Cardiovascular diseases afflict people of all races, ethnicities, genders, religions, ages, sexual orientations, national origins and disabilities. The American Heart Association is committed to ensuring that our workforce and volunteers reflect the world's diverse population. We know that such diversity will enrich us with the talent, energy, perspective and inspiration we need to achieve our mission: building healthier lives, free of cardiovascular diseases and stroke.

For information on upcoming American Heart Association Scientific Conferences, visit my.americanheart.org.
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<th>Tuesday, February 3</th>
<th>Wednesday, February 4</th>
<th>Thursday, February 5</th>
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<tr>
<td>7:30 am</td>
<td>7:00–7:45 am</td>
<td>Breakfast Symposium: Animal Models for Understanding Kawasaki Disease</td>
<td>7:00–8:00 am</td>
<td>7:30–8:30 am Continental Breakfast</td>
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<td>8:00 am</td>
<td>8:00–9:00 am</td>
<td>Animal Models</td>
<td>8:00–9:15 am Break</td>
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<tr>
<td>8:30 am</td>
<td>9:00–9:15 am Break</td>
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<td>8:15–9:30 am Imaging and Surveillance</td>
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<tr>
<td>9:30 am</td>
<td>9:45–10:15 am</td>
<td>Opening Remarks and Welcome</td>
<td>9:30–9:45 am Break</td>
<td>9:30–9:45 am Presentation of Awards</td>
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<tr>
<td>10:00 am</td>
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<td>Diagnosis/Biarkers Part 1 (Sponsored by Roche Diagnostics)</td>
<td>9:45–11:45 am Natural History and Prognosis Part 1</td>
<td>9:45 am Announcement of Next Meeting and Closing</td>
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<tr>
<td>10:30 am</td>
<td>10:15–10:45 am</td>
<td>Yuki Lynn Takahashi Memorial Lecture</td>
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<tr>
<td>11:00 am</td>
<td>10:45–11:15 am</td>
<td>Epidemiology Part 1</td>
<td>11:15–11:45 am Break</td>
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<td>11:30 am</td>
<td>11:45 am–noon</td>
<td>Break</td>
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<tr>
<td>Noon–1:30 pm</td>
<td>Noon–11:00 am</td>
<td>Lunch Symposium: Immunology of Kawasaki Disease (Sponsored by Seattle Children’s Hospital and Research Institute)</td>
<td>Noon–1:00 pm Lunch Symposium: Discovery Through Multi-Institutional Collaboration</td>
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<td>1:30 pm</td>
<td>1:15–1:45 pm Break</td>
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<td>2:00 pm</td>
<td>1:45–2:30 pm Genetics of Kawasaki Disease</td>
<td>1:00–1:15 pm Break</td>
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<td>2:30 pm</td>
<td>2:30–3:30 pm Genetics/Pathology/Immunology</td>
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<td>4:00 pm</td>
<td>3:00–3:30 pm Poster Session I</td>
<td>1:00–1:15 pm Break</td>
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<tr>
<td>5:00 pm</td>
<td>5:00–6:15 pm Etiology/Pathophysiology</td>
<td>1:00–1:15 pm Break</td>
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<td>5:30 pm</td>
<td>5:00–6:30 pm Medical Treatment Part 2</td>
<td>1:00–1:15 pm Break</td>
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<tr>
<td>6:00 pm</td>
<td>5:00–6:30 pm Poster Session II</td>
<td>1:00–1:15 pm Break</td>
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<tr>
<td>6:30 pm</td>
<td>6:30–8:00 pm Welcome Reception</td>
<td>1:00–1:15 pm Break</td>
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Legend: Poster Sessions     Conference Sessions     Other

Program at a Glance

**Council on Cardiovascular Disease in the Young (CVDY)**

The Council on Cardiovascular Disease in the Young actively supports the mission to improve the health of children and adults with congenital heart disease and cardiovascular disease acquired during childhood through research, education, prevention, and advocacy. Learn more at my.americanheart.org/cvdycouncil

You become a member of the Council on Cardiovascular Disease in the Young, by selecting it as your Scientific Council when you join AHA/ASA Professional Membership.

**Are You a Member?**

Members receive even more resources than before.

Learn more about how you can access the best science and professionals in your field and across multiple disciplines. Professional Membership benefits include:

- The AHA research grant application fee is being waived for members. Apply today at my.americanheart.org/research.
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- Free access to Science OnDemand® Products — over $300 value**
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*Specific benefits depend upon your membership level.
**Restrictions apply. Visit my.americanheart.org/membership for more information.
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## Contact Information

If you have questions after reading this program, contact the American Heart Association National Center, Dallas, Texas:

- **Telephone**: 888.242.2453 toll-free 214.570.5935
- **Fax**: 214.706.5255
- **Email**: scientificconferences@heart.org
- **Website**: my.americanheart.org/ikds

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- **Telephone**: 800.787.8984 toll-free 301.223.2327
- **Email**: ahaonline@lww.com
Dear Colleagues:

On behalf of the Program Committee of the Eleventh International Kawasaki Disease Symposium, it is our pleasure to welcome you to Honolulu. The meeting promises to be lively, with presentations on new breakthroughs in epidemiology, etiology, genetics, pathology, pathogenesis, diagnosis, therapy and outcomes of Kawasaki disease. This meeting seeks to broaden the educational mission of these symposia by including a parent symposium. We hope to bring clinicians and scientists from around the globe together to share their common interest in and new knowledge of Kawasaki disease.

Our hope is that through these presentations we will sow the seeds of future collaborations and cooperation, which will be highlighted in the Symposium, with the goal of enhancing clinical care of children with this important illness.

As your hosts for the meeting, please let us know if there is anything we can do to enrich your stay in Hawaii.

We thank you all for traveling such long distances to share your insights and expertise and look forward to greeting all of you here in Honolulu.

With Best Regards,

Anne Rowley, MD
Program Committee Co-Chair

Brian McCrindle, MD, MPH, FAHA
Program Committee Co-Chair

Letter from the Chairs
The American Heart Association gratefully acknowledges the support from the following:

Kawasaki Disease Foundation
Cardiac Children’s Foundation Taiwan
The Chemo-Sero-Therapeutic Research Institute
Council on Cardiovascular Disease in the Young
Japan Blood Products Organization
Japan Kawasaki Disease Research Center
Nihon Pharmaceutical Co., Ltd.
Roche Diagnostics
Seattle Children’s Hospital and Research Institute
Teijin Pharma Limited

Program Committee

The American Heart Association is grateful to the members of the Program Committee for their dedication and leadership in planning this program.

Brian McCrindle, MD, MPH, FAHA, Hospital for Sick Children, Toronto, Ontario, Canada
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Junbao Du, MD, Peking University First Hospital, Beijing, PR China
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Masaru Miura, MD, Tokyo Metropolitan Children’s Medical Center, Tokyo, Japan
Yoshikazu Nakamura, MD, Jichi Medical University, Tochigi, Japan
Eeva Salo, MD, Helsinki University Hospital, Helsinki, Finland
Kei Takahashi, MD, Toho University, Ohashi Medical Center, Tokyo, Japan
Masaru Terai, MD, Tokyo Women’s Medical Center, Tokyo, Japan
Adriana Tremoulet, MD, University of California-San Diego, San Diego, CA
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Rae Yeung, MD, PhD, Hospital for Sick Children, Toronto, ON
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Rae Yeung, MD, PhD, Hospital for Sick Children, Toronto, Ontario
### Room Locator

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<td>Speaker Resource Room</td>
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<td>Lunch Symposium</td>
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<td>General Session</td>
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<td><strong>3:30–5:00 PM</strong></td>
<td>Poster Session 1</td>
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<td><strong>1:00–1:15 PM</strong></td>
<td>Break</td>
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<tr>
<td><strong>1:15–2:45 PM</strong></td>
<td>General Session</td>
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<td><strong>2:45–3:00 PM</strong></td>
<td>Break</td>
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<tr>
<td><strong>3:00–5:00 PM</strong></td>
<td>General Session</td>
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<td><strong>5:00–6:30 PM</strong></td>
<td>Poster Session 2</td>
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<tr>
<td><strong>5:00–6:30 PM</strong></td>
<td>Parent’s Association Symposium</td>
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<tr>
<td><strong>6:30–9:00 PM</strong></td>
<td>Reception and Dinner</td>
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<th>Friday, Feb. 6, 2015</th>
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<tr>
<td><strong>7:00–11:00 AM</strong></td>
<td>Speaker Resource Room</td>
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<td><strong>7:00–10:30 AM</strong></td>
<td>Registration</td>
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<tr>
<td><strong>7:30–8:30 AM</strong></td>
<td>Continental Breakfast</td>
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<tr>
<td><strong>8:30–9:45 AM</strong></td>
<td>General Session/ Adjourn</td>
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</table>
Program Description

This 3½-day conference includes lectures, discussions, and oral/poster presentations focusing on the latest advances in Kawasaki disease. Kawasaki disease is the major cause of acquired childhood heart disease in developed countries. Children who develop significant coronary artery aneurysms as a result of Kawasaki disease have a lifetime increased risk of myocardial ischemia, infarction and sudden death. The study of Kawasaki disease and its treatment are likely to yield important answers to general questions in cardiovascular health and disease that apply equally to pediatric and adult populations.

The Eleventh International Kawasaki Disease Symposium seeks to address the influence of genetics on disease susceptibility and outcomes, the mechanisms of coronary artery damage following severe acute inflammation, the role of immune modulation and other novel therapies in preventing artery damage, the potential use of serum biomarkers for diagnosis and prognosis, the use of newer imaging techniques to assess abnormalities of the coronary arteries and myocardium, and new therapies regarding anticoagulation and vascular health. Current data regarding the worldwide epidemiology will be highlighted.

Since the historic first International Kawasaki Disease Symposium in 1984, the international symposium has been held every three years in Japan, the United States or Taiwan, drawing attendees from all continents.

Who Should Attend

The audience will consist of pediatric and adult cardiologists, pediatricians and pediatric subspecialists in immunology, infectious disease and rheumatology; cardiovascular surgeons; pathologists; basic scientists in genetics, molecular biology, microbiology and cardiovascular pathophysiology; public health officials from county and state agencies and the Centers for Disease Control and Prevention; epidemiologists; and nurses working in pediatric cardiology and public health who have an interest in Kawasaki disease.

Learning Objectives

After completing this program, participants will be able to:

1. Summarize prevailing hypotheses regarding KD etiology, and discuss emerging research supporting or contradicting these hypotheses.

2. Summarize current findings regarding diagnostic and prognostic biomarkers for KD, and their potential significance to clinical practice.

3. Summarize the most recent research and clinical findings regarding genetic susceptibility to KD and to KD coronary artery disease.

4. Summarize the most recent research and clinical findings regarding IVIG mechanism of action and the efficacy of additional or alternative therapies.

5. Review evidence regarding the two distinct arterial processes that can lead to myocardial ischemia or infarction.

6. Review available imaging modalities for their ability to assess for presence of thrombosis and luminal myofibroblastic proliferation.

7. Summarize technical principles and current evidence supporting use of various imaging modalities in determining KD prognosis and optimal long-term follow-up.

8. Review evidence regarding the efficacy, safety and long-term expected outcomes of revascularization options for KD patients.

9. Review current understanding, recent findings and unresolved issues regarding optimization of thromboprophylaxis in KD patients.
Program Information (continued)

**Continuing Medical Education Accreditation — Physicians**
The American Heart Association is accredited by the Accreditation Council for Continuing Medical Education to provide continuing medical education for physicians.

The American Heart Association designates this live activity for a maximum of 23.75 AMA PRA Category 1 Credits™. Physicians should claim only the credit commensurate with the extent of their participation in the activity.

All persons who develop and/or control educational content in CME/CE activities sponsored by the American Heart Association will disclose to the audience all financial relationships with any commercial supporters of this activity as well as with other commercial interests whose lines of business are related to the CME/CE-certified content of this activity. In addition, presenters will disclose unlabeled/unapproved uses of drugs or devices discussed in their presentations. Such disclosures will be made in writing in course presentation materials.

**Continuing Medical Education Accreditation — Physician Assistants**
AAPA accepts certificates of participation for educational activities certified for AMA PRA Category 1 Credit™ from organizations accredited by ACCME or a recognized state medical society. Physician assistants may receive a maximum of 23.75 hours of Category 1 credit for completing this program.

**Continuing Education Accreditation — Nurse Practitioners**
American Academy of Nurse Practitioners (AANP) accepts AMA PRA Category 1 Credit™ from organizations accredited by the ACCME.

**Continuing Education Accreditation — Nurses**
The American Heart Association is accredited as a provider of continuing nursing education by the American Nurses Credentialing Center’s Commission on Accreditation.

The maximum number of hours awarded for this CE activity is 23.75 contact hours.

**Steps for Successful Completion**
To successfully complete this activity, learners must fully participate in the sessions. In addition, learners must provide feedback that will be used for evaluative and outcomes measurement purposes. Learners’ participation will be verified, and learners will be required to provide evaluative feedback before CME/CE credit can be claimed. Add 2 new sections:

**Speaker Resource Room**
The Speaker Resource Room is located in the Sea Pearl 4 room. Speakers are asked to deliver their presentations on CD-ROM, DVD-ROM or a USB storage device to the Speaker Resource Room at least 3 hours before the start of the session in which they will speak. It is imperative that you review your presentation in the Speaker Resource Room if it contains video files or was created on a Mac. Speakers will be directed to a preloading station where a technician will be on hand to load the presentations. Speakers may also use this room to review and practice their presentations on both PCs and Mac computers. The Speaker Resource Room will be open during these following hours:

- Monday, Feb. 2 ....................... 1:00–7:00 PM
- Tuesday, Feb. 3 ...................... 7:00 AM–5:00 PM
- Wednesday, Feb. 4 ................. 7:00 AM–5:00 PM
- Thursday, Feb. 5 ................... 7:00 AM–5:00 PM
- Friday, Feb. 6 ....................... 7:00–11:00 AM

**Conference Registration Hours**
- Monday, Feb. 2 ....................... 1:00–5:00 PM
- Tuesday, Feb. 3 ...................... 7:00 AM–7:00 PM
- Wednesday, Feb. 4 ................. 7:00 AM–7:00 PM
- Thursday, Feb. 5 ................... 7:00 AM–7:00 PM
- Friday, Feb. 6 ....................... 7:00–10:30 AM
Program Information

Simultaneous Translation
Simultaneous translation will be provided for the conference sessions. Oral presentations and question-and-answer sessions will be conducted in English or Japanese with simultaneous translation by on-site translators. Headsets will be available for all attendees who wish to use these services.

Abstract Presentations
Abstract presentations for the 2015 International Kawasaki Disease Symposium are embargoed for release at the time of presentation or time of AHA news event. Information may not be released before the scheduled presentation time.

Abstracts will be published in the May online edition of the AHA journal Circulation.

Abstracts O.01–O.75 will be presented orally throughout the program.

Abstracts 1–225 will be presented as posters in these Sessions:

<table>
<thead>
<tr>
<th>Poster Session</th>
<th>Date</th>
<th>Time</th>
<th>Abstract Range</th>
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<tr>
<td>Poster Session 01</td>
<td>Tuesday, Feb. 3</td>
<td>3:30–5:00 PM</td>
<td>1–111</td>
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<tr>
<td>Poster Session 02</td>
<td>Thursday, Feb. 5</td>
<td>5:00–6:30 PM</td>
<td>120–225</td>
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Abstract poster presenters are asked to comply with the set-up and tear-down schedule shown below:

**Poster Session 01**
- Set-up time: Tuesday, Feb. 3, 8:30 AM–1:30 PM
- Attended time: Tuesday, Feb. 3, 3:30–5:00 PM
- Tear-down time: Wednesday, Feb. 4, before NOON

**Poster Session 02**
- Set-up time: Thursday, Feb. 5, 8:30 AM–1:30 PM
- Attended time: Thursday, Feb. 5, 5:00–6:30 PM
- Tear-down time: Friday, Feb. 6, before 9:00 PM

Web Resources

**HealthJobsPlus**
The American Heart Association and Lippincott Williams & Wilkins (a Wolters Kluwer business) are proud to offer HealthJobsPlus. HealthJobsPlus provides a first-rate source for those seeking and posting jobs by connecting qualified healthcare professionals with top-notch employers. Go to http://healthjobsplus.com to learn more.

**Professional Education Center – learn.heart.org**
Please visit learn.heart.org to register/claim your CME certification using the conference’s unique code. AHA is the premier provider in quality science, evidence-based, continuing education for healthcare professionals. Our course offerings are available in a multitude of formats including live presentations and online activities. The Professional Education Center website also provides access to webcasts, satellite broadcasts and podcasts.

**my.americanheart.org**
My AmericanHeart for Professionals is the American Heart Association/American Stroke Association’s powerful Internet resource for healthcare professionals. The site has become a valuable tool for countless professionals devoted to the fight against cardiovascular disease and stroke. Depending on the level of membership selected, AHA/ASA Professional Members may have access to all 12 AHA scientific journals, clinical updates, core clinical textbooks, statements and practice guidelines, continuing education, professional membership information, breaking medical news and much more.
**Policy Information**

**Disclaimer**
The 2015 International Kawasaki Disease Symposium is a scientific and educational conference to exchange and discuss research results and scientific developments in the field of cardiovascular disease. Accordingly, the American Heart Association cannot and does not offer any assurance or warranty of the accuracy, truthfulness or originality of the information presented at the conference.

**Embargo Guidelines**
Abstracts, lectures and presentations in IKDS 2015 are embargoed for release at the time of presentation. Information may not be released before the scheduled presentation time.

**Photography and Audio/Visual Recording Policy**
No person may record any portion of the AHA Scientific Sessions, scientific conferences, and the AHA/ASA International Stroke Conference, whether by video, still or digital photography; audio; or any other recording or reproduction mechanism. This includes recording of presentations and supporting A/V materials and of poster presentations and supporting poster materials. Additionally, science information shared by investigators during a meeting is confidential and often unpublished data. Taking photos of or recording the content of meeting room slides is also prohibited, and is considered intellectual piracy and unethical. Attendees who ignore this policy will be asked to leave the educational session and are at risk of losing their badge credentials.

The American Heart Association (AHA) will take photographs and video during its conferences and may display, reproduce and/or distribute them in AHA educational, news or promotional material, whether in print, electronic or other media, including the AHA website. Your registration for an AHA conference grants AHA the right to use your name, image and biography for such purposes as well as any other purpose. All photographs and/or videos become the property of AHA.

**No-Smoking Policy**
AHA policy prohibits smoking in conference meeting rooms and exhibits/registration areas. Thank you for your cooperation.

**Seating/Badge Requirement**
Seating is on a first-come, first-served basis. According to fire code, a session must be closed if the room fills to capacity. You must wear your name badge at all times during the symposium. Nonregistered guests may not be permitted into the sessions or food and beverage events. Be sure to remove your badge when you leave the conference or your hotel room.

The American Heart Association reserves the right to revoke or deny attendance to any registered participant, speaker, exhibitor, news media reporter or photographer of presentations or activities at AHA/ASA scientific conferences and meetings.

*Please note: The American Heart Association shall not be liable for cancellation of the 2015 International Kawasaki Disease Symposium caused by labor strikes, civil disorders, fires, weather conditions, or other acts of God or for any damages or losses resulting from such cancellations.*
Tuesday, February 3

Opening Remarks
9:45–10:00 AM
Coral 3
Elliott Antman, MD, President, American Heart Association, Brigham and Women’s Hospital, Associate Dean for Clinical/Translational Research, Harvard Medical School, Boston, MA

Welcome and Introduction
10:00–10:15 AM
Coral 3
Greg Chin, Kawasaki Disease Foundation, Ipswich, MA
Tomisaku Kawasaki, MD, Japan Kawasaki Disease Research Center, Tokyo, Japan
Brian McCrindle, MD, MPH, FAHA, The Hospital for Sick Children, Toronto, Ontario, Canada
Anne Rowley, MD, Northwestern University Feinberg School of Medicine, Chicago, IL

Yuki Lynn Takahashi Memorial Lecture
10:15–10:45 AM
Coral 3
Moderator:
Masato Takahashi, MD, Seattle Children’s Hospital, Washington School of Medicine, Seattle, WA

10:15 Lessons from Epidemiologic Studies of Kawasaki Disease in Japan
Yoshikazu Nakamura, MD, MPH, FFPH, Jichi Medical University, Tochigi, Japan

Epidemiology Part 1
10:45–11:45 AM
Coral 3
Moderators:
Ermias Belay, MD, Centers for Disease Control and Prevention, Atlanta, GA
Yoshikazu Nakamura, MD, MPH, FFPH, Jichi Medical University, Tochigi, Japan

10:45 Challenges of Epidemiologic Studies of Kawasaki Disease in Resource Limited Countries
Surjit Singh, MD, Post Graduate Institute of Medical Education and Research, Chandigarh, India

11:00 Epidemiology of Kawasaki Disease in South Korea, 2009-2011
Gi Beom Kim, Seoul Natl Univ Children’s Hosp, Seoul, Korea, Republic of; Ji Whan Han, Uijeongbu St. Mary’s Hosp, Uijeongbu, Korea, Republic of; Yong Won Park, Inje Univ Seoul Paik Hosp, Seoul, Korea, Republic of; Min Seob Song, Inje Univ Haeundae Paik Hosp, Busan, Korea, Republic of; Young Mi Hong, Ewha Womans Univ Hosp, Seoul, Korea, Republic of; Dong Soo Kim, Severance Children’s Hosp, Seoul, Korea, Republic of

11:15 Validation of Kawasaki Disease Incidence Assessment as Derived from Health System Administrative Databases vs. Active Retrospective Surveillance in Ontario, Canada
Cedric Manlhiot, Sunita O’Shea, Bailey Bernknopf, Michael Labelle, Mathew Mathew, Nita Chahal, Brian W. McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

11:30 Monitoring the Occurrence of Kawasaki Syndrome in the United States
Ryan A. Maddox, Marissa K. Person, Lindsay J. Joseph, Dana L. Haberling, Ctrs for Disease Control and Prevention, Natl Ctr for Emerging and Zoonotic Infectious Diseases, Atlanta, GA; Claudia A. Steiner, Dept of Health and Human Services, Agency for Healthcare Res and Quality, Rockville, MD; Lawrence B. Schonberger, Ermias D. Belay, Ctrs for Disease Control and Prevention, Natl Ctr for Emerging and Zoonotic Infectious Diseases, Atlanta, GA

Break
11:45 AM–12:00 PM
Coral Lounge
Lunch Symposium
Epidemiology Part 2
12:00–1:15 PM
Coral 3

Moderators:
Adriana Tremoulet, MD, University of California
San Diego School of Medicine, La Jolla, CA
Hiroshi Yanagawa, MD, FFPH, Jichi Medical
University, Tochigi, Japan

12:00 Kawasaki Disease with Down Syndrome: O.4
Low Risk for Igiv Resistance and
Coronary Artery Abnormalities
Shinichi Takatsuki, Toho University Omori
Medical Center, Tokyo, Japan; Masato
Yokozawa, Hokkaido Medical Center for
Child Health and Rehabilitation, Hokkaido,
Japan; Masae Ono, Tokyo Teishin Univ
Hospital, Tokyo, Japan; Masako Fujinawa,
Horoyuki Ida, Jikei Univ Hospital, Tokyo,
Japan; Hideki Motomura, Horoyuki
Morichu, Nagasaki Univ, Nagasaki, Japan; Mio Taketazu, Junichi Oki, Asahikawa-Koisi
General Hospital, Hokkaido, Japan; Shigeaki
Nonoyama, Nafi Defense Medical College,
Tokyo, Japan; Tatsuya Kawano, Kenji Ihara,
Oita Univ Hospital, Oita, Japan; Sachiko
Kido, Hyogo Prefectural Kobe Children’s
Hospital, Hyogo, Japan; Junko Shiono,
Ibaragi Children’s Hospital, Ibaragi, Japan; Shiro Tsuchiya, Soka Municipal Hospital,
Saitama, Japan; Keiji Tsuchiya, Japan
Red Cross Medical Center, Tokyo, Japan;
Teruhumi Goushi, Nakatsu Municipal Hospital,
Osaka, Japan; Shuhei Ogata, Masahiro Ishii,
Kitazato Univ Hospital, Kanagawa, Japan;
Fukiko Ichida, Toyama Univ Hospital, Tokyo,
Japan; Tsutomu Saji, Toho University Omori
Medical Center, Tokyo, Japan

12:05 The Incidence and Outcome of
Kawasaki Shock Syndrome:
2003–2013
Sara Kristen Sexson Tejtel, Andrea A.
Ramirez, Thomas Seery, Amy Liou,
Debra Canter, Marietta DeGuzman,
Caroly A. Altman, Texas Childrens Hosp/
Baylor Coll of Med, Houston, TX

12:10 Epidemiology of Kawasaki Disease in
Canada (2004–2011)
Brian W. McCrindle, Sunita O’Shea,
Brendan Lew, Sameer Masood; The
Hosp for Sick Children, Toronto, ON,
Canada; Dirk Bock, London Health
Sciences Ctr, London, ON, Canada;
Lillian S. Lai, Children’s Hosp of Eastern
Ontario, Toronto, ON, Canada; Rejane F.
Dillenburg, McMaster Univ Children’s
Hosp, Hamilton, ON, Canada; Bailey
Bernknopf, Nita Chahal, Rae SM Yeung,
Cedric Manlihot, The Hosp for Sick
Children, Toronto, ON, Canada

12:15 The Clinical Risk Factors of
Intravenous Immunoglobulin
Resistance and Coronary Artery
Lesion of Kawasaki Disease:
Retrospective Analysis of 602 Cases
Lijian Xie, Cuizhen Zhou, Renjian Wang,
Tingting Xiao, Jie Shen, Min Huang,
pediatric cardiology, Shanghai Children’s
Hospital, Shanghai, China

12:20 Rashless Kawasaki Disease (KD):
Colorado’s Experience
Marsha S. Anderson, Samuel R.
Dominguez, Heather R. Heizer, Pei-Ni
Jone, Jesse Davidson, Mary P. Glode,
Children’s Hosp Colorado, Aurora, CO

12:25 French Observatory of Kawasaki
Disease in Adults: 24 Observations
Jean-Baptiste Faison, Jean Verdier Hosp,
Bondy, France; Pascal Seve, Univ Hosp,
Lyon, France; Emmeline GommaMesen,
internal medicine, Béziers,
France; Claire Dauphin, Gabriel Montpied
Hosp, Clermont-Ferrand, France; Alfred
Mahr, St Louis Hosp, Paris, France; Cedric
Landron, Univ Hosp, Poitiers, France;
Costedoat-Chalumeau Nathalie, Cochin
Hosp, Paris, France; Olivier Epaulard,
Univ Hosp, Grenoble, France; Le Thi
Huong Boutin, Pitie Salpêtrière Hosp,
Paris, France; Maryam Piram, Bicetre
Hosp, Paris, France; Arnaud Hot, Edouard Heriot Hosp,
Lyon, France; Gihane Chalhoub, internal
medicine, Metz, France; Jean-Marc
Galemoip, internal medicine, Charleville-
Mézières, France; Guillaume Marchand,
Bizet Hosp, Paris, France; Sébastien
Humbert, Philippe Humbert, Univ Hosp,
Besançon, France; Philippe Morlat, Univ Hosp,
Bordeaux, France; Xavier Puéchal,
Loic Guillemin, Cochin Hosp, Paris, France;
Isabelle Koné-Paut, Bicetre Hosp, Paris,
France; Olivier Fain, Saint Antoine Hosp,
Paris, France
12:30 Risk Factors Associated with Recurrence of Kawasaki Disease in Mexican Children
Giovanni Sorcia-Ramirez, Luis M. Garrido-Garcia, Instituto Nacional de Pediatría, Mexico City, Mexico

12:40 Update of 2011-2014 Kawasaki Disease Surveillance in Emilia Romagna, a Northern Region of Italy
Elena Corinaldesi, Ramazzini Hosp, Carpi, Italy; Giorgia Difazio, pediatric unit, Reggio Emilia, Italy; Elisa Mazzoni, Chiara Landini, Maggiore Hosp, Bologna, Italy; Barbara Bigucci, pediatric unit, Rimini, Italy; Maria Chiara Casadei, pediatric unit, Cesena, Italy; Gabriella Testa, pediatric unit, Ferrara, Italy; Cristina Cicero, pediatric unit, Piacenza, Italy; Alessia Palladini, pediatric unit, Ravenna, Italy; Luca Pierantoni, Sant’Orsola Hosp, Bologna, Italy; Paola Sogno Vallin, pediatric unit, Imola, Italy; Francesca Iami, pediatric unit, Modena, Italy; Marianna Fabi, pediatric cardiology unit, Sant’orsola Hospital, Bologna, Italy

12:45 Kawasaki Disease in the Maghreb Community in Quebec
Arbia A. Gorrab, Div of Pediatric Cardiology, CHU Ste-Justine, Univ of Montreal, Montreal, QC, Canada; Asma Abed Bouaziz, Dept of Pediatrics, Regional Hosp of Ben Arous, Faculty of Med of Tunis El Manar, Ben Arous, Tunisia; Linda Spigelblatt, Dept of Pediatrics, Maisonneuve-Rosemont Hosp, Univ of Montreal, Montreal, QC, Canada; Anne Fournier, Nagib Dahdah, Div of Pediatric Cardiology, CHU Ste-Justine, Univ of Montreal, Montreal, QC, Canada

12:50 Incidence Rate of Recurrent Kawasaki Disease in Japan (2003-2012)
Daisuke Sudo, Ooshima Prefecture Hosp, Amami, Japan; Yosikazu Nakamura, Jichi Medical Univ, Shimotsuke, Japan

12:55 Multicenter Retrospective Study of the Clinical Course of Kawasaki Disease in Latin American Children
Andrea Salgado, Pontificl Catholical Univ of Chile, Santiago, Chile; Rolando Ulloa-Gutierrez, Hosp Nacional de Niños “Dr. Carlos Sáenz Herrera”, San Jose, Costa Rica; Dora Estripeaut, Hosp del Niño, Ciudad Panama, Panama; Kathia Luciani, Hosp de Especialidades Pediátricas de la Caja del Seguro Social, Ciudad Panama, Panama; Olguita Del Agulla, Hosp Edgardo Rebagliati, Lima, Peru; German Camacho-Moreno, Hosp de la Misericordia, Bogota, Colombia; Enrique Faugier, Hosp Infantil de México Federico Gómez, Mexico D.F., Mexico; Lucila Martínez-Medina, Centenario Hosp Miguel Hidalgo, Aguas Calientes, Mexico; Eduardo López-Medina, Ctr de Estudios en Infectologia Pediátrica, Cali, Colombia; Giannina Izquierdo, Hosp de Niños “Dr. Exequiel González Cortés”, Santiago, Chile; Sandra Beltran, Clínica Colsanitas, Bogota, Colombia; Luisa B. Gamez, Hosp Infantil de Chihuahua, Ciudad de México, Mexico; Adrian Collia, Sanatorio Mater Dei, Buenos Aires, Argentina; Lorena Franco, Nora Bueno, Hosp Infantil Municipal de Córdoba, Cordoba, Argentina; Carlos Daza, Hosp Materno Infantil José Domingo de Obaldía, Chiriqui, Panama; Mariella Vargas-Gutierrez, Susan Li-Chan, Hosp Nacional de Niños “Dr. Carlos Sáenz Herrera”, San Jose, Costa Rica; Natalia Lara, Hosp de la Misericordia, Bogota, Colombia; Jacqueline Levy, Hosp del Niño, Ciudad Panama, Panama; Alejandro Ellis, Sanatorio Mater Dei, Buenos Aires, Argentina; Isabel Hurtado, Ctr de Estudios en Infectologia Pediátrica, Cali, Colombia; Erika K. Berry, Adriana H. Tremoulet, Kawasaki Disease Res Ctr, Univ of California, San Diego, San Diego, CA; REKAMLATINA-2 Study Group

1:00 Discussion

Break
1:15–1:45 PM
Coral Lounge
Program Agenda (continued)

Genetics of Kawasaki Disease Panel
1:45–2:30 PM
Coral 3
Moderators:
Jane Burns, MD, University of California San Diego
School of Medicine, La Jolla, CA
Yoshihiro Onouchi, MD, PhD, Chiba University
Graduate School of Medicine, Chiba, Japan

1:45 Martin Hibberd, PhD, The Genome Institute of
Singapore, Singapore, Republic of Singapore

1:57 Yi-Ching Lee, PhD, Institute of Cellular and
Organismic Biology, Academia Sinica, Taipei, Taiwan

2:09 Yoshihiro Onouchi, MD, PhD, Chiba University
Graduate School of Medicine, Chiba, Japan

2:21 Discussion

Genetics/Pathology/Immunology
2:30–3:30 PM
Coral 3
Moderators:
Taco Kuijpers, MD, PhD, Academic Medical Center, Amsterdam, Netherlands
Anne Rowley, MD, Northwestern University
Feinberg School of Medicine, Chicago, IL

2:30 Comprehensive Genotyping of the
FGFR2/3 Locus Reveals a Novel
Association of FGFR2C-ORF with
Susceptibility to Kawasaki Disease
Taco W. Kuijpers, Carlene E. Tacke,
Academic Medical Ctr, Amsterdam,
Netherlands; Sietse Q. Nagelkerke,
Sanquin Res and Landsteiner Lab,
Amsterdam, Netherlands; Willemijn B.
Breunis, Academic Medical Ctr,
Amsterdam, Netherlands; Long T. Hoang,
Eileen Png, Genome Inst of Singapore,
Singapore, Singapore; Judy Geissler,
Sanquin Res and Landsteiner Lab,
Amsterdam, Netherlands; Michael W.
Tanc, Academic Medical Ctr, Amsterdam,
Netherlands; Justine A Ellis, Anne L.
Ponsonby, Murdoch Childrens Res Inst,
Parkville, Australia; Sonia Davila, Chiea C.
Khor, Genome Inst of Singapore, Singapore,
Singapore; Martin de Boer, Joris van der
Heijden, Sanquin Res and Landsteiner
Lab, Amsterdam, Netherlands; Karin
Fijnvandraat, Academic Medical Ctr,
Amsterdam, Netherlands; E. van der
Schoot, Timo K. van den Berg, Sanquin
Res and Landsteiner Lab, Amsterdam,
Netherlands; Rae S. Yeung, The Hosp
of Sick Children, Toronto, ON, Canada;
Michael L. Levin, Imperial Coll London,
London, United Kingdom; David Burgner,
Murdoch Childrens Res Inst, Parkville,
Australia; Chisato Shimizu, Jane C. Burns,
UC San Diego Sch of Med, La Jolla, CA;
Martin L. Hibberd, Genome Inst of
Singapore, Singapore, Singapore

2:45 Whole Genome Sequencing of a
Six-member African-American
Family with Two Kawasaki Disease-
Affected Siblings Identifies Novel
Susceptibility Variants
Jihoon Kim, Div of Biomedical Informatics,
Depts of Med, Univ of California San
Diego, La Jolla, CA; Chisato Shimizu,
Depts of Pediatrics, Univ of California
San Diego, La Jolla, CA; Hai Yang,
Olivier Harismendy, Div of Biomedical
Informatics, Depts of Med, Univ of California
San Diego, La Jolla, CA; Long Truong
Hoang, Genome Inst of Singapore,
Singapore, Singapore; Eric Levy, Div of
Biomedical Informatics, Depts of Med,
Univ of California San Diego, La Jolla,
CA; Rolando Cimaz, Univ of Florence,
Florence, Italy; David Burgner, Murdoch
Childrens Res Inst, The Royal Children’s
Hosp, Parkville, Australia; Rae S. Yeung,
Univ of Toronto, The Hosp for Sick
Children, Toronto, ON, Canada; Chiea
Chuen Khor, Sonia Davila, Genome
Inst of Singapore, Singapore, Singapore;
Michael Levin, Imperial Coll London,
London, United Kingdom; Taco W.
Kuijpers, Univ of Amsterdam, Emma
Children’s Hosp Academic Medical Ctr,
Amsterdam, Netherlands; Martin L.
Hibberd, Genome Inst of Singapore,
Singapore, Singapore; Lucila Ohno-
Machado, Div of Biomedical Informatics,
Depts of Med, Univ of California San
Diego, La Jolla, CA; Jane C. Burns,
Depts of Pediatrics, Univ of California
San Diego, La Jolla, CA; the International
Kawasaki Disease Genetics Consortium
3:00 Histopathological Analysis of Sudden Death Adults with Coronary Artery Aneurysms
Kei Takahashi, Toshiaki Oharaseki, Yuki Yokouchi, Yasunori Enomoto, Toho Univ Ohashi Medical Ctr, Tokyo, Japan; Kino Hayashi, Kumiko Asakura, Tokyo Medical Examiner’s Office, Tokyo, Japan; Kazuyuki Saito, Dept of Forensic Med, Juntendo Univ Sch of Med, Tokyo, Japan; Aya Takada, Dept of Forensic Med, Saitama Medical Univ Faculty of Med, Tokyo, Japan

3:15 Fine Specificity of Natural Regulatory T Cells that Modulate Vascular Inflammation
Alessandra Franco, Ranim Touma, Robert L. Padilla, Adriana H. Tremoulet, Univ of California San Diego, La Jolla, CA; John Sidney, Alessandro Sette, La Jolla Inst for Allergy and Immunology, La Jolla, CA; Jane C. Burns, Univ California San Diego, La Jolla, CA

5:00 Microbiome Analysis in Kawasaki Disease
Kristine Wylie, PhD, The Genome Institute, Washington University School of Medicine, St. Louis, MO

5:15 Deep RNA Sequencing Reveals a Transcriptional Profile of Cytotoxic T Lymphocyte Activation, Antigen Presentation, Immunoglobulin Production, and Type I Interferon Response in Kawasaki Disease Arteritis

5:30 Inositol 1,4,5 triphosphate 3-kinase C Regulates NLRP3 Inflammasome Activation in Kawasaki Disease
Martin P. Alphonse, Trang T. Duong, The Hosp for Sick Children, Toronto, ON, Canada; Chisato Shimizu, UCSD, La Jolla, CA; Long T. Hoang, Genome Inst of Singapore, Singapore, Singapore; Brian W McCrindle, The Hosp for Sick Children, Toronto, ON, Canada; Alessandra Franco, UCSD, La Jolla, CA; Stephane Schurmans, Univ de Liege, Belgium, Belgium; Dana J. Philpott, Univ of Immunology, Toronto, ON, Canada; Martin L. Hibberd, Genome Inst of Singapore, Singapore, Singapore; Jane C. Burns, UCSD, La Jolla, CA; Taco W. Kuijpers, Sanquin Blood Supply, Netherlands, Netherlands; Rae S. Yeung, The Hosp for Sick Children, Toronto, ON, Canada

5:45 Analysis of the Mechanisms of Intravenous Immunoglobulin-resistant Kawasaki Disease Using iPS Cell Technology
Kazuyuki Ikeda, Kyoto Prefectural Univ of Med, Kyoto, Japan; Tomonaga Ameku, Yui Nomiya, Masahiro Nakamura, Shinichi Mae, Satoshi Matsui, Ctr for iPS Cell Res and Application (CiRA), Kyoto Univ, Kyoto, Japan; Tomoyo Yahata, Akiko Okamoto-Hamaoka, Chinsu Suzuki, Ayako Yoshiko, Yuki Kuchitsu, Kyoto Prefectural Univ of Med, Kyoto, Japan; Akira Watanabe, Kenji Osafune, Ctr for iPS Cell Res and Application (CiRA), Kyoto Univ, Kyoto, Japan; Kenji Hamaoka, Kyoto Prefectural Univ of Med, Kyoto, Japan
Program Agenda (continued)

6:00  Lysyl Oxidase Expression in the Patients with Kawasaki Disease
     Chisato Shimizu, Cassidy YunJing Huang, Anne Phan-Huy, Andrea Salgado, UCSD Sch of Med, La Jolla, CA; Lilia Antonio, Univ de La Frontera, Temuco, Chile; John T. Kanegaye, Adriana H. Tremoulet, Alessandra Franco, Jane C. Burns, UCSD Sch of Med, La Jolla, CA

Welcome Reception
6:30–9:00 PM
Great Lawn

Wednesday, February 4

Breakfast Symposium
Animal Models for Understanding Kawasaki Disease
7:00–7:45 AM
Coral 3
Moderators:
Moshe Arditi, MD, Cedars-Sinai Medical Center, Los Angeles, CA
Rae Yeung, MD, PhD, The Hospital for Sick Children, Toronto, Ontario, Canada

7:00  Moshe Arditi, MD, Cedars-Sinai Medical Center, Los Angeles, CA
7:12  Kei Takahashi, MD, Toho University Ohashi Medical Center, Tokyo, Japan
7:24  Rae Yeung, MD, PhD, The Hospital for Sick Children, Toronto, Ontario, Canada
7:36  Discussion

Break
7:45–8:00 AM
Coral Lounge

Animal Models
8:00–9:00 AM
Coral 3
Moderators:
Jun Abe, MD, PhD, National Research Institute for Child Health and Development, Tokyo, Japan
Kei Takahashi, MD, Toho University Ohashi Medical Center, Tokyo, Japan

8:00  Gut Microflora Influences Pathology in the Kawasaki Disease Vasculitis Mouse Model
     Daiko Wakita, Ceders-Sinai Medical Ctr, Los Angeles, CA; Yosuke Kurashima, Yoshihiro Takasato, The Univ of Tokyo, Tokyo, Japan; Yungho Lee, Kenichi Shimada, Shuang Chen, Timothy R. Crother, Ceders-Sinai Medical Ctr, Los Angeles, CA; Michael C. Fishbein, UCLA, Los Angeles, CA; Thomas JA Lehman, Hosp for Special Surgery, New York, NY; Hiroshi Kiyono, The Univ of Tokyo, Tokyo, Japan; Moshe Arditi, Ceders-Sinai Medical Ctr, Los Angeles, CA

8:15  Identification of Pathogenic Cardiac Cd11c+ Macrophages in Nod1-mediated Coronary Arteritis, a Murine Model of Kawasaki Disease
     Yoshitomo Motomura, Shunsuke Kanno, Hisanori Nishio, Toshiro Hara, Dept of Pediatrics, Graduate Sch of Medical Sciences, Kyushu Univ, Fukuoka, Japan; Sho Yamashita, Div of Molecular Immunology, Medical Inst of Bioregulation, Kyushu Univ, Fukuoka, Japan

8:30  Angiotensin Receptor Blocker, Losartan Suppresses Coronary Arteritis in a Murine Model of Kawasaki Disease –Effectiveness of IVIG versus Losartan
     Eisuke Suganuma, Tokai University School of Medicine, Iseharashi, Kanagawa, Japan

8:45  The Role of CD40L and CD40 in the Pathogenesis of Kawasaki Disease
     Leon Parsaud, Parmian Arjmard, Univ of Toronto, Toronto, ON, Canada; Trang T. Duong, Hosp for Sick Children Res Inst, Toronto, ON, Canada; Rae S. Yeung, Univ of Toronto, Toronto, ON, Canada

Break
9:00–9:15 AM
Coral Lounge
**Program Agenda (continued)**

**Diagnosis/Biomarkers Part 1**

9:15–11:15 AM

(Sponsored by Roche Diagnostics)

**Coral 3**

**Moderators:**

Wilbert Mason, MD, Children’s Hospital Los Angeles, Los Angeles, CA

Junbao Du, MD, Peking University First Hospital, Beijing, China

10:15 An Improved Point-of-Care Differentiation of Kawasaki Disease from Other Febrile Illnesses

Shiying Hao, Bo Jin, Zhou Tan, Zhen Li, Jun Ji, Stanford Univ, Stanford, CA; Adriana Tremoulet, Jane C. Burns, Univ of California San Diego, La Jolla, CA; Harvey J. Cohen, Xuefeng B. Ling, Stanford Univ, Stanford, CA

10:30 Identification of Kawasaki Disease-specific Molecules in the Sera as Microbe-associated Molecular Patterns

Takeshi Kusuda, Yasutaka Nakashima, Kenji Murata, Shunsuke Kanno, Kyushu University, Fukuoka, Japan; Yumi Mizuno, Fukuoka Children’s Hosp and Medical Ctr for Infectious Disease, Fukuoka, Japan; Kazunobu Ouchi, Kawasaki Medical Sch Hosp, Kurashiki, Japan; Kenji Waki, Kurashiki Central Hosp, Kurashiki, Japan; Toshio Hara, Kyushu University, Fukuoka, Japan

10:45 NT-proBNP Based Algorithm for Diagnosis and Treatment of Kawasaki Disease – Are we there yet?

Audrey Dionne, Léamarie Meloche-Dumas, Anne Fournier, Nagib Dahdah, Div of Pediatric Cardiology, CHU Ste-Justine, Montreal, QC, Canada

11:00 BCGits as a Clinical Diagnosis Marker in Mexican Children with Kawasaki Disease

Jose A. Castillo-Moguel, Mario A. Ynga-Durán, Eduardo Galvez-Cultiva, Cesar Carrasco, Giovanni Sorcia-Ramirez, Luis M Garrido-García, Instituto Nacional de Pediatría, Mexico City, Mexico

**Break**

11:15–11:45 AM

**Coral Lounge**

10:15 Macrophage Activation Syndrome Associated with Kawasaki Disease

Giuseppe A. Latino, Cedric Manthiot, Brian W. McCrindle, Nita Chahal, Rae S. Yeung, The Hosp for Sick Children, Toronto, ON, Canada

10:30 Transcriptional Profiling Discriminates Complete and Incomplete KD from Human Adenovirus

Preeti Jaggi, Asuncion Mejias, Nationwide Children’s Hosp, Columbus, OH; Adriana Tremoulet, Jane Burns, Rady Children’s Hosp, San Diego, CA; Wei Wang, Octavio Ramilo, Nationwide Children’s Hosp, Columbus, OH

10:45 Novel Biomarker for Early Diagnosis of Kawasaki Diseases

Tai-Ming Ko, Inst of Biomedical Sciences, Academia Sinica, Taipei, Taiwan; Ho-Chang Kuo, Dept of Pediatrics and Kawasaki Disease Ctr, Kaohsiung Chang Gung Memorial Hosp, Kaohsiung, Taiwan; Jeng-Sheng Chang, Dept of Pediatrics, China Medical Univ Hosp, Taichung, Taiwan; Shih-Ping Chen, Yi-Min Liu, Hui-Wen Chen, Inst of Biomedical Sciences, Academia Sinica, Taipei, Taiwan; Fuu-Jen Tsai, China Medical Univ Hosp, Taichung, Taiwan; Yi-Ching Lee, Inst of Cellular and Organismic Biology, Academia Sinica, Taipei, Taiwan; Chien-Hsiun Chen, Jer-Yuarn Wu, Yuan-Tsong Chen, Inst of Biomedical Sciences, Academia Sinica, Taipei, Taiwan

10:00 Tenascin-C can be a Novel Prognostic Biomarker for Kawasaki Disease

Kyoko Imanaka-Yoshida, Mie Univ Graduate Sch of Med, Tsu, Japan; Yoshiaki Okuma, Takeji Matsushita, Michiaki Hlroo, Natl Ctr of Global Health and Med, Tokyo, Japan; Kei Takahashi, Toho Univ, Tokyo, Japan
Lunch Symposium
11:45 AM–12:45 PM
Immunology of Kawasaki Disease
(Sponsored by Seattle Children’s Hospital and Research Institute)
Coral 3
Moderators:
Toshiro Hara, MD, PhD, Kyushu University, Fukuoka, Japan
Michael Portman, MD, Seattle Children’s Research Institute, Seattle, WA

11:45 Fc Gamma Receptors and Immune Modulation in Kawasaki Disease
Michael Portman, MD, Seattle Children’s Research Institute, Seattle, WA

12:15 Immunogenetic Architecture of Kawasaki Disease
Sadeep Shrestha, PhD, University of Alabama at Birmingham, Birmingham, AL

Break
12:45–1:00 PM
Coral Lounge

Diagnosis/Biomarkers Part 2
1:00–2:15 PM
Coral 3
Moderators:
David Burgner, MD, Murdoch Children’s Research Institute, Parkville, Australia
Ben Saji, MD, Toho University, Tokyo, Japan

1:00 Kawasaki Disease and Systemic Juvenile Idiopathic Arthritis – Two Ends of the Same Spectrum
Rae S. Yeung, Mira van Veenendaal, Cedric Manlihot, Rayfel Schneider, Brian W. McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

1:15 Coronary Artery Dilatation in Viral Myocarditis Mimics Coronary Artery Findings in Kawasaki Disease
Soha Rached-d’Astous, Ibtissama Boukas, Anne Fournier, Marie-Josée Raboisson, Nagib Dahdah, CHU Sainte-Justine Div of Pediatric Cardiology, Montreal, QC, Canada

1:30 Fever Patterns in KD Patients after Treatment with IVIG
Preeti Jaggi, Wei Wang, Beth Printz, Nationwide Children’s Hosp, Columbus, OH; Jane Burns, Rady Children’s Hosp, San Diego, CA; John Kovalchin, Nationwide Children’s Hosp, Columbus, OH; Adriana Tremoulet, Rady Children’s Hosp, San Diego, CA

1:45 The Incidence of Abnormal Electroencephalographic Findings and Mild Encephalitis/encephalopathy with a Reversible Splenial Lesion in Kawasaki Disease
Naomi Nakagawa, Masahiro Kamada, Yukiko Ishiguchi, Yuji Moritoh, Kengo Okamoto, Hiroshima City Hosp, Hiroshima, Japan

2:00 Persistent Subacute/Chronic Coronary Arteritis in Kawasaki Disease 40 (KD): Histologic, RNA and Protein Evidence

Hideko Ogawa Memorial Lecture
2:15–2:45 PM
Coral 3
Moderator:
Hirohisa Kato, MD, Kurume University, Kurume, Japan

2:15 Challenges in Performing Clinical Trials in Kawasaki Disease
Jane Newburger, MD, Harvard Medical School, Boston, MA

Break
2:45–3:15 PM
Coral Lounge
### Medical Treatment Part 1
#### 3:15–4:45 PM
**Coral 3**

**Moderators:**
- Stanford Shulman, MD, Ann & Robert H. Lurie Children’s Hospital of Chicago, Chicago, IL
- Tohru Kobayashi, MD, The Hospital for Sick Children, Toronto, Ontario

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<tr>
<td>3:15</td>
<td>Assessment of Kawasaki Disease Risk Scores for Predicting Coronary Artery Aneurysms at a North American Center</td>
<td>Mary Beth F. Son, Kimberlee Gauvreau, Susan Kim, Alexander Tang, Fatma Dedeoglu, David R. Fulton, Mindy S. Lo, Robert P. Sundel, Jane W. Newburger, Boston Children’s Hosp, Boston, MA</td>
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<tr>
<td>3:30</td>
<td>Efficacy and Safety of Treatment with Immunoglobulin Plus Steroid for Kawasaki Disease: A Prospective Observational Study</td>
<td>Koichi Miyata, Naoya Fukushima, Yoshihiko Morikawa, Tokyo Metropolitan Children’s Medical Center, Tokyo, Japan; Yoshiaki Okuma, Nat’l Ctr for Global Health and Med, Tokyo, Japan; Masahiro Misawa, Tokyo Metropolitan Bokutoh Hospital, Tokyo, Japan; Mitsuhiko Hara, Tokyo Metropolitan Hiroo Hospital, Tokyo, Japan; Hiroyuki Yamagishi, Keio University School of Medicine, Tokyo, Japan; Masaru Miura, Tokyo Metropolitan Children’s Medical Center, Tokyo, Japan</td>
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<td>4:00</td>
<td>Infliximab for Kawasaki Disease Patients Who Did Not Respond to the Initial Therapy: A Japanese Nationwide Surveillance</td>
<td>Tohru Kobayashi, Gunma Univ Graduate Sch of Med, Gunma, Japan; Shinichi Takatsuki, Tsutomo Saji, Toho Univ Omori Medical Ctr, Tokyo, Japan; Tomoyoshi Sonobe, Ikuryo Clinic, Tokyo, Japan; Shunichi Ogawa, Nippon Medical Sch, Tokyo, Japan; Hirotaro Ogino, Kansai Medical Univ Kori Hosp, Osaka, Japan; Yosikazu Nakamura, Jichi Medical Univ, Shimotsuke, Japan; Kenji Hamaoka, Kyoto Prefectural Univ of Med, Kyoto, Japan</td>
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<tr>
<td>4:15</td>
<td>Kawasaki Disease Refractory to Primary IVIG Treatment – Use of 45 Scoring Systems and Predictive Modelling Based on Data from Singapore Children</td>
<td>Swee Chye Quek, Yao Guang Leow, Dimple D. Rajgor, Terence Lim, Chew Kiat Heng, Robert Grignani, Dept of Paediatrics, Yong Loo Lin Sch of Med, Natl Univ of Singapore AND Khoo Teck Puat – Natl Univ Children’s Medical Inst, Natl Univ Health System, Singapore, Singapore</td>
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<td>4:30</td>
<td>A Phase I/IIa Dose Escalating, Open-label Study of Atorvastatin in Children with Acute Kawasaki Disease and Coronary Artery Abnormalities</td>
<td>Adriana H. Tremoulet, Univ of California San Diego Sch of Med, La Jolla, CA; Pei-Ni Jone, Samuel Dominguez, Marsha Anderson, Heather Heizer, Mary Glode, Jane C. Burns, Univ of Colorado Sch of Med, Denver, CO</td>
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#### Break
4:45–5:00 PM
**Coral Lounge**

### Medical Treatment Part 2
#### 5:00–6:30 PM
**Coral 3**

**Moderators:**
- Marian Melish, MD, Kapi’olani Medical Center for Women and Children, Honolulu, HI
- Masaru Miura, MD, Tokyo Metropolitan Children’s Medical Center, Tokyo, Japan

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<td>5:00</td>
<td>Prediction of IVIG Resistance Using Kawasaki Disease Risk Scores and Baseline Coronary Z-Scores at a Single North American Center</td>
<td>Mary Beth F. Son, Susan Kim, Kimberlee Gauvreau, Alexander Tang, Fatma Dedeoglu, David Fulton, Mindy S. Lo, Robert P. Sundel, Jane W. Newburger, Boston Children’s Hosp, Boston, MA</td>
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**Program Agenda** (continued)
5:15  Intravenous Immunoglobulin-Associated Hemolysis in Kawasaki Disease  
Rae S. Yeung, Fiona Almeida, Vahid Khajoee, Nita Chahal, Trent Mizzi, Sarah Schwartz, Brian W. McCrindle, Wendy Lau, The Hosp for Sick Children, Toronto, ON, Canada

5:30  Factors Associated with Development of Coronary Artery Aneurysms after Kawasaki Disease are Generally Similar for Those Treated Promptly Versus Those with Delayed or No Treatment  
Mallory L. Downie, Cedric Manlhiot, Tarveer H. Collins, Nita Chahal, Rae S. Yeung, Brian W. McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

5:45  Favorable Outcome of Patients with Kawasaki Disease Treated with Unified Protocol with Cyclosporine A as the Third Line Therapy  
Hiromichi Hamada, Takafumi Honda, Kumi Yasukawa, Takuya Matsui, Masaru Terai, Tokyo Women’s Medical Univ Yachiyo Medical Ctr, Yachiyo, Japan

6:00  Effects of Anti-TNF-alpha Antibody Therapy on IVIG-resistant Patients with Kawasaki Disease  
Hiroshi Masuda, Jun Abe, Shinji Oana, Akira Ishiguro, Nao Tsuchida, Hirokazu Sakai, Shuichi Ito, Hiroshi Ono, Hitoshi Kato, Natl Ctr for Child Health and Development, Tokyo, Japan

6:15  Infliximab Use and Cardiac Outcome in Infants ≤6 Months Old: A Two Center Retrospective Study  
Adriana Tremoulet, Univ of California San Diego, La Jolla, CA; Andrea Salgado, Pontifica Univ Catolica de Chile, Santiago, Chile; Negas Ashouri, Children’s Hosp Orange County, Orange, CA; Erika Berry, Univ of California San Diego Sch of Med, La Jolla, CA; Sonia Jain, Xiaoying Sun, Univ of California San Diego, La Jolla, CA; Jane C. Burns, Univ of California San Diego Sch of Med, La Jolla, CA

Thursday, February 5

Breakfast Symposium  
7:00–8:00 AM  
To Be or Not to Be Scored: Impact of Coronary Artery Z-score Systems on the Assessment of Cardiac Outcomes in Kawasaki Disease (Sponsored by the Cardiac Children’s Foundation–Taiwan)  
Coral 3

Moderators:  
Nagib Dahdah, MD, University of Montreal, Montreal, QC, Canada  
Hung-Chi Lue, Professor Emeritus, National Taiwan University; President, Cardiac Children’s Foundation Taiwan

7:00  Development of Normative Values and Classification Schemes  
Cedric Manlhiot, BSc, The Hospital for Sick Children, Toronto, Canada

7:20  Incorporating Z Scores into Care Algorithms  
Ming-Tai Lin, MD, PhD, National Taiwan University Hospital, Taipei, Taiwan

7:40  Beyond the Lumen: Imaging Function and Structure  
Yoshihide Mitani, MD, PhD, Mie University Graduate School of Medicine, Tsu City, Japan

Break  
8:00–8:15 AM  
Coral Lounge

Imaging and Surveillance  
8:15–9:30 AM  
Coral 3

Moderators:  
Atsuko Suzuki, MD, Tokyo Teishin Hospital, Tokyo, Japan  
Mei-Hwan Wu, MD, PhD, FACC, National Taiwan University Hospital, Taipei, Taiwan

8:15  Occult Coronary Artery Dilatation: An Unrecognized Category of Coronary Involvement  
Soha Rached-d’Astous, Nour Rached-d’Astous, CHU Sainte-Justine Div of Pediatric Cardiology, Montreal, QC, Canada; Frederic Dallaire, Univ of Sherbrooke Div of Pediatric Cardiology, Montreal, QC, Canada; Nagib Dahdah, CHU Sainte-Justine Div of Pediatric Cardiology, Montreal, QC, Canada
8:30  Alteration of Left Ventricular Performance and Aortic Elastic Properties in Patients After Kawasaki Disease With Coronary Artery Aneurysm Even Without Cardiac Ischemia
Jun Oyamada, Hiraka General Hospital, Yokote, Japan; Shunsuke Shimada, Mieko Okazaki, Manatomo Toyono, Akita Univ, Akita, Japan

8:45  Utility of Adenosine Cardiac Stress MRI to Evaluate Ischemia in Patients with Kawasaki Disease
Michael J. Campbell, Piers Barker, Jennifer Li, Duke Univ, Durham, NC

9:00  Myocardial Fibrosis in Patients with a History of Kawasaki Disease: A Pilot Study
Susan M. Dusenbery, Jane W. Newburger, Kimberlee Gauvreau, Annette Baker, Andrew J. Powell, Boston Childrens Hosp, Boston, MA

9:15  Coronary Circulation Assessed by Transthoracic Echocardiography During Exercise Test is Impaired in Patients after Kawasaki Disease Even with Regressed Coronary Arterial Lesions
Manatomo Toyono, Shunsuke Yamada, Akita Univ Graduate Sch of Med, Akita, Japan; Jun Oyamada, Hiraka General Hosp, Yokote, Japan; Shunsuke Shimada, Mieko Aoki-Okaaki, Akita Univ Hosp, Akita, Japan; Kenji Harada, Harada Kids’ Clinic, Akita, Japan; Tsutomu Takehashi, Akita Univ Graduate Sch of Med, Akita, Japan

9:30–9:45 AM
Coral Lounge

9:45  Medium-term Outcomes of Coronary Artery Aneurysms after Kawasaki Disease: A Study from the North American Kawasaki Disease Registry
Brian W. McCrindle, Cedric Manlhiot, The Hosp for Sick Children, Toronto, ON, Canada; Kristen Sexson, Texas Children’s Hosp, Baylor Coll, Houston, TX; Pei-Ni Jone, Children’s Hosp Colorado, Aurora, CO; Mathew Mathew, The Hosp for Sick Children, Toronto, ON, Canada; Kambiz Norozi, London Health Sciences Ctr, London, ON, Canada; Kevin C. Harris, BC Children’s Hosp, Vancouver, BC, Canada; Alana Hughes, Nemours/DuPont Hosp for Children, Wilmington, DE; Anne Ferris, New York Presbyterian Hosp, Columbia Univ, New York, NY; Frederic Dallaire, CHU Sherbrooke, Sherbrooke, QC, Canada; Andrew M. Crean, Toronto General Hosp, Toronto, ON, Canada; Nagib Dahdah, CHU Sainte-Justine, Montreal, QC, Canada; North American Kawasaki Disease Registry

10:00  Fate of Kawasaki Disease Giant Coronary Aneurysm: Analysis of the Last 10 Years Nationwide Survey in Japan
Ryuji Fukazawa, Dept of Pediatrics, Nippon Medical Sch, Tokyo, Japan; Kenji Hamaoka, Kyoto Prefectural Univ of Med, Graduate Sch of Medical Scienc, Kyoto, Japan; Tsutomu Saji, First Dept of Pediatrics, Toho Univ Omori Medical Ctr, Tokyo, Japan; Hitoshi Kato, Dept of Cardiology, Natl Ctr for Child Health and Development, Tokyo, Japan; Hiroyuki Suzuki, Dept of Pediatrics, Wakayama Medical Univ, Wakayama, Japan; Etsuko Tsuda, Dept of Pediatrics Cardiovascular Surgery, Natl Cardiovascular Ctr, Osaka, Japan; Mamoru Ayusawa, Dept of Pediatrics, Nihon Univ Sch of Med, Tokyo, Japan; Masaru Miura, Div of Cardiology, Tokyo Metropolitan Children’s Medical Ctr, Tokyo, Japan; Tohru Kobayashi, Div of Cardiology, Tokyo Metropolitan Children’s Medical Ctr, Tokyo, Japan; Toru Kobayashi, Div of Cardiology, Tokyo Metropolitan Children’s Medical Ctr, Tokyo, Japan;
of Clinical Pharmacology and Toxicology, the Hosp for Sick Children, Toronto, ON, Canada; Shunichi Ogawa, Dept of Pediatrics, Nippon Medical Sch, Tokyo, Japan

10:15 Kawasaki Disease Complicated by Coronary Artery Aneurysms: Mortality and 40-year Outcomes Cedric Manlhiot, The Hosp for Sick Children, Toronto, ON, Canada; Andrew M. Crean, Univ Health Network, Toronto, ON, Canada; Nigel Fernandopulle, Brendan Lew, Tanveer H. Collins, Nita Chahal, Brian W. McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

10:30 Coronary Artery Stenosis Risk and Progression in Kawasaki Disease Patients: Experience at a U.S. Tertiary Pediatric Center Alok Patel, Margaret Bruce, Whitney Harrington, Michael Portman, The University of Washington, Seattle, WA

10:45 Estimation of the Severity of Coronary Artery Aneurysm by Z-score of the Internal Diameter in Kawasaki Disease Naoya Fukushima, Masaru Miura, Tokyo Metropolitan Children's Medical Ctr, Fuchu, Japan; Toru Kobayashi, Div of Clinical Pharmacology and Toxicology, The Hosp for Sick Children, Toronto, Toronto, QC, Canada; Shigeto Fuse, NTT East Japan Sapporo Hosp, Sapporo, Japan; Tsutomu Saji, First Dept of Pediatrics, Toho Univ Omori Medical Ctr, Tokyo, Japan; Hiroyuki Yamagishi, Dept of Pediatrics, Keio Univ, Fuchu, Japan; Taichi Kato, Dept of Pediatrics, Nagoya Univ, Nagoya, Japan; Kenji Hamaoka, Dept of Pediatric Cardiology and Nephrology, Kyoto Prefectural Univ of Med Graduate Sch of Medical Science, Kyoto, Japan; Yuichi Nomura, Dept of Pediatrics, Kagoshima Univ, Kagoshima, Japan; Ryuji Fukazawa, Dept of Pediatrics, Nippon Medical Sch Hosp, Tokyo, Japan; Hitoshi Kato, Dept of Cardiology, Natl Medical Ctr for Children and Mothers, Tokyo, Japan; Keiichi Hirose, Dept of Pediatrics, Univ of Toyama Graduate Sch of Med, Toyama, Japan; Kenji Suda, Dept of Pediatrics and Child Health Cardiovascular Res Inst Kurume Univ Sch of Med, Kurume, Japan


11:15 Characteristics and Fate of Systemic Artery Aneurysm Caused by Kawasaki Disease Shinsuke Hoshino, Shiga Univ of Medical Science, Shiga, Japan; Etsuko Tsuda, Osamu Yamada, Natl Cerebral and Cardiovascular Ctr, Osaka, Japan

11:30 Long-term Outcome of Patients with Giant Coronary Aneurysms Caused by Kawasaki Disease: A 30-year Experience in a Single Center in Taiwan Wan-Ling Chih, Ming-Tai Lin, Ching-Hao Chang, Chun-An Chen, Shue-Nan Chiu, Chun-Wei Lu, Jou-Kou Wang, Mei-Hwan Wu, Natl Taiwan Univ Children's Hosp, Taipei, Taiwan

Break 11:45 AM–12:00 PM Coral Lounge

Lunch Symposium 12:00–1:00 PM Discovery Through Multi-Institutional Collaboration Coral 3 Moderators: Jane Newburger, MD, MPH, Harvard Medical School, Boston, MA Kenji Hamaoka, MD, PhD, Kyoto Prefectural University of Medicine, Kyoto, Japan

12:00 The North American Kawasaki Disease Registry Brian McCrindle, MD, MPH, FAHA, The Hospital for Sick Children, Toronto, Ontario, Canada
12:10 **International Kawasaki Disease Genetic Consortium**  
Taco W. Kuijpers, MD, PhD, Emma Children's Hospital, Amsterdam, Netherlands

12:20 **Red de Emfermedad de Kawasaki en America Latina (Latin America Kawasaki Disease Network)**  
Adriana Tremoulet, MD, University of California-San Diego, San Diego, CA

12:30 **The KAICA Trial of Cyclosporine for Severe Kawasaki Disease**  
Akira Hata, PhD, Chiba University Graduate School of Medicine, Chiba, Japan

12:40 **Discussion**

1:00–1:15 PM  
**Break**  
*Coral Lounge*

**Richard Rowe Memorial Lecture**  
*1:15–1:45 PM*  
*Coral 3*  
**Moderator:** Brian McCrindle, MD, MPH, FAHA, The Hospital for Sick Children, Toronto, Ontario, Canada

1:15 **Risk Stratification and Outcome in Patients with Coronary Artery Lesions**  
Etsuko Tsuda, MD, Department of Pediatrics, National Cardiovascular Center, Osaka, Japan

**Natural History and Prognosis Part 2**  
*1:45–2:45 PM*  
*Coral 3*  
**Moderators:** Michael Gewitz, MD, New York Medical College, Valhalla, NY; Shiro Naoe, Toho University Ohashi Medical Center, Tokyo, Japan

1:45 **Exercise Response in Children and Adolescents Late After Kawasaki Disease According to Early Coronary Status**  
Nagib Dahdah, Div of Pediatric Cardiology, CHU Ste-Justine, Montreal, QC, Canada; Michael Portman, Div of Pediatric Cardiology, Seattle Children Hosp, Seattle, WA

2:00 **Carotid Intima-media Thickness in Patients with a History of Kawasaki Disease**  
Sanne Dietz, Carline Tacke, Emma Children's Hosp, Academic Medical Ctr, Amsterdam, Netherlands; Johan Gort, Academic Medical Ctr, Amsterdam, Netherlands; Irene Kuijpers, Emma Children's Hosp, Academic Medical Ctr, Amsterdam, Netherlands; Eric de Groot, Imagelabonline & Cardiovascular, Amsterdam, Netherlands; Albert Wiegman, Emma Children's Hosp, Academic Medical Ctr, Amsterdam, Netherlands; Barbara Hutton, Academic Medical Ctr, Amsterdam, Netherlands; Taco Kuijpers, Emma Children's Hosp, Academic Medical Ctr, Amsterdam, Netherlands

2:15 **Corticosteroid Pulse Therapy for Acute Kawasaki Disease: Consideration for the Long-Term Prognosis of Coronary Artery Lesions**  
Atsushi Kitagawa, Masahiro Ishii, Yoshiiito Ogihara, Shouhei Ogata, Kitasato Univ, Kanagawa, Japan; Motofumi Iemura, Kenji Suda, Kurume Univ, Kurume, Fukuoka, Japan

2:30 **Coronary Vessel Wall Imaging by Using Multi-detector Computed Tomography and Outcomes in Patients Long After Kawasaki Disease: Potential for Risk Stratification**  
Hiroyuki Ohashi, Kakuya Kitagawa, Hirohumi Sawada, Hitoteshi Hayakawa, Shoichiroy Otsuki, Noriko Yodoya, Hajime Sakuma, Yoshihiro Komada, Yoshihide Mitani, Mie Univ Graduate Sch of Med, Tsu City, Mie Prefecture, Japan

2:45–3:00 PM  
**Break**  
*Coral Lounge*
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<td>3:00–4:15 PM</td>
<td>Medical Management and Revascularization</td>
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<td>Masahiro Ishii, MD, Kitasato University, Kanagawa, Japan</td>
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<td>Shunichi Ogawa, MD, Nippon Medical School, Tokyo, Japan</td>
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<td>Safety and Efficacy of Warfarin Therapy in Kawasaki Disease</td>
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<td>Annette L. Baker, Jenna Murray, Boston Childrens Hosp, Boston, MA</td>
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<td>3:15</td>
<td>Thrombosis and Thromboprophylaxis for Patients with Giant Coronary Artery</td>
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<td>Aneurysms after Kawasaki Disease: A Study from the North American Kawasaki Disease Registry</td>
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<td>Cedric Manlhiot, The Hosp for Sick Children, Toronto, ON, Canada;</td>
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<td>William T. Mahle, Children’s Healthcare, Emory Univ, Atlanta, GA;</td>
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<td>Kevin D. Hill, Duke Univ Medical Ctr, Durham, NC;</td>
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<td>Jennifer S. Li, Duke Univ Medical Ctr, Atlanta, GA; Dawn Tucker,</td>
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<td>Children’s Mercy Hosp, Kansas City, MO; Ashwini Kulkarni,</td>
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<td>Stollery Children’s Hosp, Edmonton, AB, Canada; Lillian S. Lai,</td>
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<td>Children’s Hosp of Eastern Ontario, Ottawa, ON, Canada; Brett Anderson,</td>
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<td>New York Presbyterian Hosp, Columbia Univ, New York, NY; Aaron K. Olson,</td>
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<td>Seattle Children’s Hosp, Seattle, WA; Brian W. McCrindle, The Hosp for</td>
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<td>Sick Children, Toronto, ON, Canada; North American Kawasaki Disease</td>
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<td>3:30</td>
<td>The Spectrum of Cardiovascular Lesions Requiring Intervention in Young Adults after Kawasaki Disease</td>
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<td>John B. Gordon, San Diego Cardiac Ctr, San Diego, CA; Lori B. Daniels,</td>
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<td>Andrew M. Kahn, Univ of California, San Diego Dept of Med, La Jolla, CA;</td>
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<td>Matthew Vejar, Chisato Shimizu, Jane C. Burns, Univ of California,</td>
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<td>San Diego Dept of Pediatrics, La Jolla, CA</td>
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<td>3:45</td>
<td>Long-term Results of Percutaneous Transluminal Coronary Rotational</td>
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<td>Atherectomy for Localized Stenosis Caused by Kawasaki Disease</td>
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<td>Etsuko Tsuda, Shinsuke Hoshino, Yasuhide Asaumi, Yosuke Hayama,</td>
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<td>Osamu Yamada, Natl Cerebral and Cardiovascular Ctr, Suita, Japan</td>
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<td>4:00</td>
<td>Statin Alleviates Persistent Coronary Arterial Inflammation Long After Kawasaki Disease – A Serial Fluorodeoxyglucose Positron Emission Tomography Study</td>
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<td>Kenji Suda, Nobuhiro Tahara, Akhiro Honda, Hironaga Yoshimoto, Shintaro</td>
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<td>Kishimoto, Yoshiyuki Kudo, Hayato Kaida, Toshi Abe, Takafumi Ueno,</td>
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<td>Yoshihiro Fukumoto, Kurume University Sch of Med, Kurume City, Japan</td>
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<td>4:15</td>
<td>Lifestyle and Psychosocial Issues</td>
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<td>Moderators:</td>
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<td>Annette Baker, BSN, MSN, CPNP, Children’s Hospital, Boston, MA</td>
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<td>Greg Chin, Kawasaki Disease Foundation, Ipswich, MA</td>
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<td>4:15</td>
<td>Transition to Adult Care</td>
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<td>Adrienne Kovacs, PhD, University Health Network, Toronto, ON</td>
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<td>4:45</td>
<td>Factors Associated with Illness Impact after Diagnosis of Kawasaki Disease and Coronary Artery Complications</td>
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<td>Nita Chahal, Ahlexxi Jelen, The Hosp for Sick Children, Toronto, ON,</td>
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<td>Canada; Janet Rush, The Univ of Toronto, Toronto, ON, Canada; Katherine</td>
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<td>Boydell, Cedric Manlhiot, Renee Sananes, Brian W. McCrindle, The Hosp</td>
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**Poster Session 2**

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**Parents Association Symposium**

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**Reception and Dinner**

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<td>6:30–9:00 PM</td>
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**Program Agenda (continued)**

**Friday, February 6**

**Continental Breakfast**
7:30–8:30 AM
Coral Lounge

**SUMMARY and DISCUSSION**
8:30–9:30 AM
Coral 3

**Moderators:**
Brian McCrindle, MD, MPH, FAHA, Hospital for Sick Children, Toronto, Canada
Anne Rowley, MD, Northwestern University Feinberg School of Medicine, Chicago, IL

8:30  **Jane Burns, MD**, University of California San Diego School of Medicine, La Jolla, CA

8:30  **Jane Newburger, MD**, Harvard Medical School, Boston, MA

**Presentation of Awards**
9:30–9:45 AM
Coral 3

**Presenters:**
Tomisaku Kawasaki, MD, Japan Kawasaki Disease Research Center, Tokyo, Japan
Kathryn Taubert, PhD, American Heart Association, Dardagny, Switzerland

**Announcement of the Next Symposium and Closing**
9:45 AM
Coral 3
Oral Abstract Presentations

O.01
Epidemiology of Kawasaki disease in South Korea, 2009-2011

Gi Beom Kim, Seoul Natl Univ Children’s Hosp, Seoul, Korea, Republic of; Ji Whan Han, Uijeongbu St. Mary’s Hosp, Uijeongbu, Korea, Republic of; Yong Won Park, Inje Univ Seoul Paik Hosp, Seoul, Korea, Republic of; Min Seob Song, Inje Univ Haeundae Paik Hosp, Busan, Korea, Republic of; Young Mi Hong, Ewha Womans Univ Hosp, Seoul, Korea, Republic of; Dong Soo Kim, Severance Children’s Hosp, Seoul, Korea, Republic of

We assessed the recent epidemiologic features of Kawasaki disease in South Korea from the nationwide survey conducted between 2009 and 2011. We collected data regarding the incidence, symptoms, treatment, and coronary complications associated with acute Kawasaki disease by sending questionnaires to the 100 hospitals that have pediatric residency programs. We received complete responses from 73 hospitals and partial responses from 14 hospitals. A total of 13,031 cases of Kawasaki disease were reported from the 87 hospitals (3,941 in 2009, 4,635 in 2010, and 4,455 in 2011). The male to female ratio was 1.44:1, and the median age at diagnosis was 28 months. From the questionnaires with complete responses, we noted that the incidence of Kawasaki disease per 100,000 children less than 5 years of age was 115.4 in 2009, 132.9 in 2010, and 134.4 in 2011 (average rate, 127.7). Kawasaki disease occurred more frequently during summer (June, July, and August) and during winter (December and January). The recurrence rate was 3.83% (387 of 10,100). The mean total duration of fever was 5.6 ± 2.4 days. The most common symptom was conjunctival injection (88.2%). The standard dose of intravenous immunoglobulin was administered to 93.6% (9,453 of 10,100), and non-responder rate was 11.6%. Coronary aneurysm occurred in 1.9% (180 of 9,028) though giant aneurysm developed in 0.26% (26 of 9,882) of patients over 3 years. Two patients had myocardial infarction. No mortality was reported during this period. In conclusion, the average annual incidence of Kawasaki disease in South Korea has continuously increased to 134.4 per 100,000 children less than 5 years of age in 2011, which is the second highest incidence of Kawasaki disease worldwide, following its incidence in Japan.

O.02
Validation of Kawasaki Disease Incidence Assessment as Derived from Health System Administrative Databases vs. Active Retrospective Surveillance in Ontario, Canada

Cedric Manlhiot, Sunita O'Shea, Bailey Bernknopf, Michael Labelle, Mathew Mathew, Nita Chahal, Brian W. McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

Introduction: Historically, 2 methods have been used to determine the incidence of Kawasaki disease (KD): active or passive surveillance, or the use of administrative databases. Given the increasing regulatory requirements, mainly around patient privacy, periodic retrospective surveillances have become increasingly challenging. Administrative databases are not curated datasets and doubts have been cast on their accuracy.

Methods: The Hospital for Sick Children has been conducting retrospective triennial surveillances of KD since 1995 by contacting all hospitals in Ontario and manually reviewing all cases through chart review, reconciling inter-hospital transfers and multiple readmissions. We queried the Canadian hospital discharge database (Canadian Institute for Health Information) for hospitalizations associated with a diagnosis of KD between 2004-9. The administrative dataset was manually reviewed; patient national health number, institution and dates of admission/discharge were used to identify inter-hospital transfers, readmission and follow-up episodes.

Results: The Canadian hospital discharge database reported 1,685 admissions during the study period (281±44 per year) for Ontario. Manual review of the dataset identified 219 (13%) as inter-hospital transfers (56, 26%), readmissions (122, 56%), admissions for follow-up of coronary artery aneurysms (14, 6%) or hospital admissions not related to KD (27, 12%). When these admissions were removed, the total...
number of incident cases for the study period was 1,466 (244±45 per year). The retrospective triennial surveillance identified 1,373 KD cases during the same period (229±33 per year). The Canadian hospital discharge database overestimated the number of cases in all 6 years by an average of 6.7±5.9%. The overestimation likely comes from patients who were originally diagnosed with KD but in whom the diagnosis of KD was subsequently excluded (historically ~5-6%).

**Conclusions**: Reliance on administrative data to determine incidence of KD is possible and accurate; data should be manually reviewed to remove non-incident cases and estimates should be adjusted to reflect the expected proportion of patients in whom the diagnosis of KD will be subsequently excluded.

**C. Manlhiot**: None. **S. O’Shea**: None. **B. Bernknopf**: None. **M. Labelle**: None. **M. Mathew**: None. **N. Chahal**: None. **B.W. McCrindle**: None.

### O.03 Monitoring the Occurrence of Kawasaki Syndrome in the United States

**Ryan A Maddox**, Marissa K Person, Lindsay J Joseph, Dana L. Haberling, Ctrs for Disease Control and Prevention, Natl Ctr for Emerging and Zoonotic Infectious Diseases, Atlanta, GA; Claudia A Steiner, Dept of Health and Human Services, Agency for Healthcare Res and Quality, Rockville, MD; Lawrence B Schonberger, Ermias D Belay, Ctrs for Disease Control and Prevention, Natl Ctr for Emerging and Zoonotic Infectious Diseases, Atlanta, GA

**Objectives.** To describe the occurrence of Kawasaki syndrome (KS) in the United States.

**Methods.** The Kids’ Inpatient Database (KID; 2003, 2006, 2009, 2012) and the Nationwide Inpatient Sample (NIS; 2001-2011) were analyzed to determine KS-associated hospitalization rates and trends; the United States Centers for Disease Control and Prevention (CDC; 2010-July 2014) passive KS surveillance database was analyzed to assess the frequency of coronary artery abnormalities (CAAs) among reported KS cases meeting the CDC KS case definition.

**Results.** The KS-associated hospitalization rate for children <5 years of age using the KID was 18.1 (95% CI: 16.0-20.2) per 100,000 children in 2012, 20.0 (95% CI: 17.8-22.2) in 2009, 21.3 (95% CI: 18.9-23.7) in 2006, and 19.7 (95% CI: 17.7-21.7) in 2003. The 2012 KS-associated hospitalization rate was 21.0 (95% CI: 18.6-23.4) among males <5 years of age and 15.0 (95% CI: 13.0-17.0) among females. Asians/Pacific Islanders had the highest rate among all racial groups, 29.6 (95% CI: 22.2-37.4). The average annual KS-associated hospitalization rate for children <5 years of age using the NIS was constant from 2001-2011 at 18.8 per 100,000 per year (95% CI: 17.3-20.3; p=0.16) with peaks in 2005 (27.0 per 100,000; 95% CI: 19.3-34.7) and, to a lesser extent, in 2010 (22.6 per 100,000; 95% CI: 16.6-28.5). The CDC surveillance database included 497 physician-diagnosed KS cases <18 years of age reported with onset occurring January 1, 2010 through July 31, 2014; about three-quarters (n=372) of the cases met the CDC KS case definition. Among KS cases meeting this definition that also contained complication data, 18.7% (69/369) had CAAs reported; among Asian/Pacific Islander children, 24.7% (18/73) had CAAs reported. Almost all KS cases in the database (98.1%, 363/370) were treated with intravenous immunoglobulin.

**Conclusions.** Analyses of KID and NIS data did not indicate any increase in KS-associated hospitalization rates for children <5 years of age in the United States through 2012. CAAs continue to occur at a comparable rate with past reports.

**R.A. Maddox**: None. **M.K. Person**: None. **L.J. Joseph**: None. **D.L. Haberling**: None. **C.A. Steiner**: None. **L.B. Schonberger**: None. **E.D. Belay**: None.

### O.04 Kawasaki Disease With Down Syndrome: low Risk For Ivig Resistance And Coronary Artery Abnormalities

**Shinichi Takatsuki**, Toho university Omori medical center, Tokyo, Japan; Masato Yokozawa, Hokkaido Medical center for child health and rehabilitation, Hokkaido, Japan; Masae Ono, Tokyo Teishin Univ hospital, Tokyo, Japan; Masako Fujiwara, Horoyuki Ida, Jikei Univ hospital, Tokyo, Japan; Hideki Motomura, Horoyuki Moriuchi, Nagasaki Univ, Nagasaki, Japan; Mio Taketazu, Junichi Oki, Asahikawa-Koisei General hospital, Hokkaido, Japan; Shigeaki Nonoyama, Natl Defense Medical college, Tokyo, Japan; Tatsuya Kawano, Kenji Ihara, Oita Univ hospital, Oita, Japan; Sachiko
Oral Abstract Presentations

Kido, Hyogo Prefectural Kobe Children’s hospital, Hyogo, Japan; Junko Shiono, Ibaragi Children’s hospital, Ibaragi, Japan; Shiro Tsuchiya, Soka Municipal hospital, Saitama, Japan; Keiji Tsuchiya, Japan Red Cross Medical center, Tokyo, Japan; Teruhumi Goushi, Nakatsu Municipal hospital, Osaka, Japan; Shuhei Ogata, Masahiro Ishii, Kitazato Univ hospital, Kanagawa, Japan; Fukiko Ichida, Toyama Univ hospital, Tokyo, Japan; Tsutomu Saji, Toho university Omori medical center, Tokyo, Japan

Background: Japanese nationwide survey reported that Down syndrome (DS) is less-frequently occurring comorbidity in Kawasaki disease (KD). Thus, no studies have focused treatment response and risk for coronary artery abnormalities (CAAs) in KD with DS. The aim of this study was to evaluate clinical manifestations, treatment response and incidence of CAAs in KD with DS.

Methods: We retrospectively reviewed the medical records of KD with DS from 2005 through 2012. Data were collected according to survey questionnaires from 16 hospitals.

Results: The response rate was 80% and the survey questionnaires from 16 KD patients (11 boys and 5 girls) with DS were collected. Age at diagnosis was 3 years (8 months to 12 years). Eight children (50%) were diagnosed incomplete KD. Five children had previous history of repaired congenital heart disease (AVSD 2, VSD+ASD 1, ASD 2, PDA 1). Of all, 8 children were classified as high risk group based on Kobayashi score. Twelve children received IVIG and 3 children were treated with only high dose aspirin. All 15 children were responded to initial treatment. In the remaining one girl with incomplete KD, the clinical symptoms spontaneously resolved. CAAs were not detected by echocardiography during follow-up.

Conclusions: All DS children with KD were responded to initial IVIG or aspirin therapy despite the high risk of IVIG resistance and none of children had CAAs. Therefore, our finding suggested DS is not a risk factor for IVIG resistance and developing CAAs in KD.

**O.06 Epidemiology of Kawasaki Disease in Canada (2004-2011)**

**Brian W. McCrindle**, Sunita O’Shea, Brendan Lew, Sameer Masood, The Hosp for Sick Children, Toronto, ON, Canada; Dirk Bock, London Health Sciences Ctr, London, ON, Canada; Lillian S. Lai, Children’s Hosp of Eastern Ontario, Toronto, ON, Canada; Rejane F. Dillenburg, McMaster Univ Children’s Hosp, Hamilton, ON, Canada; Bailey Bernknopf, Nita Chahal, Rae S.M. Yeung, Cedric Manlhiot, The Hosp for Sick Children, Toronto, ON, Canada

**Introduction:** We have previously documented in consecutive triennial systematic surveillances a rise in the incidence of KD in Ontario, Canada between 1995 and 2004 followed by a stabilization at 24-26 cases per 100,000 children <5 year old per year between 2004 and 2009. Previous studies have been limited to the province of Ontario; we sought to determine the incidence of KD across Canada and by province.

**Methods:** We queried the Canadian hospital discharge database (Canadian Institute for Health Information) for hospital admissions associated with a discharge diagnosis of KD (either primary or secondary) between 2004 and 2011. Multiple admissions for a given patient were not counted as separate incident cases unless >2 months from the original admission and associated with IVIG treatment. Denominators were derived from population data from the 2001, 2006 and 2011 Censuses.

**Results:** The annual incidence of KD during the study period was 21.9, 6.8 and 1.1 cases per 100,000 children <5 years, 5-9 years and 10-14 years old, respectively (4,340 cases total). Stratification by region showed the lowest incidence to be in Saskatchewan (11.8/100,000 children <5 year old), followed by Manitoba (17.3), Alberta (17.7), Quebec (18.1), British Columbia (20.6), Atlantic Provinces (22.5) and finally Ontario (27.5, similar to that noted on previous systematic surveillances). The incidence remained stable over the study period, confirming the plateau reached in the previous systematic Ontario surveillance between 2004-2009. An increased incidence was noted for children <5 years old, male gender and winter months. There was a moderate correlation between proportion of the provincial population of Asian descent and KD incidence (r=0.58). Coronary artery aneurysms affected 5.8% of patients, and 1.9% experienced major cardiac complications or had cardiac interventions.

**Conclusions:** The previous increase in the incidence of KD has plateaued, indicating that the true annual incidence fluctuates between 20-22 and 24-27 cases per 100,000 children <5 years for Canada as a whole, and 24-27 cases for the province of Ontario. Differences in annual incidence observed between provinces remain to be explained, but may reflect racial, genetic or environmental factors.

**B.W. McCrindle:** None. **S. O’Shea:** None. **B. Lew:** None. **S. Masood:** None. **D. Bock:** None. **L.S. Lai:** None. **R.F. Dillenburg:** None. **B. Bernknopf:** None. **N. Chahal:** None. **R.S. Yeung:** None. **C. Manlhiot:** None.
O.07
The Clinical Risk Factors of Intravenous Immunoglobulin Resistance and Coronary Artery Lesion of Kawasaki Disease: Retrospective Analysis of 602 Cases

lijian xie, Cuizhen Zhou, Renjian Wang, Tingting Xiao, Jie Shen, Min Huang, pediatric cardiology, shanghai children's hospital, shanghai, China

Introduction
The incidence of Kawasaki disease (KD) in China is increasing for years. The current coronary artery lesion (CAL) incidence is 5-10% in KD with intravenous immunoglobulin (IVIG) treatment. And the 10-20% KD patients still exhibit IVIG resistance. However, little clinical evidence on the occurrence of either CAL or IVIG resistance for big KD sample study in China during the past decade.

Objective
In order to find clinical risk factors of CAL and IVIG resistance of KD in China.

Methods
We retrospectively analyzed the clinical manifestations, laboratory results, treatment and complications of cardiac vascular of 602 KD cases from 2007 to 2012 admitted at Shanghai Children's Hospital. The SAS 9.2 edition was used for statistical analysis. The mean ± standard deviation or the median were used for measurements. Case numbers and percentages were used for the count number. The t-test and the Mann-Whitney test were both used for mean comparisons. Single factor and multi-factor logistic regression analyses were used to analyze the risk factors.

Results
1. The KD gender male to female ratio was 1.85:1. The KD median age was 2.0 years old (one month to 11.7 years old). 20.1% cases (121 of 602) exhibited CAL. There was no difference of CAL incidence between the gender (p=0.09). 2. The incidence of bright red cracked lips (p=0.001), peeling of the skin of the toes (p=0.021) and perianal skin peeling (p=0.031) are less in group with CAL. 3. Among the 602 cases, there were 525 cases that were sensitive to IVIG therapy. 100 of those cases had CAL with an incidence of 19.1%. Among the 26 IVIG resistance cases, there were 9 cases with CAL with an incidence of 34.6%, which was higher than the IVIG sensitive group (p=0.05). 4. ESR (p=0.014), CRP (p=0.017), PLT (p=0.003) and Hb (p=0.032) were much higher in the IVIG resistance group than the IVIG sensitive group, even though the IVIG resistance group started the IVIG treatment earlier (p=0.003). 5. Logistic regression analysis was conducted to show that GPT≥80IU/L was the independent risk factor of IVIG resistance, risk ratio was 2.945 (p=0.012).

Conclusion
This research suggests that risk factors of clinical evidence for IVIG resistance and CAL in KD.

Key words
Kawasaki disease, intravenous immunoglobulin, coronary artery lesion


O.08
Rashless Kawasaki Disease (KD): Colorado's Experience

Marsha S Anderson, Samuel R Dominguez, Heather R Heizer, Pei-Ni Jone, Jesse Davidson, Mary P Glode, Children's Hosp Colorado, Aurora, CO

Objective: Published studies describe Incomplete KD, but rashless KD has not been well characterized. We describe a 10 year experience with rashless KD patients, diagnosed based on the presence of a compatible illness and coronary artery lesions (CALs).

Methods: We prospectively collected cases of rashless KD with CALs diagnosed at Children's Hospital Colorado from 7/1/2004-6/30/2014. Patient charts were reviewed for demographic, clinical, laboratory, and diagnostic information.

Results: 11 patients were identified (median age 3.7 yrs), representing 10.3% (11/107) of all KD patients with CALs diagnosed during the same time period. Diagnosis was made on median day of illness (DOI) 8 (range 4-17 days), and patients had a median of 4 (range 2-7) healthcare contacts prior to diagnosis. All patients (100%) had the presence or history of conjunctival injection and 8/11 (72.7%) had oral changes. Five patients had only 2 major clinical features in addition to fever; 1 patient had one. All patients had very elevated inflammatory markers. Infectious Disease consultants suspected KD and recommended treatment prior to echocardiogram (ECHO) results in 8/11 (72.7%), recommended treatment if ECHO abnormal in 2/11 (18.1%), and in 1/11 (9.2%) KD was thought to be unlikely, but the diagnosis
was made by ECHO.

Conclusions: 10.3% of KD patients with CALs at our institution presented without a rash. As rash is often considered a defining characteristic of KD, some children with rashless KD are likely not being identified and treated. Providers should consider the diagnosis of KD in patients with unexplained fever, conjunctivitis, and elevated inflammatory markers.


O.09
French observatory of Kawasaki disease in adults: 24 observations.

Jean-Baptiste Fraison, Jean Verdier Hosp, Bondy, France; Pascal Seve, Univ Hosp, Lyon, France; Emmeline Gommard-Mennesson, Internal medicine, Béziers, France; Claire Dauphin, Gabriel Montpied Hosp, Clermont-Ferrand, France; Alfred Mahr, St Louis Hosp, Paris, France; Cedric Landron, Univ Hosp, Poitiers, France; Costedoat-Chalumeau Nathalie, Cochin Hosp, Paris, France; Olivier Epaudal, Univ Hosp, Grenoble, France; Le Thi Huong Boutin, Pitie Salpêtrière Hosp, Paris, France; Maryam Piram, Bicetre Hosp, Paris, France; Arsène Mekinian, Saint Antoine Hosp, Paris, France; Pascal Roblot, Univ Hosp, Poitiers, France; Eric Oziol, Internal medicine, Béziers, France; Arnaud Hot, Edouard Herriot Hosp, Lyon, France; Gihane Chalhoub, Internal medicine, Metz, France; Jean-Marc Galempoix, Internal medicine, Charleville-Mézières, France; Guillaume Marchand, Bizet Hosp, Paris, France; Sébastien Humbert, Philippe Humbert, Univ Hosp, Besançon, France; Philippe Morlat, Univ Hosp, Bordeaux, France; Xavier Puéchal, Loic Guillemin, Cochin Hosp, Paris, France; Isabelle Koné-Paut, Bicetre Hosp, Paris, France; Olivier Fain, Saint Antoine Hosp, Paris, France

Introduction
Kawasaki disease (KD) is a vasculitis that occurs mostly among children and exceptionally in adults. We report data from a French observatory of adult KD.

Patients and methods:
Adult patients diagnosed with KD in 16 French centers were included. Patients were classified as complete KD or incomplete KD according to IKDC or probable KD.

Results:
We included 24 patients with a median age of 29 years (22-39) and a sex ratio (M/F) 2.42. 12 complete KD, 9 incomplete KD and 3 probable KD without any other cause. Time to diagnosis was 13 days (10-20.5). Main events were: fever (100%), extremities changes (21/24, 87.5%), rash (22/24, 92%), conjunctivitis (16/24, 66%), cheilitis (15/24, 63%), strawberry tongue (11/24, 46%), adenopathy (10/24, 42%), cardiac abnormalities (11/24, 46%), cardiogenic shock (n = 1), myo-pericarditis (n = 3) and left heart failure (n = 1).

Median CRP was 228mg/L (166-311), SGOT: 68 IU/L (51-139), SGPT: 125 IU/L (69-190), platelets 372 G/L (209-630) and leukocytes 16 G/L (8.3-20).

Cardiac involvement was researched in 23 patients (96%) by achieving: echocardiography (20/24), coronary scanners (6/24), coronary angiography (5/24), cardiac MRI (2/24) and stress tests (2/24).

An arteritic vascular disease was found in 11 patients (46%): coronary aneurysms (8/24, 33%), coronary arteritis (10/24, 42%) and peripheral arteritis (2/24, 8.3%) with acute lower limb ischemia (1/24, 4.2%) and splenic infarction (1/24, 4.2%).

Patients received: intravenous immunoglobulin (17/24, 71%); aspirin (21/24, 88%). After 6 months, it persisted 5 aneurysm (20.8%). Complications noticed during the last follow-up were: heart failure (1/24, 4.3%), aneurysm (3/24, 12.5%).

Conclusion:
The adult KD is a rare disease that can have bad prognosis in short or long term and leave irreversible damage. The high rate of cardiac complication could be due to the long diagnosis delay, the absence of the gold standard treatment in 30% of cases or a selectional bias due to the difficulty to diagnose this disease in adulthood.

J. Fraison: None. P. Seve: None. E. Gommard-Mennesson: None. C. Dauphin: None.
O.10
Risk Factors Associated with Recurrence of Kawasaki Disease in Mexican Children

GIOVANNI SORCIA-RAMIREZ, LUIS M GARRIDO-GARCIA, INSTITUTO NACIONAL DE PEDIATRIA, MEXICO CITY, Mexico

Background. Kawasaki disease (KD) is an acute febrile illness characterized by systemic vasculitis. Recurrences of KD (defined as at least three clinical signs of KD in addition to fever ≥ 5 days), presenting ≥ 14 days after the return to baseline from the index episode is reported in approximately 3-4% of all cases in Japan.

Objective. To assess the frequency and determined the risk factors associated with recurrences of KD in patients treated at the Instituto Nacional de Pediatría in Mexico City.

Material and Methods. An observational, comparative, retrospective and case-control study of all patients diagnosed with recurrent KD in our Institution from August 1995 and May 2014 was performed. The clinical presentation, laboratory results, treatment used and coronary artery abnormalities in the recurrent-KD and non-recurrent KD groups were analyzed and compared.

Results. We included 371 patients with KD diagnosed at our institution; we had 19 recurrences of KD (5.1%), 16 patients had one recurrence, 1 patient had 2 recurrences and 1 patient had 3 recurrences of KD. 17 cases or our cases were male (89.4%) with mean age at diagnosis of the first episode of 31.63 ± 36.40 months and with a median of 16 months of the new event after the initial episode (1 to 60 mo.).

In bivariate analysis, male gender (p < 0.037), central nervous system manifestations in the acute phase of KD (p < 0.053) and coronary aneurysms at diagnosis (p < 0.05) showed statistical significance. There were no factors associated with recurrence in a multivariate analysis.

Conclusions: This is a very small series of KD with a slightly increased rate of recurrence compared with the rate of recurrences reported in the literature. But to allow an early recognition of a new event, a previous history of KD should be considered to initiate treatment and to achieve better outcomes in the recurrent cases.

G. Sorcia-ramirez: None. L.M. Garrido-garcia: None.
O.13
Kawasaki disease in the Maghreb community in Quebec

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Background: The real incidence of Kawasaki disease (KD) in the Maghreb countries (Morocco, Algeria, and Tunisia) is unknown. It is estimated low according to the literature. However, the number of Maghrebi children living in Quebec (QC) affected by KD seems important. We sought to determine the incidence of KD among Maghrebi children in QC, Canada, and to study its epidemiological and clinical features and to clarify possible risk factors related or superimposed to their immigration.

Methods: A retrospective study of KD in Maghrebi children living in QC (n=24) (1996-2013), compared to reports from Fes, Morocco (n=23) a doctoral thesis published in 2010 (2001-2009) and from Tunisia (n=31) collected in five university hospitals with four from the Great Tunis and one from Nabeul city (1996-2013). There are no reports available from Algeria. The “country of origin” specific population in the Province of QC was obtained from Statistics Canada.

Results: The annualized incidence rate (AIR) of KD among Maghrebi children in QC was 9.58/100,000 children under 5 years (Standard-Denominator (SD)). This is 6 times higher in QC (5.57/SD and 19.02/SD among Tunisian and Moroccan descents) vs Tunisia (Nabeul Governorate) and Morocco (Fes) (0.95/SD and 3.15/SD). Personal and family history of allergy were significantly higher in QC 42% (10/24) and 75% (18/24), respectively, whereas these features were reported near 0% in both reports from Morocco and Tunisia. The prevalence of incomplete KD criteria was relatively high in the 3 series 46% (11/24) in QC vs 43% (10/23) and 35% (11/31); (p=NS). Diagnosis was late (gt day 10 of fever) in 1/24 (4%) in QC vs 7/23 (30%) in Morocco and 11/31 (35%) in Tunisia; (p 0.01). IVIG were administered in the acute phase to all patients in QC, 5/23 in Morocco and 28/31 in Tunisia. However coronary complications were more common in QC 42% (10/24) vs 22% (5/23) vs 19% (6/31) (p=0.02). Aneurysms were significantly associated with the incomplete form in the 3 groups (p=0.01).

Conclusions: The observed AIR of KD in the Maghreb community in QC is higher than the countries of origin where underdiagnosis is possible. Atopy may still be a risk factor in QC. The coronary artery disease seems linked not only to therapeutic delay but also to the underlying terrain.

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years, with a high incidence within the 12 months from the first episode. The observed person-year categorized by some variables is calculated, such as sex, age at first episode, period of time after the initial episode, presence of cardiac sequelae in the acute (within 2 months) and late (after 2 months) stage, exposure to intravenous gamma globulin (IVGG) therapy, presence of additional IVGG administration, and exposure to steroid therapy. Using those data, incidence rate of recurrent Kawasaki disease and incidence rate ratio are calculated according to such variables, and potential risk factors for recurrence of Kawasaki disease are discussed.

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O. 15
Multicenter Retrospective Study of the Clinical Course of Kawasaki Disease in Latin American Children

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BACKGROUND:
Little is known about the burden of Kawasaki disease (KD) in Latin America (LA). The LA KD network (REKAMLATINA) was established in 2013 and has 120 physicians in over 85 hospitals in 20 countries. Its goal is to characterize the epidemiology of KD in LA children, to understand the disease impact, and plan for studies that address the specific needs of LA children with KD.

METHODS:
Retrospective review of 437 children 1 echo, worst CA status was evaluated for either the RCA or LAD. IVIG therapy response was classified as resistant (fever ≥ 38°C more than 36 hrs after completion of IVIG), responsive or unknown.

CONCLUSIONS:
This is the first multicenter report describing the clinical course and treatment of KD in LA. Differences in the care of KD patients were observed among participating countries, specially regarding obtaining echos at baseline and follow up. Also, KD could be an important cause of antibiotic misuse in LA. More research is needed to describe how KD care in LA is influenced by local and economical factors, the available resources, and to standardize treatment in resource- limited settings.

O.16
Comprehensive Genotyping Of The FCGR2/3 Locus Reveals A Novel Association Of FCGR2C-ORF With Susceptibility To Kawasaki Disease

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The human FCGR2/3 locus contains highly homologous genes encoding the five major receptors for IgG (Fc-gamma receptors, FcγRs). In two prior GWAS on Kawasaki disease (KD), a SNP in FCGR2A (131H>R; rs1801274) was identified to be associated with disease susceptibility. However, the FCGR2/3 locus contains multiple single nucleotide polymorphisms (SNPs) and copy number variations (CNVs), which were not covered by the detection platforms used in the GWAS. In this study we therefore focused on further fine-mapping of this locus to investigate the association of the different genetic variations with KD susceptibility. A highly accurate and validated multiplex ligation-dependent probe amplification (MLPA) assay was used to analyze all functionally relevant SNPs and CNVs within this locus. In a genetic association study involving case-control and family-based testing with 1028 patients with KD, the previous finding of FCGR2A-131H as a susceptibility marker for KD was confirmed (OR 1.16; 95%CI 1.08-1.32, meta-P = 0.01). In addition, we found a novel significant association of the FCGR2C-ORF haplotype with susceptibility to KD (OR 1.34; 95% confidence interval 1.11-1.62, meta-P = 0.003). FCGR2C-ORF leads to the expression of an extra, functionally activating FcγR (i.e. FcγRIIIa) on myeloid cell types and NK cells. Being absent in Asian individuals, the FCGR2C-ORF haplotype only contributed to KD susceptibility in European subjects, independent of the established association with FCGR2A-H131R. We did not find any significant association of CNV of the locus with susceptibility to KD.

Our data point to an important role of the activating FcγRs in KD pathology. We hypothesize that the identified functional SNPs might alter the balance between the activating and inhibitory FcγRs leading to unbalanced inflammation and KD.


O.17
Whole Genome Sequencing of a six-member African American family with two Kawasaki disease-affected siblings identifies novel susceptibility variants

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Oral Abstract Presentations (continued)

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We performed Whole Genome Sequencing (WGS) of a 6-member African American (AA) family with 2 of the 4 children affected with KD. We identified 6,712,158 unique variants across all 6 individuals. We first analyzed the quartet of mother/father/affected sibs and then compared variants in the 2 affected vs. 2 unaffected sibs. Assuming a recessive inheritance model, we identified 49,591 transmitted candidate homozygous variants exclusively present in both affected sibs compared to their parents. The affected vs. unaffected sibling analysis generated 64,187 candidate homozygous variants exclusively present in both affected sibs compared to their parents. The affected vs. unaffected sibling analysis generated 64,187 candidate homozygous variants exclusive to the affected sibs. The intersection of the two analyses identified 20,943 variants of which 303 – in 117 genes – were predicted to be deleterious. We validated the findings in a cohort of 405 KD subjects and 6,252 normal controls using 4,060,864 imputed genotypes. Association analysis of the imputed GWAS dataset for KD susceptibility using the allelic and recessive tests in PLINK found 438,343 SNPs (nominal P-value < 0.05). Of these, 17 variants in 10 genes were also among the 303 variants from the family analysis. These genes were ANGPT1, AS3MT, C10orf32, CMIP, CNNM2, LRG1, MMP1, NT5C2, SLK, and TLR6. Of these, ANGPT1, MMP1, and TLR6 have been previously associated with KD. For SLK (serine-threonine protein kinase 2) rs10786779 located in the promoter, the homozygous A allele (risk) genotype showed significantly higher expression (p=0.04) in a cohort of 141 acute vs. convalescent mixed ethnic KD subjects on the Illumina HumanRef-12 V4 BeadChip.

Conclusion: This is the first analysis of WGS in KD and the first to focus on genetic susceptibility in AA children who are second only to Asian children in susceptibility to KD. This exploratory analysis provides new validated variants that may likely contribute to KD susceptibility in AA children.


O.18
Histopathological Analysis Of Sudden Death Adults With Coronary Artery Aneurysms

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Histopathological study on coronary arterial lesions of adult autopsy cases who had a history of Kawasaki disease (KD) in childhood or who had coronary artery aneurysms (CAANs) was performed to analyze the relationship between post-inflammatory arterial lesions and atherosclerosis.

[Materials and Methods] Five autopsy cases who contracted KD at childhood and 11 autopsy cases who had giant CAANs at autopsy although a history of KD was not confirmed were included in this study. The age at death ranged from 18 to 57 years old. Forty-eight coronary artery (CA) branches from 16 autopsies were histologically examined focusing on the atherosclerosis which developed on the post-inflammatory lesions.

[Results] CAANs occurred in 30 arteries among 48 CA branches. CAANs were classified into 2 types; dilated CAANs (22 branches) and recanalized CAANs (8 branches). Dilated CAANs: The early atherosclerotic
lesions, which corresponded to Type III or less of AHA classification, were seen in 16 CAs, and among them 6 branches had thrombotic luminal occlusion caused by the intimal erosion. On the other hand, the advanced atherosclerotic lesions corresponding to Type IV or more were observed in 6 of 22 branches and thrombotic occlusion of the lumen was observed in 5 of 6 CA branches. The cause of those thrombotic occlusion was estimated the rupture of atheroma.

Recanalized CAANs: All atherosclerotic lesions developed in the recanalized CAANs were classified to the early lesions. Thrombotic occlusion was seen in 1 of 8 branches. Non-CAANs: There were 18 CAs with no aneurysm formation. The majority of Non-CAANs (16 of 18 branches) showed early atherosclerotic lesions (Type I or II), but 2 branches of 1 patient showed the advanced atherosclerotic lesion and the lumen was occluded by the fresh thrombus caused by intimal erosion.

[Conclusion] This histological study targeted at the post-inflammatory CA lesions in adult suggests two things: 1) Though advanced atherosclerotic lesions were often observed in the dilated CAANs, the atherosclerosis in the recanalized CAANs and Non-CAANs was still in early stage. 2) The erosion of the intima plays an important role in a formation of the thrombotic occlusion in the post-inflammatory arterial lesions even in adulthood.


O.19
Fine Specificity Of Natural Regulatory T Cells That Modulate Vascular Inflammation

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Objective: We recently defined that a critical mechanism of IVIG therapy in KD patients is the activation and expansion of natural regulatory T cells (nTreg) that recognize the heavy constant region (Fc) of IgG1. Lack of circulating Fc-specific nTreg in the sub-acute phase of KD strongly correlates with arterial complications. Notably, Fc-specific nTreg are always detectable in circulation in healthy donors, suggesting their importance in maintaining vascular homeostasis. Here we aim at the characterization of the fine specificity of these nTreg by testing the immunogenicity of synthetic peptides (> 97% purity) 15 amino acid long, overlapping 10 amino acids, spanning the whole Fc protein.

Methods: To define the immunodominant Fc sequences for nTreg expansion, T cell lines have been established with pools of two consecutive overlapping peptides been generated from PBMC ex vivo from: 1) healthy donors, 2) sub-acute KD subjects (2 weeks after IVIG), and 3) KD subjects that received IVIG 1-2 years earlier. IL-10 secretion and CD4+ CD25high T cell expansion have been the read-outs in these experiments.

Results: 14 peptides have been defined immunogenic in all the 3 cohorts with several peptides recognized by the large majority of the subject studied, including patients with arterial complication that did not respond to the whole Fc protein. The algorithm prediction of the HLA binding affinity of these nTreg peptide epitopes suggests that these immunodominant regions of the Fc protein are promiscous for HLA binding and very good candidate for future therapeutic use.

Clinical relevance of the findings: Immunodominat Fc peptides are an optimized, low cost alternative to IVIG, potentially capable to overcome the lack of nTreg responses in KD patients that develop arterial complications.


O.20
Deep RNA Sequencing Reveals a Transcriptional Profile of Cytotoxic T Lymphocyte Activation, Antigen Presentation, Immunoglobulin Production, and Type I Interferon Response in Kawasaki Disease Arteritis


Introduction: Subacute/chronic arteritis (SA/C) and luminal myofibroblastic proliferation are the pathologic processes that can continue in Kawasaki Disease (KD) coronary arteries after the second week of illness, when acute neutrophilic necrotizing arteritis has subsided. The specific dysregulated immune pathways in SA/C arteritis have been unknown, hampering the development of effective immunomodulatory therapies for patients not responding to intravenous gammaglobulin therapy. Controversy exists as to whether the arteritis is lymphocyte- or macrophage-mediated.

Hypothesis: Based on our histopathologic studies, we hypothesized that the immune transcriptome of SA/C KD arteritis was primarily lymphocyte- rather than macrophage-mediated.

Methods: RNA was isolated from paraffin-embedded CA tissues, and samples passing quality control assays were subjected to deep RNA sequencing (101 nt paired-end reads, 40-100 million reads/sample). Reads were aligned to the human genome, and HTseq used to determine read counts. DESeq was used to test for differential gene expression in CA tissues from 8 KD children (median age=7 mo, median 4 wks and all >2 weeks after onset) compared to 7 controls with normal CAs (median age=5 mo). Pathways analysis was performed using Ingenuity iReport™.

Results: 1074 differentially expressed genes were identified with >1.5-fold change and q-value <0.05. The most significantly upregulated pathways included cytotoxic CD8 T lymphocyte, dendritic cell and toll-like receptor (TLR) signaling, and antigen presentation. Immunoglobulin and type I interferon-stimulated genes were significantly upregulated. 50 immune response genes encoding secreted proteins were upregulated and are candidate biomarkers of KD arteritis.

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Conclusions: The immune transcriptional profile in KD CA tissues after the second week of illness is primarily lymphocyte-mediated and compatible with an antiviral immune response. This first report of the KD CA transcriptome identifies specific dysregulated immune response pathways that can inform the development of new therapies for and biomarkers of KD vasculitis, and provides direction for future etiologic studies of this potentially fatal childhood illness.


O.21
Inositol 1,4,5 triphosphate 3- kinase C regulates NLRP3 Inflammasome activation in Kawasaki disease

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Background: ITPKC controls calcium homeostasis and was identified in genome-wide studies to be associated with susceptibility and severity of KD. NLRP3 is activated by danger signals, leading to inflammasome activation and release of IL-1beta and IL-18. Ca^{2+} mobilization mediates NLRP3 activation. We studied the contribution of ITPKC and NLRP3 inflammasome activation in KD.

Methods: Cytokine levels were measured using ELISA. Gene expression was assayed using Illumina HumanHT-12v4. EBV-transformed B-cell lines from KD patients with different ITPKC genotypes were used to study the gene and protein expression and Ca^{2+} flux using qRT-PCR, Western blot analysis, and FACS respectively. In vivo and in vitro analyses from ITPKC-deficient and wildtype mice were performed using ELISA, spinning disc confocal and Westerns, to determine cytokine release, Ca^{2+} flux and protein expression responses.
Results: Children with KD show increased circulating IL-1beta, IL-18, IL-1RA and IL18BP protein during acute phase of KD (KD n=48, febrile controls n=41 p<0.001). NLRP3 and its associated inflammasome complex, and the IL-1[Unsupport Character - Symbol Font &#61538;] receptor genes were upregulated nearly two fold during the acute KD compared to matched convalescent controls (n=171, p<0.001). Pathway analysis showed specific up-regulation of NLRP3 related genes. The KD-associated genetic polymorphism in ITPKC (rs28493229) is functional, directly modulating [Ca2+]i mobilization resulting in NLRP3 activation and increased production of IL-1beta and IL-18, as demonstrated by gene expression, circulating protein levels and functional assays of PBMCs and immortalized cell lines from affected children. These biologic data are partnered with evidence showing resistance to IVIG therapy in those with the ITPKC polymorphism associated with the highest basal and stimulated [Ca 2+]i levels. Studies using ITPKC -deficient mice in an animal model of KD support the molecular, cellular and clinical findings in affected children. Significance: ITPKC regulates NLRP3 activation via control of [Ca2+]i, pointing to the key role of calcium mobilization in the immunopathogenesis of KD.


O.22
Analysis of The Mechanisms of Intravenous Immunoglobulin-resistant Kawasaki Disease Using iPS Cell Technology

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Introduction
Although the treatment of intravenous immunoglobulin (IVIG) significantly resolves inflammation, 10-20% of Kawasaki disease (KD) patients have persistent or recurrent fever after the administration of IVIG, and IVIG-resistant patients have a particularly high risk of developing coronary artery abnormalities. The mechanisms of IVIG-resistant KD have been analyzed using the patients’ leukocyte samples. However, vascular endothelial cells (ECs), closely related to the vasculitis of KD, have not been examined in the previous reports. We propose a hypothesis that ECs are mainly involved in the etiology of IVIG-resistance.

Methods
The purpose of this study is to establish new in vitro disease models of vasculitis using induced pluripotent stem cell (iPSC) technology, and clarify the mechanisms of IVIG-resistance in KD. Dermal fibroblasts or T cells from 2 IVIG-resistant and 2 IVIG-responsive KD patients were reprogrammed by episomal vectors encoding Oct3/4, Sox2, Klf4, L-Myc, LIN28, and p53 shRNA. The iPSC lines were then differentiated into ECs by using a previously-reported differentiation method, and the EC samples were subjected to the microarray analyses.

Results
The KD patient-derived iPSCs could be differentiated into ECs. The gene expression profiles were compared between iPSC-derived ECs (iPS-ECs) generated from IVIG-resistant and IVIG-responsive KD patients. We found the expression of chemokine X, which stimulates migration of monocytes and T-lymphocytes through its receptors, was significantly up-regulated in iPS-ECs from IVIG-resistant KD patients compared with those from IVIG-responsive patients. The Principle Component Analysis (PCA) was performed, but the gene expression levels showed no significant differences between the groups. The Gene Set Enrichment Analysis (GSEA) revealed that the gene sets related to IL-6, NRAS (a member of the RAS oncogene family) and breast cancer were up-regulated in iPS-ECs from IVIG-resistant KD patients compared with those from IVIG-responsive patients. The Principle Component Analysis (PCA) was performed, but the gene expression levels showed no significant differences between the groups. The Gene Set Enrichment Analysis (GSEA) revealed that the gene sets related to IL-6, NRAS (a member of the RAS oncogene family) and breast cancer were up-regulated in iPS-ECs from IVIG-resistant KD patients.

Conclusions
Taking into account that the concentration of IL-6 has been reported to be elevated in acute phase of IVIG-resistant KD, our results suggest...
that the up-regulation of IL-6 related genes in ECs might be involved in the pathogenesis of IVIG-resistant KD.


O.23
Lysyl Oxidase Expression In The Patients With Kawasaki Disease

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Background
Histologic study of inflamed coronary arteries from the Kawasaki disease (KD) patients shows infiltration by immune effector cells, IL-17-producing myofibroblasts, and breaks in the internal elastic lamina. Transcripts from genes associated with cell trafficking (e.g. paxillin) are elevated in whole blood from acute KD patients. Lysyl oxidase (LOX) is a multifunctional protein affecting monocyte and smooth muscle cell migration, elastogenesis, and endothelial-to-mesenchymal transition. LOX promotes cell motility through paxillin phosphorylation, which influences T-cell trafficking via the calcium signaling pathway. We investigated the role of LOX in the pathogenesis of KD.

Methods
Agilent microarray data using whole blood were analyzed for differential expression of enzymes in the LOX family (LOX, LOX-like (L)1-4) in acute and convalescent KD samples (n=19). LOXL1 results were validated using RT-PCR in an independent cohort (n=20). LOXL1 transcripts levels were measured in KD whole blood, peripheral blood mononuclear cells (PBMC), T-cell clones, B-cell lines, and myeloid dendritic cells from acute KD patients.

Immunohistochemical staining for LOXL1 was performed on coronary arteries from a KD patient who died on illness day 7.

Result
LOXL1 expression by microarray was 3.2-fold higher in acute than convalescent samples (p<0.001) and was validated in an independent cohort by RT-PCR (5.4-fold higher, p<0.001). LOXL1 transcripts levels were 2-35 times higher in PBMC compared to whole blood (n=8). KD T cell clones had higher LOXL1 transcript levels than B-cells and dendritic cells. Immunohistochemical staining showed LOXL1-expressing inflammatory cells and smooth muscle cells in the coronary artery walls.

Conclusion
LOXL1 may increase inflammation in acute KD by promoting the motility of infiltrating T cells and smooth muscle cells through focal adhesion formation. However, LOXL1 may also participate in arterial wall repair by crosslinking collagen and elastin. Statins inhibit focal adhesion formation and thus cell trafficking but not the crosslinking mediated by LOXL1. Studies of LOXL1 protein levels and paxillin phosphorylation in PBMC may further our understanding of their role in KD pathogenesis.


O.24
Gut Microflora Influences Pathology in the Kawasaki Disease Vasculitis Mouse Model

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Background: Kawasaki Disease (KD) is the leading cause of acquired heart disease in the US. We have demonstrated the critical role of innate immune responses via IL-1R/MyD88 signaling in the Lactobacillus casei cell wall extract (LCWE)-induced KD mouse model. The diversity and composition of microflora (both bacterial and fungal) have been associated with the regulation and alterations of immune responses and various pathologies. However, the role of gut microbiota in immunopathology of
KD has not been investigated.
Objective: To evaluate the role of gut microflora in development of coronary arteritis, and vascular abnormalities in KD mouse model.
Methods and Results: We investigated the role of gut microflora in the LCWE-induced KD mouse model, using Specific-Pathogen Free (SPF) and Germ Free (GF) mice (C57BL/6). GF mice showed a significant decrease of KD lesions, including coronary arteritis compared with SPF mice. The development of LCWE-induced AAA, which we recently discovered in this mouse model, was also markedly diminished in GF mice. In addition to GF mice, we also investigated the specific role of commensal fungi, and determined whether altered fungal burden in this KD mouse model contributes to disease severity. To deplete fungi in the gut microflora, we exposed pregnant SPF mice and their offspring to fluconazole (antifungal) in their drinking water for 5 wks and induced KD. The fluconazole treated mice had significantly reduced coronary arteritis, and AAA compared to controls. Since Dectin-1 has emerged as a key receptor that recognizes β-1,3-glucans found in the cell wall of nearly all fungi, we next induced KD in Dectin-1 deficient mice. Dectin-1 deficient mice also had significantly reduced KD lesions such as coronary arteritis compared with WT mice.
Conclusions: We demonstrate here that gut microflora play a critical role in the development of KD vasculitis in LCWE-induced mouse model. Our results suggest that fungi in the intestinal microbiota may specifically control the induction and severity of KD vasculitis, which may be mediated by Dectin-1. These findings provide a new perspective on the potential role of the microbiome in KD pathogenesis and may offer new diagnostic and therapeutic strategies for KD patients.


O.25 Identification Of Pathogenic Cardiac Cd11c+ Macrophages In Nod1-mediated Coronary Arteritis, A Murine Model Of Kawasaki Disease

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Kawasaki disease is characterized by granulomatous inflammation of coronary arteries. We previously reported that a synthetic Nod1 ligand FK565 induced coronary arteritis in mice similar to that of Kawasaki disease. However, the molecular mechanism underlying this site-specific vasculitis has remained elusive. We found that CD11c+ MHC class II+ cells were accumulated in heart of FK565-treated mice prior to arteritis development, which was abolished in Nod1-/- mice. In vivo depletion of mononuclear phagocytes or CD11c+ cells prevented the arteritis, whereas elimination of T cells, B cells, NK cells, and neutrophils did not alter the pathology. Morphological features and gene expression signature of the cardiac CD11c+ MHC class II+ cells suggested that this population was closely related to macrophages. Notably, various inflammatory cytokines, chemokines, lysosomes and MMPs were expressed in these cardiac CD11c+ macrophages, suggesting that this population contributed to tissue destruction. Next, we determined whether Nod1 in hematopoietic cells or non-hematopoietic cells were important for this arteritis. Bone marrow chimera mice using WT and Nod1-/- mice indicated that Nod1 in non-hematopoietic host cells, rather than in hematopoietic cells, was important for the accumulation of the cardiac CD11c+ macrophages and arteritis development. Among non-hematopoietic cells, cardiac endothelial cells abundantly produced chemokines in response to FK565. In this respect, CCR2-deficient mice exhibited decreased cardiac CD11c+ macrophages and compromised inflammation. These results suggested that Nod1 activation in endothelial cells triggers accumulation of cardiac CD11c+ macrophages, which is a prerequisite for the development of coronary arteritis.

Model of Kawasaki Disease. -Effectiveness of IVIG versus Losartan-

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Background: Although intravenous immunoglobulin (IVIG) is an established treatment for Kawasaki disease (KD), 5% of KD patients treated with IVIG still have coronary involvement. Angiotensin receptor blockers (ARBs), beside their antihypertensive effects, also suppress cell infiltration in atherosclerosis. However, the efficacy of ARB for KD has not been established.

Objective: We aimed to elucidate if ARB ameliorates coronary arteritis (CA) in a murine model of KD, introduced by Lactobacillus casei wall extract (LCWE). We also aimed to verify whether ARB’s effects are different from those of IVIG.

Method: 4-week-old male mice were intraperitoneally injected with LCWE (L, n=15) or PBS (P, n=15). 5 days later, those mice were given IVIG (1g/kg, L+IVIG, n=8), or ARB (losartan 100mg/L in drinking water for 2 wks, L+ARB, n=18). 2 weeks after LCWE injection, histological assessment of the heart and measurement of plasma cytokine levels were performed. IL-6 and mannose receptor (MR) mRNA expressions in the aortic root were studied (n=5 each group) in an additional experiment.

Results: CA score was significantly increased by LCWE (L: 8.3±0.5 vs. P: 2.9±0.5, p<0.0001). ARB significantly ameliorated CA (L+ARB: 5.1±0.7 vs. L, p=0.008). The effect of IVIG on CA was milder and not significant (L+IVIG: 6.0±0.9 vs. L). Of note, macrophage infiltration was dramatically decreased by ARB but not by IVIG. IVIG treatment ameliorated serum levels of IL-1β, IL-10 and TNF-α in a milder fashion than ARB. Interestingly, serum IL-6 level was suppressed by ARB, but not by IVIG. Locally upregulated mRNAs of IL-6 and MR were significantly ameliorated by ARB, with milder effects by IVIG.

Conclusions: ARB, rather than IVIG, exerts powerful anti-CA effects with suppressing local macrophage infiltration and systemic/local inflammatory cytokines. Thus, ARB potentially exerts additive anti-CA effects in KD under IVIG treatment.

E. Suganuma: None.

O.27
The Role Of CD40L And CD40 In The Pathogenesis Of Kawasaki Disease

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Kawasaki Disease (KD) is characterized by acute, systemic inflammation followed by a persistent immune response localized to the coronary arteries. Lactobacillus Casei Cell Wall Extract (LCWE) contains among its active ingredients a superantigen (SAg) that induces coronary arteritis in mice. LCWE induces massive immune activation followed by apoptosis or anergy. Previous work has shown that co-stimulatory signals can rescue a subset of SAg-reactive T-cells from apoptosis. CD40-CD40L (ligand) are members of the TNF superfamily which play a role in T-cell co-stimulation. Moreover, genome wide association studies have implicated CD40/CD40L as candidate genes in the pathogenesis of KD. We hypothesize that co-stimulation via the CD40 pathway regulates survival of SAg-reactive T-cells during disease development. Using thymidine proliferation assay and flow cytometry we show that activation of CD40 signaling via agonistic anti-CD40 antibody or recombinant soluble CD40L (rsCD40L) upregulates CD86 (ligand responsible for CD28 signaling) expression, reduces active-caspase-3 expression, indicating decreased cell death and promotes lymphocyte proliferation. Additionally, using CD28 deficient mice we show that lymphocytes do not proliferate in response to SAg plus CD40 stimulation indicating that CD28 is the intermediary that mediates the proliferative effects of CD40 activation. Furthermore, platelets, which are markedly elevated in KD, produce approximately 90% of the soluble CD40L in the circulation. We show that activated platelets (CD62P+) express CD40L and promotes cell survival as evidenced by enhanced lymphocyte proliferation. Likewise, the absence of CD40L negates the proliferative effects of platelet mediated proliferation. Lastly, to determine the role of CD40 stimulation on in vivo development of KD, LCWE was injected into B6 and CD40L deficient mice. We show that inflammation in the coronary arteries does not develop in the absence of CD40L. Therefore, CD40L plays a critical role in immune activation
via upregulation of CD86 on antigen presenting cells leading to enhanced co-stimulation and T-cell survival.


O.28 Macrophage Activation Syndrome Associated with Kawasaki Disease

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Introduction: Macrophage activation syndrome (MAS) is a life threatening disease that is increasingly recognized in children with inflammatory conditions including Kawasaki disease (KD). We describe the prevalence, clinical features and outcomes of patients with MAS secondary to KD.

Methods: All patients diagnosed and treated for KD at The Hospital for Sick Children between 2001 and 2013 were included and reviewed for features of MAS. A diagnosis of MAS required 4 out of the following clinical findings: fever, hepatosplenomegaly, cytopenia in at least 2 cell lines, hyperferritinemia, hypofibrinogenemia and/or hypertriglyceridemia, and presence of biopsy-proven hemophagocytosis.

Results: Of 1,020 patients included in this study, 21 met MAS diagnostic criteria for an incidence of 2.1% (95% CI: 1.4-3.1%). All patients had fever, 9 (43%) hepatosplenomegaly, 10 (47%) hypofibrinogenemia and/or hypertriglyceridemia, 19 (90%) hyperferritinemia, 19 (90%) cytopenia, and 7 (33%) biopsy-confirmed hemophagocytosis. MAS was associated with: older age at KD diagnosis (median 5.7 vs. 3.0 years, p=0.06), longer fever duration prior to diagnosis (median 10 vs. 6 days, p=0.01), and higher incidence of incomplete KD (57% vs. 32%, p=0.04) and confirmed infection during acute phase (48% vs. 19%, p=0.02). Treatment included multiple IVIGs for 12 patients (57%), methylprednisolone for 15 (71%), oral prednisone for 13 (62%) and cyclosporine for 2 (10%). Median total duration of fever was 13 days (vs. 7 days, p=0.001), duration of fever after first IVIG treatment was 4 days, and median duration of hospital stay was 6 days (vs. 3 days, p=0.01). 5 patients received pRBC transfusions, 3 required ICU care, 1 had severe CNS involvement, and 1 developed multisystem organ failure dying 28 days after admission. Mild transient coronary dilatation was seen in 3 patients.

Conclusions: The clinical presentation of KD and MAS are quite similar. Both entities are syndrome complexes defined by massive immune activation and share pro-inflammatory cytokine signatures. MAS is a rare but important complication with KD. Further research is needed to optimize diagnosis and management.


O.29 Transcriptional Profiling Discriminates Complete and Incomplete KD from Human Adenovirus

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Background: The diagnosis of Kawasaki disease (KD) is often difficult to distinguish from HAdV. Objective: 1) To characterize the specific transcriptional profiles of KD patients versus acute HAdV infection 2) To determine whether the molecular distance to health (MDTH) score (a molecular score that reflects the perturbation derived from whole genome transcriptional analysis) correlates with response to therapy.

Methods: Whole blood RNA samples collected in Tempus tubes were analyzed using Illumina chips and GeneSpring software 7.4 from 76 pediatric patients with complete KD, 13 with incomplete KD, and 19 patients with HadV, and 20 age- and sex-matched healthy controls (HC). We used class comparison algorithms (Mann-Whitney p< 0.01, Benjamini-Hochberg, and 1.25- fold change filter) and modular analysis to define the KD profiles; class prediction algorithm was used to identify genes that best differentiate KD and HAdV. Results: Statistical group comparisons identified 7,899 genes differentially expressed in 39 complete KD patients versus HC (KD biosignature). This signature was validated in another 37 patients with complete KD and in 13 patients with incomplete KD. Modular analysis in children with complete KD demonstrated overexpression of inflammation, neutrophils, myeloid cell, coagulation cascade, and cell cycle genes. The class prediction
algorithm identified 25-classifier genes that differentiated children with KD vs HAdV infection in two independent cohorts of patients with 92% (95% CI [73%-99%]) sensitivity and 90% [67%-98%] specificity. MDTH scores in KD patients significantly correlated with the baseline c-reactive protein (R=0.29, p=0.008) and was four fold higher than in children with HAdV (p<0.01). In addition, KD patients that remained febrile 36 hours after treatment with IVIG (non-responders) demonstrated higher baseline, pre-treatment MDTH values compared with responders [12,290 vs. 5572 respectively; p=0.009].

**Conclusion:** Transcriptional signatures can be used as a tool to discriminate between KD and HAdV infection, and may also provide prognostic information.


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O.30
**Novel Biomarker for Early Diagnosis of Kawasaki Diseases**

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Kawasaki disease (KD) is the most common cause of acquired heart disease in young children and has been suggested to be an immune-mediated condition, which was supported by our previous findings that FCGR2A, BLK, and CD40 are KD susceptibility genes. However, diagnosing KD can be difficult especially at early stage of the disease because of its varied clinical manifestations and lack of specific laboratory tests. The aim of the present study was to identify biomarkers that may aid in the early diagnosis of KD. We conducted a three-phase study: discovery, replication, and blinded validation. The 214 children with fever and clinical features suggestive of KD were recruited in Taiwan from separate geographic medical centers. By using an unbiased, large-scale, quantitative protein array, we globally analyzed the profiles of cytokines, chemokines, and cell adhesion molecules in their plasma samples. During the discovery phase [n (KD) = 37, n (control) = 20], the expression of one cell adhesion molecules, two chemokines, and three cytokines (Th-17-related), (named gene-1~6) were upregulated during the acute phase in KD patients compared to that in the controls. Receiver-operating characteristic analysis of the combined discovery and replication data [n (KD) = 77, n (control) = 77] showed that the level of gene-3 had high area under the curve values (AUC, 0.94). Using the optimal cut-off value to predict KD, the sensitivity and specificity of the gene-3 was found to be 90% and 87%, respectively. Blinded validation study also confirmed the excellent discrimination of gene-3 in identifying KD cases from non-KD cases among subjects who were highly suspected KD cases, including incomplete KD or febrile cases with scarlet fever, even in the very early stage (<4 days). With intravenous immunoglobulin treatment, levels of gene-3 returned to normal. Furthermore, we also found the downstream receptor of gene-3 was activated in the T cells of acute KD patients. Taken together, the newly identified biomarker, gene-3, may be useful in diagnosing KD and monitoring patients’ treatment responses. The selective increase of gene-3 in KD also reveals that a novel unique signal pathway involved in KD, which may provide a critical clue for further investigating the pathogenesis of KD.


O.31
**Tenascin-C can be a Novel Prognostic Biomarker For Kawasaki Disease**

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Tenascin-C (TNC) is an extracellular matrix glycoprotein sparsely detected in normal but highly expressed in pathological condition associated with inflammation in variety of tissues. By taking advantage of its specific expression, TNC is applicable as a biomarker and a molecular imaging target for diagnosis of disease activity for ventricular remodeling. In blood vessels, the expression of TNC in normal is generally low but strong expression is linked with several pathological conditions such as pulmonary artery hypertension, coronary atherosclerotic intima, and aortic aneurysm/dissection. We hypothesized that TNC could be useful for evaluating disease activity of Kawasaki Disease (KD). We measured serum level of TNC of 174 patients with KD using ELSA and found that the TNC level was significantly higher than that of the controls, and the initial treatment with intravenous immunoglobulin decreased the level. Combination of serum TNC and Kobayashi score increased the accuracy to identify cases at a high risk of unresponsiveness to high-dose intravenous immunoglobulin. Immunohistochemical analysis of autopsied cases showed that TNC was strongly expressed in coronary vascular lesion at acute stage of KD patients as well as in the Candida albicans-induced murine model of vasculitis/aneurysm. Biomechanical analysis demonstrated that vascular flexibility was reduced in TNC knockout mice. A combination of inflammation and mechanical stress to aorta induced dissecting aneurysm in TNC knockout mice. In vitro, TNC enhanced macrophage migration and cytokine synthesis, meanwhile TNC synthesis was up-regulated by various pro-inflammatory cytokines. These results suggest that TNC is expressed in vascular lesion of KD reflecting active inflammation, which has diverse functions to modulate not only inflammatory response but also regulate vascular remodeling and aneurysm formation. TNC could be a key molecule in pathophysiology and a promising biomarker of KD.


O.32
An Improved Point-of-care Differentiation Of Kawasaki Disease From Other Febrile Illnesses

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Background - Kawasaki disease (KD) shares many clinical features with other pediatric febrile illnesses (FC). Clinical confusion can lead to a missed or delayed diagnosis that increases the risk of coronary artery damage. In the present study, we improved our previous KD diagnostic algorithm for point-of-care diagnosis.

Methods and Results - We reviewed clinical records of 534 acute KD and 318 FC patients (development dataset) and subsequent 268 acute KD and 161 FC patients (validation dataset). KD subjects met the American Heart Association definition. Using clinical data and lab test results, we integrated our previously developed linear discriminant analysis (LDA)-based clinical model with a newly developed decision tree-based algorithm to improve KD diagnosis. To train the decision trees, subcohorts were constructed based upon the 5 KD classic criteria. Our 1st clinical model (LDA) stratified the subjects into FC (FC diagnosis, negative predictive value NPV >=95%), undecided (88/802 KD, 167/479 FC), and KD (KD diagnosis, positive predictive value PPV >=95%) subgroups. The subsequent 2nd clinical model (decision trees) further classified the undecided group into FC, undecided, and KD subgroups, resulting in a much-improved algorithm with only 59/479 FC (Specificity>76%) and 26/802 KD (Sensitivity>95%) undetermined.

Conclusions - Our computer-based algorithm that incorporates only clinical findings and readily available clinical laboratory data now has sufficient sensitivity and specificity in distinguishing acute KD from FC patients that a multicenter, prospective clinical trial is warranted to test the performance of the diagnostic algorithm against the gold standard of expert clinical opinion.

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O.33
Identification of Kawasaki Disease-specific Molecules in the Sera as Microbe-associated Molecular Patterns
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Background: Kawasaki disease (KD) is a systemic vasculitis of unknown etiology. The innate immune system is involved in its pathophysiology at the acute phase. We have recently established a novel murine model of KD coronary arteritis by oral administration of a synthetic microbe-associated molecular pattern (MAMP). On the hypothesis that specific MAMPs exist in KD sera, we have searched them to identify KD-specific molecules and to assess the pathogenesis.

Methods: The study subjects included 117 patients with KD (median age, 21 months; range 3-96 months; male/female, 65/52) and 101 controls with other febrile illnesses (DC: median age, 16 months; range 0-121 months; male/female, 61/40), and 5 normal controls (NC: median age, 6 months; range 3-39 months; male/female, 1/4). We performed liquid chromatography-mass spectrometry (LC-MS) analysis of fractionated serum and microbial samples by ethyl acetate.

Results: KD serum samples elicited proinflammatory cytokine responses from human coronary artery endothelial cells (HCAECs). By LC-MS analysis of KD serum samples collected at 3 different periods, we detected a variety of KD-specific molecules in the lipophilic fractions that showed distinct m/z and MS/MS fragmentation patterns in each cluster. Serum KD-specific molecules showed m/z and MS/MS fragmentation patterns almost identical to those of MAMPs obtained from Bacillus cereus, Yersinia pseudotuberculosis and Staphylococcus aureus at the 1st study period, and from MAMPs from Bacillus cereus, Bacillus subtilis/Bacillus cereus/Yersinia pseudotuberculosis and Staphylococcus aureus at the 2nd and 3rd periods. These molecules decreased after intravenous immunoglobulin (IVIG) treatment.

Conclusions: We herein conclude that serum KD-specific molecules possess molecular structures common to MAMPs from Bacillus cereus, Bacillus subtilis, Yersinia pseudotuberculosis and Staphylococcus aureus. Discovery of these KD-specific molecules offers novel insight into the diagnosis and management of KD as well as its pathogenesis.


O.34

NT-proBNP based Algorithm for Diagnosis and Treatment of Kawasaki Disease - Are we there yet?

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Background Diagnosis of Kawasaki Disease (KD) can be confusing in the absence of a confirmatory test or pathognomonic finding, especially when clinical criteria are incomplete (iKD). We have lately proposed serum NT-proBNP as an adjunctive diagnostic test.

Method We retrospectively tested a new diagnostic algorithm to aid in diagnosis based on NT-proBNP (Z-score for age), coronary artery dilation (CAD) at onset, and abnormal serum albumin or CRP. The goal was to assess the performance of the algorithm with respect to CAD outcome (aneurysm, dilation, or occult dilation). Occult dilation is defined as variation of coronary artery Z-score >2 within the normal range (<2.5).

Results The algorithm was tested on 81 KD patients who had NT-proBNP on admission at our institution between 2008 and 2013. Age at diagnosis was 3.2 ± 2.6 years, with a median of 5 diagnostic criteria (range 3-6), of whom 31/81 (38.3%) had iKD. Aneurysms occurred in 16/81 (19.8%); higher prevalence in iKD, 12/31 (38.7%) versus 4/50 (8.0%) (p=0.001). CAD affected 35/81 (43.2%), and 30/81 (37.0%) had occult CAD. With the algorithm, 80/81 (98.8%) were to be treated: based on high NT-proBNP alone for 54/81 (66.7%), on onset CAD for 13/81 (16.0%), and on high CRP or low albumin for 13/81 (16.0%). (Figure 1) Results were similar when the algorithm was applied to patients with complete or incomplete criteria. The only patient “not-to-treat” with the algorithm had iKD and transient occult CAD.

Conclusion This NT-proBNP based algorithm is efficient to identify and treat patients at risk of coronary involvement, despite an apparent
selection bias of CA involvement. This paves the way for a prospective validation trial of the algorithm.

A. Dionne: None. L. Meloche-dumas: None. A. Fournier: None. N. Dahdah: None.

O.35
BCGitis as a Clinical Diagnosis Marker in Mexican Children with Kawasaki Disease

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Background. Kawasaki disease (KD) is an acute febrile illness characterized by systemic vasculitis of unknown etiology. A BCG reactivation (BCGitis) is not included in the classical clinical criteria for KD. BCGitis recently has been recognized as a clinical marker of incomplete KS in younger children in countries where BCG vaccination is mandatory. Objectives. To assess the frequency of BCGitis in the clinical profile of patients diagnosed with KD in a Mexican third level Children’s Hospital and its association with the presence of coronary artery abnormalities. (CAA) Material and Methods. An observational, comparative, retrospective and case control study of all patients diagnosed with KD at our Institution between August 1995 and May 2014 was performed. The clinical presentation, laboratory results, treatment used and coronary artery abnormalities in the BCG-reactive [BCG(+) ] and BCG-nonreactive [BCG(-)] groups were analyzed and compared. Results, We included 356 patients with KD diagnosed at our institution; 83 had BCGitis. (23.3%) The BCG(+) group was younger than the BCG(-) group, 21.2 ± 22.51 vs 44.33 ± 38.85 months (p < 0.00001). There were 17 (20.48%) incomplete cases in the BCG(+) group compared with 52 (19.11%) in the BCG(-) group without statistical significance. The BCG(+) group had a slightly shorter fever duration before IVGG treatment than the BCG(-) group. Laboratory results showed lower hemoglobin counts, higher white blood cell counts, platelet counts, CRP counts, and ALT counts in the BCG(+) group. The BCG(+) group developed CAA in 29 cases and the BCG(-) group developed CAA in 110 cases without statistical significance. Multivariate analysis showed that younger age at diagnosis (< 24 months) was the only factor significantly associated with a reaction at the BCG inoculation site in KD patients Conclusions: In Mexico, as a country with a National BCG Vaccination Program and a low incidence of KD, a reaction at the BCG inoculation site could be a useful and early diagnostic sign of KD among younger patients, especially those younger than 24 months of age.


O.36
Kawasaki Disease and Systemic Juvenile Idiopathic Arthritis - Two Ends of the Same Spectrum

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Background: Clinical similarities between Kawasaki disease (KD) and systemic Juvenile Idiopathic Arthritis (sJIA) are well known. We critically reviewed children with KD and sJIA to identify those with both diagnoses in order to characterize discriminating findings at baseline. Methods: Data from prospectively acquired KD (n=1765) and sJIA (n=112) cohorts were reviewed for common patients (1990-2011).
Those with both diagnoses (KD/sJIA n=8) were reviewed for clinical presentation, laboratory investigations, treatment regimens, coronary artery outcome and complications including macrophage activation syndrome, and results were compared to the overall KD cohort.

Results: All children with KD/sJIA fulfilled diagnostic criteria for KD and sJIA (ILAR classification). Co-diagnosis was present in 0.45% (8 of 1765) and 7.1% (8 of 112) of those with KD and sJIA, respectively. Time between diagnosis of KD and presumptive diagnosis of sJIA was a median of 24 days (IQR 21-45 days). KD/sJIA patients had bilateral conjunctival injection less frequently, lower hepatic transaminases together with signs of more intense inflammation as expressed a by higher white blood cell count and lower albumin than the KD cohort alone. All KD/sJIA patients had recalcitrant disease consisting of prolonged fever requiring multiple doses of intravenous immunoglobulin and steroids. Coronary artery abnormalities (CAAs) were observed in 5 KD/sJIA patients. Macrophage activation syndrome occurred in one KD/sJIA patient and in 0.9% and 8% of KD patients and sJIA patients respectively.

Conclusions: A small portion of our patients with KD developed subsequent sJIA. KD/sJIA patients were characterized by more intense inflammation at initial presentation, a recalcitrant disease course and a high prevalence of CAAs. These patients may provide clues to potentially shared immunopathology. The clinical presentations of MAS, KD and sJIA are quite similar with fever, rash, hepatomegaly, and lymphadenopathy. All 3 entities are syndrome complexes defined by massive immune activation. We propose that the intensity and duration of the immune response may be the key distinguishing features, which dictate which one of these clinical syndromes the affected child presents with.

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Background: Coronary artery dilatations are almost always secondary to Kawasaki disease in the pediatric population. The presence of CA involvement is used as a criterion to diagnose incomplete KD disease, which may be challenging. It has been recently demonstrated that febrile patients had larger CA size than non-febrile children in a pilot study. As there is almost always a myocarditis in the acute phase of KD disease we sought to investigate whether viral myocarditis may cause CA dilatations.

Method: This retrospective study reviewed 14 consecutive patients with a diagnosis of viral myocarditis at Saint-Justine Hospital, Montreal, from April 2000 through December 2010. Kawasaki disease was excluded in all patients. All echocardiogram studies were reviewed by an independent experienced technician for CA size and function parameters. Patients were classified in three categories: definite CA dilatation (Z-score ≥ 2.5 in one or more CA), occult CA dilatation (Z score variation ≥ 2 for the same CA on 2 different echocardiograms, but absolute Z score always < 2.5) and normal coronary artery. Demographics, laboratory values, microbial etiology testing, diagnostic studies were also collected.

Results: Mean age at presentation was 1.67 ± 3.22 years, the majority < 2 years old, and 11 (78%) were girls. Of the 14 patients 8 (57.1%) had normal CA, 3 (21.4%) had occult CA dilatation and 3 (21.4%) had definite CA dilatation. When present, CA dilatation was detected within the first 8 days of presentation. Eleven (78%) patients presented with acute onset features and the remaining 3 presented with subacute characteristics. There was no correlation between CA involvement and the intensity of LV dysfunction however (p = 0.84).

Conclusion: Patients with viral myocarditis can present CA dilatation during the acute phase of the illness. This finding should be taken into account when diagnosing patients with incomplete KD on the basis of the CA involvement as the two illnesses may present with similar features.

O.37
Coronary Artery Dilatation in Viral Myocarditis Mimics Coronary Artery Findings In Kawasaki Disease
O.38 Fever Patterns in KD Patients after Treatment with IVIG

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Objective: To determine if fever patterns in the first 36 hours after completion of intravenous immunoglobulin (IVIG) for Kawasaki disease (KD), with or without additional infliximab, can predict eventual resistance to treatment and coronary artery abnormalities (CAA).

Study design: Subjects with acute KD enrolled in a clinical trial of infliximab plus IVIG (n=96) versus placebo plus IVIG (n=94) had temperatures taken axillary and either oral or rectal every 6 hours after completion of IVIG infusion. Fever was defined as any temperature >38.0°C and resistance to treatment was defined as persistent or recrudescent fever ≥36 hours after completion of IVIG. CAA was defined as a Z-score >2.5 based on the maximum internal diameters of the proximal right coronary or left anterior descending artery. Multivariable logistic regression was performed to predict two outcomes (resistance to treatment and development of CAA) by the variables of presence of fever at 0-12, 12-24, and 24-36 hours post-IVIG. All analyses were controlled for treatment, age, and sex.

Results: After completion of IVIG, 131 subjects (68.9%) had no fever. There was no difference in the median time to defervescence between the infliximab + IVIG group (n=96) versus the IVIG alone group (n=94). Subjects who had at least one fever at 24-36 hours post-IVIG had a higher probability of having a fever at least 36 hours post-IVIG (p<0.0001, odds ratio=30.6 [95%CI 6.7-139.8]), although 11% of those who eventually responded to treatment also had fever between 24-36 hours post-completion of IVIG. Subjects who had at least one fever within the first 12 hours post-IVIG had a higher likelihood of having CAA (odds ratio=3.782, p=0.037). Of those with CAA (n=51), 43 (84%) had abnormalities on the initial baseline echocardiogram.

Conclusion: Fevers in the first 12 hours after completion of IVIG are associated with CAA, which can be demonstrated on the initial echocardiogram in the majority of CAA+ subjects. Fever 24-36 hours after IVIG completion is associated with subsequent resistance to treatment, but also occurred in 11% of responders. Our data suggest that patterns of fever can be useful as prognostic indicators of disease outcome in KD patients.

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O.39 The Incidence Of Abnormal Electroencephalographic Findings And Mild Encephalitis/encephalopathy With A Reversible Splenial Lesion In Kawasaki Disease

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Background: Central nervous system inflammation sometimes occurs in Kawasaki disease (KD). In 2012, we reported the first case of KD complicated with mild encephalitis/encephalopathy with a reversible splenial lesion (MERS) in a 14-year-old. Since then, similar cases have been reported. We studied the incidence of KD complicated with encephalitis/encephalopathy and MERS.

Methods: We selected 36 patients (22 boys and 14 girls; age: range, 5-80 months; mean, 22 months) from 42 patients who had undergone electroencephalography (EEG) before intravenous immunoglobulin (IVIG) therapy between May 2013 and August 2014. Patients with and without abnormal EEG findings were assigned to groups A and B, respectively. Age; sex; time of diagnosis; neurological symptoms; N-terminal pro-brain natriuretic peptide, serum procalcitonin, serum sodium, serum albumin, and C-reactive protein (CRP) levels; liver disorder, coronary artery lesion, and IVIG therapy response were examined. Results: Group A comprised 6 patients (17%); and group B, 30 patients (83%). Consciousness disturbance was noted in 5 of 6 patients with abnormal EEG findings, without sequelae. Patients in group A were significantly older (56.5±16.8 vs 25.0±19.9 months ) and had
higher CRP levels than those in group B (12.3±5.62 vs 6.56±3.47 mg/dL). No other parameters showed significant differences. Magnetic resonance imaging revealed edema in 2 of 5 patients and MERS in the remaining patient in group A. Pleocytosis was noted in 1 of 4 patients in group A. Cytokine II-6 and INF-γ levels were very high in the patient with MERS.

Conclusion: EEG findings indicating central nerve disorders were noted in 17% patients, a lower incidence than that reported by Mitudome et al. We performed EEG early before IVIG therapy; thus, central nerve symptoms encountered may have occurred in the early stages of the disorders. MERS was noted in 1 of 6 patients with abnormal EEG findings, or 2 of 9 patients if past cases with neurological symptoms were included, suggesting that central nerve complications occur in a certain group of KD patients.

N. Nakagawa: None. M. Kamada: None. Y. Ishiguchi: None. Y. Moritoh: None. K. Okamoto: None.

O.40 Persistent Subacute/Chronic Coronary Arteritis in Kawasaki Disease (KD): Histologic, RNA and Protein Evidence


Introduction: We identified 3 linked KD vasculopathic processes: acute self-limiting necrotizing arteritis, subacute/chronic (SA/C) arteritis and luminal myofibroblastic proliferation, most critically affecting the coronary arteries (CA). SA/C arteritis (lymphocytes, eosinophils, plasma cells) was not previously recognized, and patients with persistent coronary artery aneurysms do not currently receive immunomodulatory therapy after the initial febrile illness.

Hypotheses: SA/C arteritis in KD CA is a process of dysregulated innate and adaptive immune responses, and markers of inflammation can be detected in the sera of KD patients with persistently inflamed CAs.

Methods: RNA was isolated from paraffin-embedded CA tissues, and real-time RT-PCR arrays performed on samples passing quality control assays. RNA from KD CA with persistent subacute/chronic arteritis (n=7, 5 mo-several yrs after onset, median age=3 yr) and from CA of childhood controls (n=7, median age=10 mo) was assayed, and dysregulated genes determined (>1.5 fold change and q value <0.05). To identify if dysregulated immune markers were detected in sera of KD children with persistent CA aneurysms, ELISA cytokine array for 400 proteins was performed on sera from 4 KD patients with persistently abnormal CA echocardiograms who were otherwise asymptomatic (3-5 yrs after onset, median age 5 yrs) and 4 age/gender matched healthy childhood controls (median age 5 yrs).

Results: Ten interferon response genes and 9 Th1/Th2 response genes were upregulated in chronic KD arteritis tissues. ELISA revealed ~40 proteins with at least tenfold dysregulation in sera of KD children with persisting aneurysms compared to matched controls (q-values=0.07), while serum C-reactive protein levels were not different in the 2 groups.

Conclusions: Evidence of dysregulated immune responses can be detected in KD CA tissues months to years after onset in patients with persistent CA disease. In addition, we identified many candidate immune biomarkers of chronic KD arteritis. An immune biomarker panel would be useful to identify and monitor patients with persistent coronary arteritis in potential future clinical trials of immunomodulatory therapies for such patients.


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O.41
Assessment of Kawasaki Disease Risk Scores for Predicting Coronary Artery Aneurysms at a North American Center

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Aim: To assess the performance of established Japanese risk scores (RS) to identify patients (pts) with Kawasaki disease (KD) at high-risk for developing coronary artery aneurysms (CAA).

Methods: We reviewed clinical, laboratory and echocardiographic (echo) data for pts with KD treated with IVIG from 1/2006 to 5/2014. We defined CAA as z score $\geq 2.5$ in the right coronary artery (RCA) or left anterior descending artery (LAD) at 4-8 weeks of illness. Relationships with Kobayashi, Sano, Egami and Harada RS and CAA were examined. The maximum z score of LAD or RCA (zMax) at baseline was a covariate in logistic regression. The discrimination of each model was assessed using the c statistic.

Results: Of 268 pts with complete data, 173 (65%) were male and median age was 3.1 y (range 0.1-14.1 y). At diagnosis, 74 (28%) had $\leq 3$ classical criteria for KD, and 70 pts (26%) received IVIG retreatment. On baseline echo, 75 pts (27%) had a zMax $\geq 2.0$. CAA occurred in 15 pts (5.6%). The Harada RS predicted development of CAA (low risk = 0% (0/80), high risk=9% (12/140), $p=0.005$), but the Kobayashi, Sano, and Egami RS were not associated with CAA. CAA were associated with baseline zMax $\geq 2.0$ vs. $<2.0$ (12 [16%] vs. 3 [2%], respectively, $p<0.001$) and as a covariate in logistic regression (Table 1).

Conclusions: With the exception of the Harada score, established RS were ineffective at predicting the development of CAA at a cosmopolitan center. Baseline z scores were highly associated with CAA. However, adding baseline z scores to a logistic regression model did not improve discrimination of the RS.

<table>
<thead>
<tr>
<th>Risk Score</th>
<th>Odds Ratio (95% Confidence interval)</th>
<th>p value</th>
<th>c statistic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kobayashi High Risk ($\geq 4$)</td>
<td>0.3 (0.1, 1.6)</td>
<td>0.18</td>
<td>0.84</td>
</tr>
<tr>
<td>Maximum Z at Baseline Echo $\geq 2.0$</td>
<td>17.3 (7.7, 81.0)</td>
<td>$&lt;0.001$</td>
<td>0.77</td>
</tr>
<tr>
<td>Egami High Risk ($\geq 3$)</td>
<td>0.5 (0.1, 3.6)</td>
<td>0.43</td>
<td>0.79</td>
</tr>
<tr>
<td>Maximum Z at Baseline Echo $\geq 2.0$</td>
<td>11.4 (3.1, 42.6)</td>
<td>$&lt;0.001$</td>
<td>0.76</td>
</tr>
<tr>
<td>Sano High Risk ($\geq 2$)</td>
<td>1.9 (0.5, 7.9)</td>
<td>0.38</td>
<td>0.76</td>
</tr>
<tr>
<td>Maximum Z at Baseline Echo $\geq 2.0$</td>
<td>9.9 (2.6, 37.5)</td>
<td>$&lt;0.001$</td>
<td>0.76</td>
</tr>
<tr>
<td>Harada High Risk ($\geq 4$)</td>
<td>Ne aneurysms in low risk subgroup</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


O.42
Efficacy And Safety Of Treatment With Immunoglobulin Plus Steroid For Kawasaki Disease: A Prospective Observational Study

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[Background] Non-responders to primary intravenous immunoglobulin (IVIG) therapy with aspirin are at risk of coronary artery lesions in Kawasaki disease (KD). A randomized controlled trial (the RAISE study) indicated that prednisolone + primary IVIG improves responsiveness to treatment and coronary artery outcomes in non-responders to IVIG predicted on the basis of Kobayashi score. The present study aimed to verify the efficacy and safety of prednisolone + primary IVIG in predicted non-responders to IVIG. [Methods] We conducted a multicenter, prospective cohort study at 30 hospitals in Japan from July 2012. All KD patients received primary IVIG therapy (2 g/kg/24 h) and, if febrile at diagnosis, oral aspirin (30 mg/kg/day) and were stratified by Kobayashi
score into non-responders (score ≥5) and responders (score ≤4). The required sample size to reach statistical significance was 1,500 for KD patients and 500 for non-responders. [Results] We enrolled 868 patients with KD by the end of 2013, including 545 (63%) predicted responders and 323 (37%) predicted non-responders. Within the non-responder group, 256 patients received IVIG + prednisolone and 67 patients IVIG alone. The non-response rate to IVIG was significantly lower (17% vs. 55%, p<0.001) and the incidence of coronary artery lesions (Japanese criteria; 5% vs. 11%, p=0.06) non-significantly lower in the IVIG + prednisolone group than the IVIG alone group. These results are similar to those of the RAISE study (non-response rate of 13% and coronary artery lesion rate in non-responders of 3%). There were 10 severe adverse events (i.e., aseptic meningitis 2, liver dysfunction 2, anaphylaxis 1, hypertension 1, ventricular tachycardia 1, bacteremia 1, drug eruption 1, and gait disorder 1) and no significant between-group difference in event rate. [Conclusion] Like the RAISE study, our study suggests that prednisolone added to IVIG therapy with oral aspirin reduces the non-response rate and incidence of coronary artery lesions in predicted non-responders to IVIG with KD.


O.43 Partial and Complete Non-response to Intravenous Immunoglobulin in the Acute Treatment of Kawasaki Disease: A Matched Case-control Study

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Introduction: Patients non-responsive to intravenous immunoglobulin (IVIG) in the acute phase of Kawasaki disease (KD) are usually considered a single patient group; however, response to second-line therapy varies significantly. We sought to characterize the pattern of temperature response to IVIG infusion, and to define whether the profile was associated with response to second-line therapy in non-responders.

Methods: Patients non-responsive to IVIG (temperature >37.5°C >24 hours after the end of IVIG) were identified. Each IVIG non-responder was matched to a IVIG-responsive control patient of the same age and gender, and with the same duration of fever prior to IVIG. Hourly temperature profiles were obtained from immediately before the start of the IVIG infusion until complete defervescence.

Results: n=202 patients non-responsive to IVIG were matched (total n=404). For all, temperature reduced by 0.17 (0.06)°C per g/hr IVIG (p=0.006). Important variation in the temperature profile was noted for patients who did not defervesce with IVIG. Thus, non-responders were further classified as partial non-responders (31%) (temperature decreased to <37.5°C within 24 hours of the end of IVG infusion, but fever recurred) and complete non-responders (69%) (temperature consistently >37.5°C throughout IVIG treatment). The temperature profile during IVIG infusion was similar between complete and partial responders ([EST: -0.26 (0.11)°C per g/hr IVIG (p=0.02) for complete responders vs. EST: -0.20 (0.09)°C (p=0.02) for IVIG responders (responders vs. partial non-responders, p=0.65)]. In complete non-responders, IVIG was not associated with significant decreases in temperature (EST: -0.11 (0.14)°C, p=0.43). Factors associated with complete (vs. partial) non-response included presence of infectious symptoms, differences in multiple laboratory values and IVIG brand. Defervescence in partial non-responders was achieved with a second IVIG dose for 88% of patients compared to only 47% of complete non-responder (p=0.001).

Conclusions: Non-response to initial IVIG can be further characterized by the temperature profile, and complete non-responders may require more aggressive second-line therapy.


O.44 Infliximab For Kawasaki Disease Patients Who Did Not Respond To The Initial Therapy: A Japanese Nationwide Surveillance

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Oral Abstract Presentations (continued)

Medical Univ Kori Hosp, Osaka, Japan; Yosikazu Nakamura, Jichi Medical Univ, Shimotsuke, Japan; Kenji Hamaoka, Kyoto Prefectural Univ of Med, Kyoto, Japan

Backgrounds: In Japan, infliximab (IFX) has been used in patients with Kawasaki disease (KD) who did not respond to initial treatment. However, nationwide surveillance of the IFX for KD patients has not been reported. The objective of the present study is to reveal epidemiological and clinical features of KD patients treated with IFX.

Method: This retrospective observational study was conducted from 2007 to 2013. We sent a questionnaire to members of Japanese Society of Kawasaki disease annually and collected demographic data and clinical outcomes of KD patients treated with IFX. A total of 315 patients (208 boys and 107 girls, age at onset 37±25 months, illness days of initial treatment 4.3±1.2) from 46 hospitals were identified and analyzed in the present study.

Results: No patients received IFX as initial treatment. Over 60% of the patients were treated with IFX as first or second line additional rescue treatment. After the IFX administration, 237 patients (75.7%) became afebrile within 24 hours and 82 patients (26.0%) treated additional rescue treatments subsequently. Before IFX administration, 55 patients already had coronary artery aneurysm exceeding 4mm and 69 patients were finally affected coronary artery aneurysm exceeding 4mm. Serum level of C reactive protein were significantly decreased after IFX administration (10.6±7.2 to 4.9±4.7, P<0.001). Patients who required additional treatment after IFX showed significantly higher CRP levels before IFX compared to patients without additional treatment after IFX (12.3±8.3 vs. 10.0±6.7, P=0.049). Adverse events were observed in 50 patients (15.9%) which recovered spontaneously or after interventions.

Conclusions: IFX therapy for Kawasaki disease patients who did not respond to the initial treatment would be well tolerated and play a certain role to improve clinical course.

K. Hamaoka: None.

O.45
Kawasaki Disease Refractory To Primary IVIG Treatment - Use Of Scoring Systems And Predictive Modelling Based On Data From Singapore Children

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Objectives: Although first-line treatment for Kawasaki Disease (KD) is IVIG, some children may not respond, requiring repeat IVIG or another second-line therapy. It is important to predict non-responders for timely management decisions in this group of patients. The objective of our study was to assess the predictive value of the currently available scoring systems and propose an improved model for predicting refractory KD, based on data from KD patients in Singapore.

Method: We performed a retrospective review of the medical records (2001-2014) of 180 children with KD and identified 17 refractory cases. The 4 scoring systems; Egami, Kobayashi, Sano and Fukunishi; were applied to the data of refractory KD cohort to determine their predictive value based on sensitivities (SN) and specificities (SP). A logistic regression model was built using 5 predictors (age, AST, CRP, Hb, platelet and duration of illness) which were common among the existing models to propose a new scoring system based on our data -. The formula used was 1/(1+e^(-(-5.642839-0.192452*(zHb)-0.011597*(Age)+0.003756*(PLT)+0.009441*(CRP)+0.006015*(AST)+0.084408*(Days).

Results: The SN and SP obtained were; (1) Egami: SN 35.3%, SP 73.9% (original SN 78% and SP 76%) (2) Kobayashi: SN 23.5%, SP 67.5% (original SN 86% and SP 68%) (3) Sano: SN 18.8% and SP 88.2% (original SN 77% and SP 86%) (4) Fukunishi: SN 53.3% and SP 76.0% (original 84.6% and 87.0%). As the existing scoring systems proved less predictive in our population, we used logistic regression model to derive a formula incorporating the common variables to predict the likelihood of non-responders. This model attained an SN of 80% and SP of 80%.

Conclusion: The proposed model should be
validated prospectively in our local population for predicting unresponsiveness, and the formula can be applied to different datasets from other KD populations to test its robustness.


O.46
A Phase I/IIa Dose Escalating, Open-label Study of Atorvastatin in Children with Acute Kawasaki Disease and Coronary Artery Abnormalities

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BACKGROUND:
Although high-dose intravenous immunoglobulin plus aspirin reduces the risk of coronary artery damage, 5-10% of children with Kawasaki disease (KD) will go on to develop coronary artery aneurysms that may result in myocardial ischemia, infarction, or death. Arterial damage in KD results from immune activation and vessel wall infiltration by myofibroblasts, neutrophils, and T-cells with secretion of pro-inflammatory cytokines, elastases, and matrix metalloproteinases. Resolution of inflammation and recovery from the acute illness occurs through T-cell regulation. The 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA) reductase inhibitors, also known as statins, have extensive anti-inflammatory effects that target all of these pathways. These effects are independent of their cholesterol-lowering effect. Given these anti-inflammatory effects, statins would be a reasonable therapy to block coronary artery abnormality (CAA) progression in KD

METHODS:
We designed a Phase I/IIa, two-center, dose-escalating, 6-week open-label study of atorvastatin. Acute KD patients within the first 20 days after fever onset are eligible if they are between the ages of 2 and 17 years old, have had fever for ≥ 3 days, and have ≥ 2 clinical criteria with LAD/RCA z-score ≥ 2.5 or a coronary artery aneurysm (≥ 1.5 x the adjacent segment). Dose escalation (0.125-0.75 mg/kg/day) follows a 3+3 design with evaluations for dose limiting toxicities at 2 and 6 weeks after enrollment. The primary outcome measure is safety with secondary outcome measures including the pharmacokinetics (PK) of atorvastatin, changes in measures of oxidative stress and inflammation, enumeration and characterization of regulatory T-cells, and echocardiographic changes in the internal diameter of the coronary arteries.

RESULTS:
To date we have enrolled 9 subjects, 7 at Rady Children’s Hospital San Diego and 2 at Children’s Hospital Colorado. The median age at enrollment was 4 years with 5/9 (55%) males and a median illness day at enrollment of 6 days. The median baseline Z worst score was 3.5. The study is currently enrolling at the second dose level.

CONCLUSIONS:
The safety, tolerability, and PK of atorvastatin for acute KD patients will be established by this clinical trial.


O.47
Prediction of IVIG Resistance using Kawasaki Disease Risk Scores and Baseline Coronary Z-Scores at a Single North American Center

Mary Beth F Son, Susan Kim, Kimberlee Gauvreau, Alexander Tang, Fatma Dedegolu, David Fulton, Mindy S Lo, Robert P Sundel, Jane W Newburger, Boston Children's Hosp, Boston, MA

Aim: At a single pediatric tertiary care center, we assessed the performance of established Japanese risk scores (RS) to identify patients (pts) with Kawasaki Disease (KD) at higher risk for re-treatment (re-tx). We also sought to determine if the addition of baseline coronary Z-scores to RS could improve the prediction re-tx.

Methods: We reviewed available clinical, lab and echocardiogram (echo) data for KD pts treated from 1/2006 to 5/2014. The maximum z-score (zMax) of the right coronary artery (RCA) or left anterior descending artery (LAD) at baseline was used. Abnormal coronary arteries at baseline echo were defined as zMax ≥ 2 in the RCA or LAD. Kobayashi, Sano, Egami and Harada scores were calculated, comparing low and high risk scores to re-tx. The zMax was incorporated into each RS with 1 point added...
Oral Abstract Presentations (continued)

(+1) if baseline $z_{\text{Max}} \geq 2$. In an alternative approach, $z_{\text{Max}}$ was added as a covariate in a logistic regression model. The discrimination of each model was assessed using the c statistic. Results: Of 339 pts, 214 (63%) were male, and median age was 3.2 y (range 0.1-14.1 y). At diagnosis, 29% (97/339) had $\leq 3$ classical criteria for KD, and 25% (85/339) received IVIG re-tx. At baseline, the median $z_{\text{Max}}$ was 1.37 (-1.64-14.2) and 26% (88/339) had $z_{\text{Max}} \geq 2$. Classification as high risk by all four RS was significantly associated with re-tx ($p<0.001$-0.02). Baseline $z_{\text{Max}} <2$ vs. $\geq 2$ was also associated with re-tx (50 [21%] vs. 30 [34%), $p<0.02$). The ORs for re-tx were significant for all RS, but c-statistics were low, with a c statistic <0.7 (range of 0.57-0.61). RS +1 for $z_{\text{Max}} \geq 2$ did not improve the prediction for re-tx (c statistic 0.58-0.63). However, the addition of $z_{\text{Max}} \geq 2$ as a covariate improved the discrimination of all RS for re-tx (c-statistic 0.6-0.67).

Conclusions: Published RS for predicting IVIG resistance are associated with higher rates of re-tx in our patient population, but are not sufficient to discriminate patients at risk for re-tx. With the addition of baseline $z_{\text{Max}}$ as a covariate to the RS, prediction for re-tx was improved, although still modest. Further study in larger, multi-center studies are needed to validate these findings and to better understand the risk factors for re-tx in KD in North American children.

**M.F. Son:** None. **S. Kim:** None. **K. Gauvreau:** None. **A. Tang:** None. **F. Dedeoglu:** None. **D. Fulton:** None. **M.S. Lo:** None. **R.P. Sundel:** None. **J.W. Newburger:** None.

### O.48 Intravenous Immunoglobulin-Associated Hemolysis in Kawasaki Disease

**Rae S Yeung**, Fiona Almeida, Vahid Khajoee, Nita Chahal, Trent Mizzi, Sarah Schwartz, Brian W. McCrindle, Wendy Lau, The Hosp for Sick Children, Toronto, ON, Canada

Background: Intravenous immunoglobulin (IVIG) is the mainstay of treatment for Kawasaki Disease (KD). Due to the consolidation of IVIG manufacturers in 2008, different preparations of IVIG are currently available in Canada. An increase in adverse effects, especially hemolytic anemia, has been observed.

Objective: To characterize the natural history of IVIG-associated hemolytic anemia in KD.

Methods: A single-centre retrospective study was conducted at Toronto's SickKids Hospital between January 2002 and December 2012. Medical records of all KD patients were reviewed and hemolytic anemia identified (drop in hemoglobin $\geq 20$mg/dl post-IVIG treatment with 2 or more of the following criteria: reticulocytosis, positive direct anti-globulin test (DAT), and morphological changes on blood film). For statistical analysis, Chi-square tests and ANOVA with Tukey's post-hoc correction for multiple comparisons were utilized.

Results: Between 2002 and 2008, 2 of 370 patients diagnosed with KD who received IVEGAM had hemolytic anemia (0.5%). After 2008, the rates of IVIG-associated hemolysis were as follows: Privigen 17% (8/48, $p<0.001$), Gammagard 3.3% (4/121) and Gamunex 2.3% (3/130). Retreatment rates were significantly higher in the hemolysis group (64% vs. 22%, $p<0.001$), and there was a trend showing more patients with larger aneurysms ($Z_{\text{score}} >5$) in the hemolysis group (17% vs. 5.3%). All patients who hemolyzed had non-O+ blood types. Out of the 17 patients with hemolysis, 9 required red cell transfusions (60%). Starting in 2012, a detailed hemolysis work-up was included as standard protocol for all KD patients. Hemolysis was mediated by anti-blood group A & B antibodies resulting in DAT positivity, but no complement fixation. This extravascular hemolysis was maximal at 72 hours post-IVIG infusion and appeared to be dose dependent.

Conclusions: Hemolysis is seen in up to 17% of those receiving new IVIG preparations, which also appear to be less efficacious - associated with treatment failure and, possibly, poor coronary outcome. There are important implications for patient safety. Further study is required to develop evidence-based guidelines to improve our management of these children.

**R.S.M. Yeung:** None. **F. Almeida:** None. **V. Khajoee:** None. **N. Chahal:** None. **T. Mizzi:** None. **S. Schwartz:** None. **B.W. McCrindle:** None. **W. Lau:** None.

### O.49 Factors Associated with Development of Coronary Artery Aneurysms after Kawasaki Disease are Generally Similar for Those Treated Promptly Versus Those with Delayed or No Treatment

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McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

**Introduction:** While the risk is reduced, patients may develop coronary artery aneurysms (CAA) after Kawasaki disease (KD) despite receiving intravenous immunoglobulin (IVIG) within 10 days of onset of symptoms. Risk factors for CAA may differ compared to those patients with delayed or no treatment.

**Methods:** Patients diagnosed with KD between 1990 and 2013 were included. Patients with maximum coronary artery z-scores >5 were classified as having CAA. Separate multivariable regression models were used to determine factors associated with CAA for those with vs. without prompt treatment.

**Results:** Of 1,358 patients included, 83% were treated with IVIG within 10 days and 5.4% developed CAA. Patients who had delayed (>10 days) or no IVIG treatment were at increased odds of developing CAA (OR: 3.1, p<0.001). From 1990-2013, the proportion of patients treated promptly increased (OR: 1.05/year, p=0.006) while the total duration of fever decreased (EST: -0.10 (0.03) days/year, p=0.001). These trends were associated with a shift such that a greater proportion of the patients who developed CAA actually had been treated promptly (from <25% in 1990 to >70% in 2013, OR: 1.1/year, p=0.01). For patients with prompt treatment with IVIG, factors associated with increased odds of CAA were: longer duration of fever prior to treatment (OR: 1.2/day, p=0.04), age <1 year old (OR 3.9, p=0.001), higher pre-IVIG white blood cell count (OR: 1.05x10^9/L, p=0.007), lower hemoglobin (OR: 1.4/g/L, p=0.004) and non-response to the initial IVIG treatment (OR: 2.5, p<0.001). For patients with delayed or no treatment, factors associated with increased odds of CAA were: males (OR: 5.4, p=0.009), age <1 year old (OR: 29.9, p<0.001), lower red blood cell count (OR: 2.5-5.5x10^12/L, p=0.01) and higher platelet count at diagnosis (OR: 1.4/100x10^12/L, p=0.001). Additionally, delayed treatment with IVIG did not reduce the risk of CAA (OR: 1.9, p=0.28), and total duration of fever was not associated with CAA for this group (OR: 1.04/day, p=0.16).

**Conclusions:** Factors associated with the development of CAA are generally similar for those treated promptly vs. those with delayed or no treatment. For those with delayed diagnosis, treatment with IVIG does not appear to be effective to prevent CAA.

**Background:** Cyclosporin A (CsA), which potently suppresses inflammatory cytokines by negative regulation of nuclear factor of activated T cells pathway, may be a promising option for the treatment of Kawasaki disease (KD), especially in patients resistant to intravenous immunoglobulin (IVIG). We treat KD patients with the unified protocol using CsA after 2nd IVIG. Here we report 6 years-outcome of this treatment. Patients and Methods: From 2008 to 2014, 441 patients were treated. At the persistence or recurrence of fever at the end of the 2nd IVIG (2 g/kg for 24 hours), patients were treated with CsA (4-5mg/kg/day) through oral administration except for infants younger than 4 months old. If patients failed to become afebrile after CsA treatment, they received 3rd IVIG. All patients received aspirin 50mg/kg/day at febrile stage. Results: 419 patients became afebrile after 1st or 2nd IVIG. At this point, 2 patients had mild CALs (max 4.7 mm, 2.5mm in 2month-old infant). Among the other 22 patients (5.0%) who failed to become afebrile, one infant aged 1 month-old received 3rd IVIG. Among a total of 21 patients treated with CsA, 10 patients responded promptly to be afebrile within 5 days. The other 11 patients failed to become afebrile and received 3rd IVIG. Eight out of the 11 patients became afebrile after 3rd IVIG. Three patients developed mild CALs (max 3.1mm, 3.7mm, 5.5mm). There were no serious adverse effects in CsA treatment. A total number of patients with CAL was 5 (1.1%). The maximum CAL diameter was 5.5 mm. Conclusions: The outcome of KD patients treated with CsA and 3rd IVIG as a third line therapy is safe and favorable. CsA could be a candidate drug of the
Effects of Anti-TNF-alpha Antibody Therapy on IVIG-resistant Patients with Kawasaki Disease

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Background: Kawasaki disease (KD) patients who do not respond to initial intravenous immunoglobulin (IVIG) therapy have a higher risk of developing coronary artery lesions (CALs). Infliximab (IFX) has been reported to be effective in alleviating fever in these patients and has been increasingly used. However, little is known about how IFX suppresses inflammation in KD. We analyzed immunological parameters in KD patients who responded to IFX, as well as those who did not, after the initial IVIG and aspirin treatment. Methods: Twenty-six KD patients hospitalized and treated with IFX after initial IVIG and aspirin between August 2009 and July 2014 were enrolled in this study. We analyzed electronic medical records of baseline characteristics and laboratory data (WBC, neutrophil, lymphocyte and platelet counts, levels of GOT, GPT, Alb, Na, CRP and D-dimer), and measured plasma levels of cytokines (G-CSF, IL-6, IL-8, IL-10, IL-12p70, IL-17, TNF-α, IFN-γ, sIL-2R, sTNFR1 and sTNFR2) before and after IFX. We defined responders as patients who became afebrile within two days after IFX treatment.

Results: The median age of 17 responders (11 males and 6 females) and 9 non-responders (5 males and 4 females) was 31 mo (9-84 mo) and 39 mo (16-64 mo), respectively (p=0.65). The initiation of IFX treatment after the onset of fever was compatible in both the group (day 9 vs day 9 in medians) (p=0.85). The incidence of CALs one month after onset was 0% (0/17) and 22% (2/9), respectively (p=0.11). Observed only in responders, WBC and neutrophil counts, and the levels of CRP, D-dimer, G-CSF, IL-6, sIL-2R, TNF-α, sTNFR-1 and sTNFR-2 decreased remarkably after IFX (p<0.01). In non-responders, serum level of Na was significantly lower (p=0.04) before IFX, while WBC (p=0.04) and neutrophil (p=0.01) counts, and the levels of CRP (p=0.02), IL-6 (p=0.01), IL-10 (p=0.03) were higher. After IFX, the level of Alb (p=0.02) was lower.

Conclusions: After IFX, the level of TNF-α, together with many pro- and anti-inflammatory mediators, decreased in responders but not in non-responders. In particular, suppression of IL-6 and IL-10 was insufficient in non-responders, suggesting that inflammation mechanisms other than the TNF-α axis would be important in KD patients who are unresponsive to IFX.

characterized the KD course in infants ≤6 mos and compared to outcomes in KD pts >6 mos.

**Methods**

We retrospectively reviewed the course of 88 subjects ≤6 mos diagnosed with KD between January 2004 and December 2013 at Children’s Orange County (CHOC) and Rady Children’s Hospital San Diego (RCHSD) and compared to 632 subjects >6 mos at RCHSD. Complete and incomplete KD cases were defined based on the 2004 AHA guidelines. Subjects were classified by coronary artery (CA) status (normal, dilated, or aneurysmal CA based on RCA and LAD measurements) and by Z-score (RCHSD only). IVIG resistance was defined as fever ≥38C at least 36 hours after completion of IVIG. Fisher’s Exact test was used for comparisons.

**Results**

Of the 88 infants, 62 (70.4%) were male and 76 (86.3%) were treated at ≤10 days of illness. Treatments in the 88 pts were as follows: IVIG responder: 55 (62.5%); IVIG resistant: 13 (14.7%); infliximab for cardiac indications: 16 (18.2%); late treatment >10 days: 2 (2.3%); not treated: 2 (2.3%). Infliximab was administered to a total of 27 pts (30.7%) and was well-tolerated with rash as the only adverse event in 1 pt.

Worst CA status was “normal” in 37 (42.1%), dilated in 29 (32.9%), aneurysm in 15 (17.1%) and giant aneurysm in 7 (7.9%) pts. Of the 48 pts at RCHSD who presented within the first 10 days of illness, only 26 (54.2%) had a Z-score <2.5. Of these 26 pts, 7 (26.9%) went on to have a subsequent Z-score ≥2.5. Comparing the ≤6 mos vs. >6 mos RCHSD cohorts, there were no significant differences in number of pts treated within the first 10 days of illness (48/53, 90.5% vs. 545/632, 86.2%) or pts having incomplete presentations (12/53, 22.6% vs. 106/632, 16.8%).

**Conclusions**

There were no significant differences in the rate of incomplete KD or rate of diagnosis within the first 10 days of illness in children ≤6 mos vs. >6 mos. Infliximab use in 30.7% of the ≤6 mos old pts was safe. Infants ≤6 mos had a high rate of aneurysms (22/88, 25%) despite timely diagnosis and treatment. Better treatments are needed for this high risk group of KD pts.

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**O.53**

Occult Coronary Artery Dilatation: An Unrecognized Category Of Coronary Involvement

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**Background:**

The current definition of Coronary artery dilatation (CAD), Z-score >2.5, in KD may omit patients at higher risk of later complications. We propose a category of occult CAD with a Z-score variation ≥2 for the same CA on 2 different echocardiograms, but absolute Z-score <2.5. We compared this new category with cases of CAD and normal CA.

**Method:**

A retrospective review included 337 patients diagnosed with KD in our institution. Echographic data were retrieved for the first year following diagnosis. Patients were classified in three categories: definite CA dilatation (dCAD) with Z-score ≥2.5, occult CA dilatation (oCAD) and normal CA (nCAD). We compared inflammatory profile, IVIG treatment resistance, and timing of CA involvement.

**Results:**

There were 26.3% patients with nCAD, 32.2% with oCAD and 41.1% with dCAD. Patients with KD incomplete diagnostic criteria represented 35%, 14% and 17% for nCAD, oCAD and dCAD groups respectively (p=0.008). Median time for CAD was 7 and 9.5 days for dCAD and oCAD respectively (p=0.002). A Jonckheere trend test identified a progression of inflammatory parameters through the three groups for Platelet count (p<0.001), Albumin (p = 0.007), ESR (p = 0.04), but not for CRP (p = 0.76) and WBC (p = 0.16). There was a significant difference in treatment resistance, with 5%, 19% and 31% for nCAD, oCAD and dCAD respectively (p=0.002).

**Conclusion:**

OCAD group appears like a distinctive subgroup of KD patients showing intermediate inflammatory profiles and treatment respond in the NCAD to DCAD spectrum. Recent Z-score equations, more accurate for young patients’ CA size than former linear equations, may explain the high incidence of dCAD in this report.
Further studies are needed to define the profile and propensity to complications of this subpopulation.


O.54 Alteration of Left Ventricular Performance and Aortic Elastic Properties in Patients After Kawasaki Disease With Coronary Artery Aneurysm Even Without Cardiac Ischemia

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Introduction: Recent studies have suggested that patients after Kawasaki disease (KD) have altered arterial stiffness. However, there is little evidence of the relationship between arterial stiffness and left ventricular (LV) global function of KD patients without cardiac ischemic region. Hypothesis: We hypothesized that the alteration in the elastic properties of the ascending aorta may influence both LV function. Methods: Sixty one patients after KD (age, 6.1±4.0 years) were studied, comprising 15 patients with CAAs and 46 patients without CAA. All the patients with CAAs showed no cardiac ischemic region confirmed by myocardial perfusion SPECT. Using pulsed Doppler echocardiography combined with Doppler tissue imaging, mitral peak velocities during early diastole (E) and LV peak myocardial velocities during early diastole (e’) and systole (s’) were measured. The ratio of E/e’ was used as an index of filling pressure of the LV. From Doppler tissue imaging, Doppler-derived index of combined systolic/diastolic myocardial performance (Tei index) was calculated as a surrogate for LV global function. We also obtained aortic stiffness index (ASI), and aortic distensibility (AD) from the measurements of the ascending aorta with noninvasive evaluation of blood pressure. Results: In all the patients, febrile periods of acute stage of KD showed significantly positive correlation with ASI, and showed significantly negative correlation with AD (both p <0.05). The patients with CAAs showed significantly greater pulse pressure, LV Tei index and ASI than those without CAAs (all p <0.05). Conclusions: KD especially with CAAs showed subclinical abnormal LV performance that is related to altered central aortic elastic properties.


O.55 Utility of Adenosine Cardiac Stress MRI to Evaluate Ischemia in Patients with Kawasaki Disease

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Background: Patients with Kawasaki Disease (KD) and a history of coronary artery disease (CAD) are at risk of myocardial ischemia/infarction. Adenosine stress cardiac MRI (CMR) has been increasingly used in adults to evaluate for atherosclerotic CAD. This modality has not been widely used in the evaluation of CAD in children and young adults, but may be useful in those with a history of KD. Methods: Patients with a history of Kawasaki disease and a clinical indication for a stress cardiac MRI were prospectively enrolled in the study. SSFP cine and delayed enhancement CMR (DE-CMR) were performed in a standard manner. Adenosine stress perfusion was performed with administration of adenosine (140 ug/kg/min) for 2-4 minutes and gadolinium (0.1 mmol/kg) using a standard adult protocol. Results: A total of 13 procedures were performed between 2010 and 2014 on 8 patients with a history of KD (ages 8 to 22, 3F/5M). Seven of eight patients presented with chest pain. Seven of eight patients had documented moderate to giant aneurysms and one had a previous coronary bypass operation. Scans were performed 3-16 years after initial episodes of KD. Three of 16 (19%) scans demonstrated inducible regional ischemia in the distribution of coronary abnormalities. Of these, all underwent cardiac catheterization and 1 patient subsequently underwent coronary bypass surgery. All patients with negative scans were followed clinically with no evidence of further symptoms. Conclusion: As a non-invasive imaging modality, adenosine cardiac stress MRI is feasible in patients with KD and coronary abnormalities and
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may obviate the need for invasive studies in order to rule out significant CAD. Further studies are needed to evaluate this imaging modality as a more definitive test in the evaluation of KD and chest pain.

**M.J. Campbell:** None. **P. Barker:** None. **J. Li:** None.

**O.56**
Myocardial Fibrosis in Patients with a History of Kawasaki Disease: a Pilot Study

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Background: Myocarditis occurs in acute Kawasaki disease (KD), and case series with endomyocardial biopsy report that KD patients (pts) may have myocardial fibrosis. The new cardiac magnetic resonance (CMR) technique of myocardial T1 measurement is a noninvasive means of measuring diffuse myocardial fibrosis. We sought to assess the prevalence and risk factors for diffuse myocardial fibrosis in KD pts using CMR.

Methods: In this retrospective study, all pts with KD who had a CMR with extracellular volume fraction (ECV) measurement at Boston Children’s Hospital were included. The ECV, a measure of diffuse fibrosis, was calculated in the mid-left ventricle by measuring T1 values for blood pool and myocardium before and after gadolinium with a Look-Locker technique, and adjusting for hematocrit. Myocardium with focal fibrosis as evidenced by late gadolinium enhancement (LGE) was excluded. ECV results were compared to values from control subjects (n=20; median age 16 yrs (range, 11-36)) who had a normal CMR exam, and no history of left heart disease or cardiomyopathy. Myocardium with focal fibrosis as evidenced by late gadolinium enhancement (LGE) was excluded. ECV results were compared to values from control subjects (n=20; median age 16 yrs (range, 11-36)) who had a normal CMR exam, and no history of left heart disease or cardiomyopathy. Myocardium with focal fibrosis as evidenced by late gadolinium enhancement (LGE) was excluded. ECV results were compared to values from control subjects (n=20; median age 16 yrs (range, 11-36)) who had a normal CMR exam, and no history of left heart disease or cardiomyopathy. Myocardium with focal fibrosis as evidenced by late gadolinium enhancement (LGE) was excluded. ECV results were compared to values from control subjects (n=20; median age 16 yrs (range, 11-36)) who had a normal CMR exam, and no history of left heart disease or cardiomyopathy. Myocardium with focal fibrosis as evidenced by late gadolinium enhancement (LGE) was excluded. ECV results were compared to values from control subjects (n=20; median age 16 yrs (range, 11-36)) who had a normal CMR exam, and no history of left heart disease or cardiomyopathy. 

Results: Subjects (n=10) had a median age at CMR of 13 yrs (range, 8-36), median age at KD diagnosis of 3 yrs (0.3-11), and median time interval from diagnosis to CMR of 10 yrs (0.3-34). Nine pts had coronary aneurysms and the other 1 had mild left ventricular dysfunction. All 3 pts with a known history of myocardial infarction (MI) had a LGE pattern consistent with MI. LGE with a MI pattern was also seen in 1 additional pt without a history of MI but who had undergone coronary bypass surgery. Overall, ECV was not significantly different in KD pts and controls (0.25 ± 0.03 (range, 0.21-0.30) vs. 0.24 ± 0.03 (range, 0.18-0.28), p=0.29). One pt (10%) had an increased mean ECV (>0.28). ECV was not associated with indexed LV mass, mass/volume ratio, ejection fraction, or LGE.

Conclusions: In this small pilot study of KD pts most of whom had aneurysms, diffuse myocardial fibrosis based on ECV did not differ significantly from that in normal control subjects, although 1 in 10 pts had an ECV above the normal range. Future larger studies should compare ECV in KD pts with and without aneurysms to define the risk of myocardial fibrosis after KD and to guide future recommendations for follow-up and therapy.

**S.M. Dusenbery:** None. **J.W. Newburger:** None. **K. Gauvreau:** None. **A. Baker:** None. **A.J. Powell:** None.

**O.57**
Coronary Circulation Assessed by Transthoracic Echocardiography during Exercise Test is Impaired in Patients after Kawasaki Disease Even with Regressed Coronary Arterial Lesions

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Background: Coronary flow reserve (CFR) has important clinical implications for the evaluation of coronary circulation including Kawasaki disease (KD). Pharmacological vasodilation is generally used to induce hyperemia for the assessment of CFR; however, exercise test provides more physiological stress. Objectives: This study sought to assess CFR during exercise in patients after KD with regressed coronary arterial lesions (CALs) by transthoracic echocardiography (TTE).

Methods: Twenty KD patients were studied, comprising 8 patients with regressed CALs in the left anterior descending coronary artery (LAD) and 12 patients without CALs (median ages; 10 and 9 years, respectively). Fourteen age-matched healthy subjects were also studied as controls. We obtained peak diastolic coronary flow velocity (CFV) of the LAD by pulsed-Doppler TTE at rest and at submaximal exercise on supine ergometer. CFR was calculated as the ratio of exercise to rest CFVs.

Results: The CFV measurements were obtained...
in all the subjects. There was no significant difference in the CFVs among the patients with regressed CALs, those without CALs and the controls (30 ± 7 vs. 31 ± 10 vs. 28 ± 8 cm/s, respectively). The CFVs increased during exercise in the patients without CALs and the controls (51 ± 11 and 49 ± 10 cm/s, respectively, both p <0.05). In consequence, the CFR was lower in the patients with regressed CALs compared with those without CALs and the controls (1.3 ± 0.2 vs. 1.7 ± 0.2 and 1.7 ± 0.2, respectively, p <0.05).

Conclusions: Exercise test demonstrated impaired CFR in KD patients with regressed CALs. It suggests that these patients have risk of future myocardial ischemic events.


O.58
Medium-term Outcomes of Coronary Artery Aneurysms after Kawasaki Disease: A Study from the North American Kawasaki Disease Registry

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Background: One of the main impediments to conceiving and planning studies in children with coronary artery aneurysms (CAA) after Kawasaki disease (KD) is the lack of normative data regarding the prevalence of outcomes over time and risk factors. Methods: The North American Kawasaki Disease Registry was used to determine the prevalence of multiple clinically important outcomes of CAA after KD. All analyses were stratified by severity of CAA (small CAA with z-score = 2.5-5, medium with z-score = 5-10 and giant with z-score >10). All analyses were performed using non-parametric survival analysis.

Results: n=621 patients submitted to the Registry had complete follow-up data and were included in the analysis (280 [45%] small CAA, 139 [22%] medium and 202 [33%] giant). Time-related freedom from multiple outcomes stratified by type of CAA are reported in the Table. Reduction in z-scores was strongly associated with the initial size of the lesion, with smaller lesions being more likely to decrease to a normal dimension over time. Thrombosis and stenosis were infrequent in patients without giant CAA. For those patients with giant CAA, the risk of thrombosis, myocardial infarction, angiographically-confirmed stenosis and revascularization was substantial and persisted up to 10 years after diagnosis. In addition to larger luminal diameter, other factors associated with increased risk of adverse outcomes included larger CAA longitudinal area and complex CAA (vs. isolated lesions).

Conclusions: Only patients with giant CAA are at substantial risk of adverse clinical outcomes; future trials of pharmacological therapy targeting thrombosis and stenosis risk should focus on these patients.
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O.59
Fate of Kawasaki disease giant coronary aneurysm: Analysis of the last 10 years nationwide survey in Japan

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[Background and Objective]
Long term prognosis of Kawasaki disease (KD) with giant aneurysm is not yet well understood. We conducted a nationwide survey of KD with giant aneurysm for recent 10 years, and analyzed cardiac events of those patients.

[Methods]
Nationwide epidemiological survey of KD has been conducted every 2 years since 1970 in Japan. We performed questionnaire survey based on 16th - 21th (1999 - 2010) nationwide epidemiological data.

[Results]
We send questioners to 275 facilities asking about 415 patients who were reported to have giant aneurysm (>=8mm), and collected the data of 334 patients (80.5%). We excluded 84 non-giant aneurysm patients and 36 duplicated cases and defined finally 214 patients. Out of 214 patients, 13 deaths and 32 AMIs were described (6.1% and 15.0%, respectively). The first AMI attack was mostly reported within a few months from KD onset (medium 5 months (0 - 85 months)). AMI was occurred one time in 26 patients, and two times in 6 cases. Myocardial ischemia was observed in 80% of AMI patients, and 12 patients were received coronary artery bypass graft. Thirteen patients were reported to be dead (medium 1 month (0-23 months) from KD onset). There were 6 cardiac deaths within 1 month from KD onset (5: rupture of aneurysm, 1: AMI). The others were all caused by AMI except for 2 accidental death. Four out of 6 AMI deaths were caused by the first AMI attack. For the remaining 2 AMI deaths, the period from the first AMI to second fatal AMI was 1 month and 6 month, respectively. There were no death reported beyond 2 years from KD onset.

[Conclusion]
AMI and cardiac death of KD with giant aneurysm occurred mostly in early phase of KD onset. Coronary rupture occurs within a month after onset, and 84% AMI and all AMI death occurs within 2 years after onset. Patients survival become promising after 2 years from onset. These evidences indicate that therapeutic strategy up to 2 years after onset is extremely important for prognosis of KD with giant aneurysm.


O.60
Kawasaki Disease Complicated by Coronary Artery Aneurysms: Mortality and 40-year Outcomes

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Background: Long-term outcomes and life expectancy for children with a previous history of Kawasaki disease (KD), particularly those with coronary artery aneurysms (CAA), remain to be determined.

Methods: An inception cohort of all patients with KD assessed at The Hospital for Sick Children in Toronto between 1978 and 2013 was assembled. Patient outcomes were obtained throughout their pediatric and adult clinical follow-up as long as available. Prevalence of outcomes over time was modelled with Kaplan-Meier survival curves. Life tables from Statistics Canada were used to obtain age/gender specific cumulative mortality for the general population.

Results: The cohort included 2,623 KD patients, of whom 410 (16%) had coronary artery involvement (215 dilatation, 57 non-giant CAA
and 138 giant CAA). Average follow-up for patients with coronary artery involvement was 6.7 years (13.3 years for giant CAA); 57 and 34 patients had at least 15 and 25 years of follow-up, respectively. No patients with coronary artery dilatation or non-giant CAA had revascularization or a myocardial infarct. Freedom from revascularization (14 events) for patients with giant CAA was 90±6%, 87±7% and 80±13% at 10, 20 and 40 years of follow-up. Freedom from myocardial infarct (11 events) was 94±4%, 92±5% and 89±7% at 5, 20 and 40 years. No patients with coronary artery dilatation or non-giant CAA had revascularization or a myocardial infarct. Freedom from revascularization (14 events) for patients with giant CAA was 90±6%, 87±7% and 80±13% at 10, 20 and 40 years of follow-up. Freedom from myocardial infarct (11 events) was 94±4%, 92±5% and 89±7% at 5, 20 and 40 years. No patients with coronary artery dilatation or non-giant CAA had revascularization or a myocardial infarct.

Conclusions: Despite risks of myocardial infarction and revascularization, patients with giant CAA had life-expectancy similar to that of the general population up to the fourth decade of life. Additional follow-up will be necessary to determine if these trends continue into later decades.


O.61
Coronary Artery Stenosis Risk and Progression in Kawasaki Disease Patients: Experience at a U.S. Tertiary Pediatric Center

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Objective: Risk and natural progression of coronary artery stenosis in Kawasaki Disease is not well-defined and is a potential cause of long term morbidity, despite treatment with IVIG. We present a novel study at a US tertiary pediatric care center identifying risk factors for stenosis.

Methods: We reviewed charts of all children that underwent cardiac catheterization for coronary artery abnormalities from 1998 to January 2014 at a tertiary pediatric care center. All demographic and diagnostic data was recorded including time intervals to echocardiographic changes and catheterization confirmed cases of stenosis. Multivariate survival analysis was used to identify risk factors with stenosis formation as the main outcome measure.

Results: Fifty-two children met inclusion criteria and 18 (34.6%) developed stenosis. The highest risk group overall were children under the age of 6 months (HR 3.66, p=0.005) and those with giant coronary aneurysms (GCA). In a subset of only cases of GCA (33), children under the age of six months were at highest risk (HR 2.62, p=0.04). IVIG administration, gender, and ethnicity were statistically insignificant. The majority of individuals with GCA went on to develop stenosis (19/33). The presence of GCA was 100% sensitive for cases of stenosis.

Conclusions: This is a novel study in an American population and demonstrates a relatively high incidence of stenosis in children with KD and coronary vascular abnormalities. Overall, a majority of GCA cases progressed into stenosis, with children under the age of 6 months being at highest risk.

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O.62
Estimation Of The Severity Of Coronary Artery Aneurysm By Z-score Of The Internal Diameter In Kawasaki Disease.

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ABSTRACTS
Oral Abstract Presentations (continued)

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[Background] The standard values of normal coronary artery internal diameters in Japanese children have been recently established, making it possible to calculate Z-scores based on body surface area. The aim of this study was to clarify the appropriate cut-off points of coronary artery aneurysm (CAA) Z-scores to predict coronary events such as stenosis, obstruction, and thrombosis in patients with Kawasaki disease (KD).

[Methods] In this multicenter retrospective study, we investigated height, weight, CAA diameters measured by echocardiography in acute phase KD, and coronary events in CAA patients with KD (age 18 years or younger) who had coronary angiography from 1992 to 2011.

[Results] Interim analysis was performed on data of the 928 patients recruited from 45 institutions. Body surface area (calculated from height and weight) and CAA diameters were available in 702, 680, and 539 cases of right coronary artery (RCA), left main trunk (LMT), left anterior descending artery (LAD), respectively. Coronary events occurred in 62 RCA cases (8.8%), 8 LMT cases (1.2%), and 45 LAD cases (8.3%). Areas under the ROC curves to predict coronary events were similar for actual diameter, Z-score, and the ratio of actual diameter to that showing a Z-score of zero in each segment. The cut-off points for the actual diameter, Z-score, and ratio which yielding the highest sensitivity plus specificity were 6.3 mm, 9.6, and 3.9 times for RCA; 7.4 mm, 11.1, and 2.8 times for LMT; and 5.3 mm, 8.9, and 3.5 times for LAD.

[Conclusions] We identified cut-off Z-scores for CAA diameters useful for coronary events prediction. Attention should be paid to coronary events when the Z-score for CAA diameter is over 10.


O.63 Novel Use Of Fractal Analysis In Kawasaki Disease For Risk Prediction


Introduction
Fractal based analysis of vascular branching complexity is known to have a prognostic role in cardiovascular risk prediction and suboptimal Fractal Dimensions of retinal vessels has been shown to correlate with coronary mortality. We hypothesize that Kawasaki disease permanently alters the fractal pattern of the retinal vasculature reflecting suboptimal microcirculatory development and attendant coronary risk.

Objectives
We calculated and compared the Zone Fractal Dimension(Df) of children with a history of Kawasaki disease with a matched cohort

Methods
All subjects underwent high resolution digital retinal photography and disc-as well as macular centered photographs were digitized and used for measurement of Df using a standardized validated program performed by a single trained grader. Retinal vascular dimensions were also measured.

Results
Fifty subjects and 100 controls were examined. Subjects had a Df of 1.506 while controls had a Df of 1.432(P<0.001). Cases were controlled for age, gender and ethnicity.

Conclusion
In adult studies, a Df exceeding 1.47 has been shown to be sub-optimally high with resultant associated coronary risk. This suggests that the long term cardiovascular risks of Kawasaki disease may not only be conferred through coronary flow factors but systemic microcirculatory mal-development.

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Characteristics and Fate of Systemic Artery Aneurysm caused by Kawasaki disease

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[Background] The long-term outcome of Systemic artery aneurysms (SAA) caused by Kawasaki disease (KD) remains unknown. SAA refers to aneurysms developing anywhere in the arterial system other than the coronary circulation. SAA included peripheral artery aneurysm (PAN) and aortic artery aneurysm.

[Methods] We investigated the characteristics and the fate of SAA in 20 patients (14 males and 6 females) from their medical records and angiograms. The onset age of KD ranged from 1 to 20 months with a median of 6 months. The interval from the onset of KD to the latest angiogram ranged from 16 months to 24 years (median 18 years). The residual rate of PAN and the incidence of stenotic lesions were analyzed by the Kaplan-Meier method in 11 pts, who had undergone initial angiograms within 4 months.

[Results] The mean duration of fever was 24±12 days. All 20 patients had at least a symmetric pair of aneurysms in bilateral peripheral arteries and 16 pts (80%) had multiple PAN. The number of respective SAA was as follows, brachial artery 32, common iliac artery 20, internal iliac artery 21, abdominal aortic aneurysm 7, and others 30. The residual rates of PAN at 10 and 20 years after the onset of KD were 66% and 51%, respectively (n=42). The incidence of stenotic lesions at 10 and 20 years after the onset of KD was 6% and 25%, respectively. The diameter of PAN in the acute phase leading to stenotic lesions in the late period was more than 10.0mm.

[Conclusions] PAN occurred symmetrically and were multiple in younger infants and those with severe acute vasculitis. The fate of PAN resembles that of coronary artery aneurysms, and depends on its acute phase diameter. The larger PAN can lead to stenotic lesions in the late period.

S. Hoshino: None. E. Tsuda: None. O. Yamada: None.

Long-term Outcome of Patients with Giant Coronary Aneurysms caused by Kawasaki Disease: A 30-year Experience in a Single Center in Taiwan

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[Background] Patients with coronary artery aneurysms are at risk for thrombotic and stenotic complications later in their lives. The longitudinal changes of giant coronary aneurysms caused by Kawasaki disease (KD) and their long-term outcome are still unclear in Taiwan.

[Methods] By retrospective chart review of patients diagnosed with Kawasaki disease complicated by giant coronary aneurysms, we analyze incidence of ischemic event, survival rates, and related risk factors.

[Results] Between 1984 and 2012, 28 patients (24 male and 4 female) developed giant aneurysms. The mean age at onset and observe period was 3.8 years (range from 0.41 - 10.3 years) and 12 years (0 to 36.8 years), respectively. The initial median coronary Z-score was +5.75 (+0.62 to +19.06) in left main coronary artery, +4.49 (-0.18 to +11.19) in left anterior descending artery, +6.71 (+1.79 to +14.46) in right coronary artery. None of the giant aneurysms regressed during follow-up. The 5- and 35-year survival rates were 0.92 and 0.69, respectively. Except the three deaths, four additional male patients were diagnosed with acute myocardial infarction (AMI), and 2 of these diagnoses occurred within 1 year of KD onset. The incidence of AMI or death in patients with giant aneurysms was 26%, and 67% of the AMI occurred within the first year of KD onset. AMI/death-free survival rates were 76% and 69% at 10 and 20 years after KD onset, respectively. Ischemia event-free survival rates were 63% and 36% at 10 and 20 years after disease onset. Men tended to have AMI and ischemia, and only one ischemia patient was female. The hazard ratio of gender on the ischemia events was 2.70 (95% CI: 0.33 - 21.73, P = 0.38).
Conclusions The long-term survival of KD patients with giant coronary aneurysms is guarded. Ischemic heart disease is the major cause of morbidity and mortality. Male KD patients, once they had giant aneurysms, tend to have ischemic events. Other risk factors need to be validated in a larger cohort.


O.66 Exercise Response in Children and Adolescents Late After Kawasaki Disease According to Early Coronary Status

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BACKGROUND: Cardiovascular sequelae after Kawasaki disease (KD) are typically linked to coronary artery aneurysms. This post-hoc analysis describes response to exercise challenge late after KD to determine response according to coronary artery status. METHODS: Bruce treadmill testing was performed under an international trial in 117 KD without coronary complications (NS-KD) and 133 with coronary artery aneurysm (CAA-KD). Endurance time, heart rate, systolic and diastolic blood pressure were assessed at rest, at each treadmill stage, peak exercise and recovery. The presence of myocardial perfusion defects was assessed by Tc-99m sestamibi SPECT imaging. RESULTS: Endurance time was similar between groups (11.3 ± 2.6 min vs 11.0 ± 2.6 min, NS-KD vs CAA-KD; p=0.343). There were similar responses in all investigated parameters as well (table 1) (p=0.075-0.942). The prevalence of myocardial perfusion defects was comparable in both groups (22.2% in NS-KD and 16.5% in CAA-KD; p=0.255), but predicted lower heart rate at 1-min recovery as well as lower diastolic blood pressure at 1-min and 5-min recovery in patients with abnormal Summed Stress Score > 3 (p = 0.017-0.042); reversible defects in 12.8% of NS-KD and 11.3% of CAA-KD (p=0.708).

CONCLUSION: Compared to KD patients without CA involvement, the presence of coronary aneurysms at the sub-acute phase does not induce a differential effect on exercise parameters. In contrast, exercise induced myocardial perfusion defect late after the onset of KD correlates with abnormal recovery parameters. These data suggest that the exercise performance alone is unlikely to discriminate patients with or without coronary artery sequelae.

N. Dahdah: None. H. Gravel: None. D. Curnier: None. F. Dallaire: None. A. Fournier: None. M. Portman: None.

O.67 Carotid Intima-media Thickness In Patients With A History Of Kawasaki Disease

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Aims Kawasaki disease (KD) is an acute pediatric vasculitis with the development of coronary artery aneurysms (CAA) being recognized as a serious clinical complication of KD. It has been suggested that KD predisposes to premature cardiovascular disease (CVD) later in life, however, conflicting results have been reported. We therefore assessed the risk of CVD in patients with a history of KD.
Methods and results
Carotid B-mode ultrasound scans and measurements of carotid intima-media thickness (cIMT), a validated marker of CVD risk, were performed in 161 KD patients (119 with CAA, 42 without CAA based on worst-ever z-score; age range: 7-20 years). CIMT measurements were also performed in 82 unaffected family controls in the same age range. Differences in cIMT between patients and controls were evaluated by linear regression analyses while correcting for confounders by stepwise backward elimination. Mean cIMT (±SD) was increased in patients with KD (0.378 ± 0.030 mm versus 0.360 ± 0.027 mm; \( P \) adjusted < 0.0001). If the difference in cIMT between patients and controls was plotted against age, in patients without CAA, increased cIMT was only apparent at young age, whereas in patients with CAA increased cIMT was observed over the entire age range.

Conclusion
Our findings in KD patients show significant arterial wall changes in patients with a history of KD, in particular in those with CAA. In contrast to the cIMT findings at young age - irrespective of the absence or presence of CAA, the data demonstrate that - with age - the cIMT in KD patients without CAA became indistinguishable from controls but remained increased in the patients with CAA. The age-dependency of cIMT values could in part explain the variable and conflicting results of previous reports in KD. Furthermore, these explicit differences in cIMT between CAA-negative and CAA-positive patients may suggest that the pathophysiology of the arterial wall changes in KD differ from atherosclerosis. Finally, our results indicate that follow-up in patients with KD seems justified in patients with CAA, but may not be necessary in children without CAA.


O.68 Corticosteroid Pulse Therapy for Acute Kawasaki Disease: Consideration for the Long-Term Prognosis of Coronary Artery Lesions

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Background: The use of corticosteroids as treatment for Kawasaki disease (KD) patients is still controversial. And the effects of corticosteroids on coronary artery lesions (CALs) development and later vascular remodeling are also unclear. The purpose of this study was to compare the long term prognosis of KD with CALs between corticosteroid administration patients and no corticosteroid using patients.

Methods: Five hundred sixty nine patients with KD were studied at Kurume University Hospital from 1996 to 2004. Clinical records of 66 patients (46 males, 20 females) with CALs were reviewed. The median age at diagnosis was 1.5 (range 0.2 - 13.2) years and median follow-up period was 8.9 (range 0.1 - 16.4) years. Coronary artery sizes were measured by body surface area (BSA) adjusted z-score to using echocardiography. CALs were defined as coronary artery z-score > 2.5, and CAL regressions were defined as z-score < 2.5.

Results: Sixty four patients were treated with intravenous immunoglobulin (IVIG), and 51 (79.7%) patients were unresponsive to the initial IVIG treatment. Twenty seven (40.9%) patients were received corticosteroid pulse therapy in the acute phase. The maximum CAL z-score in the acute phase, there were not significant differences between corticosteroid administration patients and no corticosteroid using patients (5.1 ± 2.2 vs. 4.9 ± 2.3, \( p = 0.277 \)). The CAL z-score at the end of this study period, there were not significant differences between two groups (2.1 ± 2.0 vs. 2.3 ± 2.3, \( p = 0.432 \)). The ratio of CAL regression in the study period (33.3% vs. 46.2%), the mean interval between the onset of KD and CAA regression (0.6 ± 0.5 vs. 0.8 ± 0.5 years, \( p = 0.209 \)), and the ratio of coronary artery stenosis or occlusion (14.8% vs. 15.4%), there were not significant differences between two groups.

Conclusion: Corticosteroid pulse therapy for KD patients may not be worsened CALs in the acute phase and long-term after the onset.


O.69 Coronary Vessel Wall Imaging By Using Multi-detector Computed Tomography And
Outcomes In Patients Long After Kawasaki Disease: Potential For Risk Stratification

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Background: In acute coronary syndrome (ACS) in adults after Kawasaki disease (KD), acute thrombosis occurs in culprit lesions with calcified intima even in the absence of giant aneurysms (AN) or severe stenosis. Recently, multi-detector computed tomography (MDCT), a non-invasive modality, was shown to have good diagnostic accuracy of detecting IVUS-defined intimal thickening and calcification. We investigated whether MDCT-derived vessel wall lesions are associated with coronary artery lesions (CAL) and outcomes in patients long after KD.

Methods: MDCT was performed and analyzed (Vitrea fX, vs2.0, VITAL) in patients ≥10 years after KD, in which CAL were determined by ultrasound (US) during acute KD and serial CAG (if CAL was detected by US). Any discernible structure under the luminal surface with the CT density with or without areas ≥ 130 Hounsfield units, was defined as a calcified or noncalcified intima. Results: A total of 42 patients (median age 19.7 yo, male 64%, median interval after KD 17.5 y) were recruited and followed-up for 4.0 years (median) (range 0.1 -5.5): 23 (55%) patients have any CAL in any segments, including regressed AN in 42 segments, persistent AN in 27 segments, localized stenosis (LS) in 7 segments; normal coronary artery from the onset was found in 225 segments in total patients. MDCT findings revealed no intimal lesions in 271 segments, 6 non-calcified intima, and 24 calcified intima; Mean (range) value of Agatston calcium score was 140 (0-2247) with zero value in 29 (69%). Normal segments from the onset exhibited no intimal lesions (225/225, 100%); regressed AN exhibited no intima (35/42, 83%), non-calcified intima (2/42, 5%), and calcified intima (5/42, 12%); persistent AN exhibited no intima (11/27, 41%), noncalcified intima (4/27, 15%), and calcified intima (12/27, 44%); all the LSs exhibited calcified intima (7/7, 100%). In the follow-up after MDCT, a 23 year-old patient (calcium score 17) had ACS at the culprit lesion with LS <50% and calcified intima; another 16 year-old patient (calcium score 545) had asymptomatic myocardial infarction at the culprit lesion with persistent aneurysm and calcified intima. Conclusions: Coronary vessel wall imaging by using MDCT may have a potential role for risk stratification of adults after KD.


O.70 Safety and Efficacy of Warfarin Therapy in Kawasaki Disease

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Purpose: Giant aneurysms are managed with combined anticoagulation and anti-platelet therapy, heightening risk of bleeding complications. We sought to describe the safety and efficacy of warfarin for Kawasaki disease (KD) patients (pts) with giant coronary artery aneurysms (CAA, ≥8 mm). Methods: We reviewed the % time in therapeutic range (%TTR); % of INR’s in range; bleeding events, categorized as major bleeding, clinically-relevant non-major bleeding, and minor bleeding; clotting events; INRs ≥5; and INRs <1.5. Results: Our anticoagulation service managed 9 KD pts (5 male), median age 13.2 y (range 7-22 y). INR testing was prescribed weekly to monthly and was done by home monitor (n=6) or lab (n=3). Median length of warfarin therapy was 6.5 y (1.6-12.5). Goal INR was 2.0-3.0 (n=6) or 2.5-3.5 (n=3), based on CAA size and history of CAA thrombosis. All pts were treated with aspirin; 1 was on triple therapy with warfarin, aspirin, and clopidogrel. From 6/2011-6/2014, the median %INRs in range was 62% (34-93%), and median %TTR was 68% (53-92%). INRs >6 occurred in 2 pts (2 events); INRs 5 <6 in 5 pts (9 events); and INRs <1.5 in 5 pts (21 events). During warfarin therapy, 3 major bleeding events occurred in 3 pts: 1 hemorrhage in calf muscle with compartment syndrome requiring surgical clot evacuation (INR 2.5); 1 hemorrhagic ovarian cyst needing hospitalization and Vit K (INR 5.2); and 1 hemopericardium (INR 2.8) 9 days post CABG requiring readmission to the hospital, pericardiacentesis and blood transfusion. There were 2 clinically-relevant non-major bleeding events in 2 pts: 1 hospitalized for bleeding 1 wk after wisdom teeth extraction (INR 6.1) and 1 requiring cauteronization for nose bleeds. Minor

Minor
bleeding events included: a) severe recurrent nosebleeds in 3 pts, causing 4 ER visits (2 pts) and Hgb fall to 7 mg/dL (1 pt, Fe treatment); and b) heavy menses in the 2 post-pubertal females, both treated with oral contraceptives. Four of 9 pts had no bleeding events, and no pt had new CAA thrombosis. Conclusions: Bleeding complications are common in pts on warfarin and aspirin. Despite management by a hospital anticoagulation service, INRs were in range only 2/3 of the time. Studies on oral Factor Xa inhibitors as an alternative to warfarin are needed in this at-risk population.


O.71
Thrombosis and Thromboprophylaxis for Patients with Giant Coronary Artery Aneurysms after Kawasaki Disease: A Study from the North American Kawasaki Disease Registry

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Background: Children with giant coronary artery aneurysms (CAA) after Kawasaki disease (KD) are at substantial risk of thrombosis. There are currently no evidence-based guidelines for optimal thromboprophylactic therapy in these children.

Methods: The North American Kawasaki Disease Registry was queried to identify all patients with giant CAA (maximum coronary artery z-score >10) and their antithrombotic therapy. Freedom from thrombosis was modelled using the Kaplan-Meier method; thrombotic complication rate was calculated per patient-year/month of follow-up.

Results: n=202 patients with giant CAA were included, of whom 28 (14%) experienced either coronary artery thrombosis with or without myocardial infarction. Freedom from thrombotic complications was 92%, 85% and 79% at 3 months, 5 and 10 years after diagnosis, respectively. Non-pharmacological factors associated with increased risk of thrombotic complications included higher maximum coronary artery z-scores (HR: 1.7/+10 SD, p<0.001), higher number of coronary artery branches with giant CAA (HR: 2.6/branch, p<0.001), higher number of discrete CAA (HR: 1.4/aneurysm, p=0.001) and presence of complex CAA (involving the bifurcation or non-discrete; HR: 3.0, p=0.05). A total of 982 patient-years of follow-up were available for analysis (11% low molecular weight heparin (LMWH), 32% warfarin, 57% antiplatelet alone). All patients were maintained on ASA, with 47 patients (23%) also receiving clopidogrel. Patients while on LMWH had the highest event rate, at 1 event per 13 patient-years, compared to 1 per 39 on warfarin and 1 per 33 on no anticoagulant. However, LMWH was predominantly prescribed immediately after the acute phase, which is also the highest risk phase for thrombosis. When limiting analysis to events within 3 months of the acute phase, patients on LMWH had the lowest event rate at 1 per 46 patient-months, compared to 1 per 27 on warfarin and 1 per 33 on no anticoagulant (p=NS).

Conclusions: Current thromboprophylaxis strategies in patients with giant CAA have suboptimal efficacy, and residual thrombosis risk persists. New anticoagulants/antiplatelet agents should be assessed in this population to determine if they provide better, safer and more tolerable thromboprophylaxis.


O.72
The Spectrum Of Cardiovascular Lesions Requiring Intervention In Young Adults After Kawasaki Disease

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**Background:** Coronary artery aneurysms resulting from vascular inflammation associated with Kawasaki disease (KD) in childhood may remain clinically silent until adulthood. Young adults presenting with large aneurysms, unstable angina, or myocardial infarction (MI) following KD in childhood present unique challenges to the interventional cardiologist and cardiothoracic surgeon. We present a range of management issues raised by this patient population.

**Methods:** Participants who underwent cardiovascular interventions were identified from an observational cohort of 154 individuals with a history of KD enrolled in the San Diego Adult KD Collaborative. Of these 154 participants, 63 (40.9%) were originally diagnosed with KD and followed by one of the co-authors (JCB) and were designated as Cohort 1. The remaining 91 participants (Cohort 2) were referred by their physician or self-referred for participation in the study.

**Results:** Of the 154 participants, 20 (12.9%; 2 from Cohort 1 and 18 from Cohort 2) underwent cardiovascular interventions: 9 had percutaneous interventions and 11 had surgery. Twelve participants had been diagnosed with KD in childhood, 7 had a history of a KD-compatible illness in childhood, and 1 had proximal coronary artery aneurysms compatible with KD. Fourteen participants were asymptomatic until experiencing a major cardiovascular event: 8 presented with an acute MI, 3 presented with angina, 1 presented with end-stage congestive heart failure requiring cardiac transplantation, and 2 presented with extremity claudication.

**Conclusions:** Cardiovascular complications in individuals with a history of KD illustrate the following points: 1) Even small to moderate-sized aneurysms that “normalize” by echocardiography in childhood can lead to stenosis and thrombosis decades after the acute illness; 2) Coronary interventions without intravascular ultrasound may result in underestimation of vessel lumen diameter; 3) Failure to assess the extent of calcification may lead to suboptimal procedural outcomes, and 4) Patients with symptomatic peripheral aneurysms may benefit from endarterectomy or resection. Interventional cardiologists should be aware of the complications encountered in this growing population of young adults.

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**O.73**

**Long-term Results Of Percutaneous Transluminal Coronary Rotational Atherectomy For Localized Stenosis Caused By Kawasaki Disease**

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We report the results of percutaneous transluminal coronary rotational atherectomy (PTCRA) for localized stenosis caused by Kawasaki disease (KD). Thirteen male and a female, aged 5 to 29 years (median 13 years), underwent PTCRA and the interval from the PTARA to the latest angiogram ranged from 3 months to 16 years (median 6 years). The target vessels were the left anterior descending artery (3 patients), the left circumflex (2), left main trunk (2) and the right coronary artery (7). The immediate results of PTCRA were successful in all patients, and the mean stenosis degree improved from 86 ± 11% to 36 ± 13%. Five cardiac events occurred within one year (acute myocardial infarction 2, transient complete atrioventricular block 1 and re-PTCRA 2). The survival rate and cardiac event free rate at 15 years after PTCRA were 93% and 71%, respectively. For the graft patency, 4 pts who underwent PTCRA within 10 years old, had asymptomatic occlusion within 1 year. The patency rate at 15 years after PTCRA was 69%, in 10 pts who underwent it more than 10 years old. Cardiac events and restenosis occurred within a year after PTCRA. The results in patients less than 10 years old was poor. If a graft is patent in one year after procedure, long-term patency may be expected in patients more than 10 years old.

**E. Tsuda:** None. **S. Hoshino:** None. **Y. Asaumi:** None. **Y. Hayama:** None. **O. Yamada:** None.
O.74
Statin Alleviates Persistent Coronary Arterial Inflammation Long After Kawasaki Disease - A Serial Fluorodeoxyglucose Positron Emission Tomography Study -

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The patient, 42-year-old male, was suffered from Kawasaki disease (KD) at 4 month of age and left with giant left coronary artery aneurysm (CAA) and occluded giant right CAA. When he visited us at 40 years of age after long interval, a multi-detector X-ray computed tomography revealed persistent giant CAA with 12 mm in diameter at segment 6 with low density area inside of it, stenosis distal to this CAA, persistent giant CAA with 12 mm in diameter at segment 11, and total occlusion of right coronary artery orifice with recanalization. Positron emission tomography using fluorodeoxy glucose (FDG-PET) with co-registration of x-ray computed tomography showed significant FDG uptake around the left coronary orifice of the aortic wall and extending to the proximal left CAA wall with 1.48 of target-to-background ratio, indicating persistent inflammation. He has 2 risk factors of atherosclerosis, dyslipidemia and a history of smoking and, since then he has been placed on 2 mg of oral pitavastatin. With the treatment, his LDL-cholesterol has decreased (105 at baseline vs. 74 mg/dL on treatment) though HDL-cholesterol did not change significantly (31 at baseline vs. 30 mg/dl on treatment). FDG-PET after 2 years of treatment indeed showed alleviation of coronary inflammation with significantly smaller area and lower uptake of FDG on the coronary wall with 1.28 of target-to-background ratio. This case indicates that statin can alleviate persistent coronary artery inflammation long after KD and FDG-PET can be a useful monitoring tool of this process.


O.75
Factors Associated With Illness Impact After Diagnosis Of Kawasaki Disease And Coronary Artery Complications

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Background: Families with Kawasaki disease (KD) experience profound anxiety, part of which is related to uncertainties about the future. We sought to understand the personal and emotional impact of uncertainty for both parents and children with coronary artery complications.

Method: During 2013-14, 31 participants were recruited. Data collection included chart reviews of demographic factors, relevant medical history, investigations, and treatments. Parents and children completed questionnaires (uncertainty, intrusiveness, self-efficacy) and were interviewed. The qualitative data were analyzed for common themes and exemplars in order to complement the quantitative questionnaire data.

Findings: Descriptive data were compared with questionnaire scores to identify factors associated with high, negative impact using univariable linear regression models. High intrusiveness scores among parents were associated with having a child who had previous cardiac catheterization (p =.05), received anticoagulant medications (p = .04), lower education (p = .02 [mother], p = .04 [father]) and income (p = .05), and for those in whom the KD diagnosis was initially missed (p <.001). Higher uncertainty scores among children were associated with absence of chest pain (p = .04) and lower number of echocardiograms (p = .01). Parents’ uncertainty was associated with missed diagnosis (p = .02), higher education (p = .03 [mother]), and higher income levels (p = .01). Self efficacy was assessed among children >10yrs. While 3 subscales (academic, social, emotional) were analyzed, the overall self-efficacy scores increased with the presence of chest pain (p = .003) and increased aneurysms z-score (p = .03). Qualitative analysis revealed 3 main themes: 1) staying normal while hyper-vigilant; 2) optimism amid relentless worry; and 3) healthy present for a hopeful future. The themes involved contrasting sentiments, each of which was held by the child or the parent but
with varied levels of expression. 

**Summary:** Negative illness impact is associated with a more intense medical experience. Both children and parents have concerns about future outcomes and management. Coping with uncertainty involves achieving a balance between anxieties and a present and forward focus.

**001**

**Rashless Kawasaki Disease (KD): Colorado’s Experience**

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**Objective:** Published studies describe Incomplete KD, but rashless KD has not been well characterized. We describe a 10 year experience with rashless KD patients, diagnosed based on the presence of a compatible illness and coronary artery lesions (CALS).

**Methods:** We prospectively collected cases of rashless KD with CALs diagnosed at Children’s Hospital Colorado from 7/1/2004-6/30/2014. Patient charts were reviewed for demographic, clinical, laboratory, and diagnostic information.

**Results:** 11 patients were identified (median age 3.7 yrs), representing 10.3% (11/107) of all KD patients with CALs diagnosed during the same time period. Diagnosis was made on median day of illness (DOI) 8 (range 4-17 days), and patients had a median of 4 (range 2-7) healthcare contacts prior to diagnosis. All patients (100%) had the presence or history of conjunctival injection and 8/11 (72.7%) had oral changes. Five patients had only 2 major clinical features in addition to fever; 1 patient had one. All patients had very elevated inflammatory markers. Infectious Disease consultants suspected KD and recommended treatment prior to echocardiogram (ECHO) results in 8/11 (72.7%), recommended treatment if ECHO abnormal in 2/11 (18.1%), and in 1/11 (9.2%) KD was thought to be unlikely, but the diagnosis was made by ECHO.

**Conclusions:** 10.3% of KD patients with CALs at our institution presented without a rash. As rash is often considered a defining characteristic of KD, some children with rashless KD are likely not being identified and treated. Providers should consider the diagnosis of KD in patients with unexplained fever, conjunctivitis, and elevated inflammatory markers.

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**P. Jone:** None.  
**J. Davidson:** None.  
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**002**

**Historical Trends in Kawasaki Disease over Three Decades in a Single Institution**

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**Purpose:** Kawasaki disease (KD) awareness and therapy have evolved since its description in 1967. We explored historical trends since 1984 in patients (pts) treated for KD at a single institution. **Methods:** Inclusion criteria were 1) first episode of KD, and 2) treated with IVIG within 3 weeks of illness onset. Exclusion criteria were 1) evaluation solely for a second opinion, and 2) presence of congenital heart disease. We reviewed age at diagnosis, sex, race, presence of complete vs. incomplete (fever + <4 clinical criteria), days of fever at initial IVIG treatment, and incidence of retreatment. Changes in pt characteristics over time were evaluated using tests of trends.

**Results:** Of 1739 pts, 1133 met eligibility criteria. Race included 61% White, 10% Black, 11% Asian; 6% other, and 12% unknown. At diagnosis, 16% were age <1 years (yrs), 58% were 1-5 yrs, 24% were 5-12 yrs, and 2% were ≥12 yrs. The median age at fever onset was 3 yrs and has not changed significantly over time. Male to female ratio was 59% to 41% and was stable over time. Median fever duration before IVIG treatment in the whole cohort was 7 days. Within the complete vs. incomplete KD groups, illness day at treatment was stable over time. However, median days of fever before IVIG treatment...
were lower in pts with complete vs. incomplete criteria (6 vs. 8 days, respectively, p<.001). The % of pts treated with IVIG for incomplete KD increased significantly over time. Before 1989, only 1 pt (2%) was treated with IVIG for incomplete KD. From 1990-1994, 11 pts (15%) pts had incomplete criteria, whereas from 2010-2014, 45 pts (27%) received IVIG treatment with incomplete clinical criteria (p=.001). The incidence of retreatment with IVIG also increased, from 9% (1984-1989) to 23% (2010-2014, p<.001). The use of adjunctive therapies (i.e., steroids, cyclosporine, cytoxan, abciximab and/or infliximab) were documented in 104/1133 pts (9%) and increased over time (p<.001).

**Conclusions:** At a single center over 3 decades, treatment of incomplete KD, as well as retreatment with IVIG and use of adjunctive therapies have become increasingly common. Pts who had incomplete diagnostic criteria received IVIG later in their illness. Future studies should assess whether these secular trends have improved outcomes in pts with KD.


003

**Kawasaki Disease in Algerian Children: A Clinical Study**

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**Background:** Kawasaki disease (KD) is an acute multisystem vasculitis of unknown etiology that occurs predominantly in infants and young children. The incidence of KD is increasing worldwide; however the epidemiological data available for Algerian patients remains insufficient

**Objective:** To describe the demographic, clinical, and laboratory features of Algerian children with KD and to highlight the practical difficulties.

**Methods:** This retrospective study included children admitted with Kawasaki disease at the only pediatric tertiary referral hospital in Algiers over a period of 8 years from January 2006 to December 2013. **Results:** 108 patients with KD, with a mean age of 31 months (range: 8-84 months) were identified. There were 63 boys and 45 girls (sex ratio: 1.4). The clinical data were similar to previously described studies, with some difference: the cervical lymphadenopathy was less frequent: 25% (27/108). 22% (24/108) of children had evidence of cardiac complications: 20% (22/108) had coronary artery abnormalities; one child had mitral regurgitation, one had pericardial effusion. Of the 22 children with coronary abnormalities, 9 had coronary dilatation, 13 had coronary aneurysms (10 small and medium, 3 giant). These abnormalities regressed in 13 cases on follow up. During this period, catheter and surgical coronary intervention were performed to treat coronary ischemia in one patient, two years after onset. The only independent variable for prediction of coronary involvement was fever duration at the time of initial presentation (p=0.016). The therapeutic used in this study included an immunoglobulin treatment for only 63% (69/108) of the children, half of which received it within the first ten days of the onset of the disease.

**Conclusion:** This work demonstrates the necessity of a registry that will allow better appreciation of the incidence of this disease and improve the diagnosis and treatment of KD in Algeria

H. Boudiaf: None. M. Achir: None.

004

**Analysis of West Coast Atmospheric Circulation Patterns and Kawasaki Disease “Dry Spells”**

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Ctr San Diego, San Diego, CA; Marian E. Melish, , Kapiolani Medical Ctr for Women and Children., Honolulu, HI; David E. Michalik, Miller Children’s and Women’s Hosp Long Beach, Long Beach, CA; Sameer Pathare, Children’s Hosp of Orange County, Orange, CA; Michael Portman, Seattle Children’s Hosp, Seattle, WA; Heather Schultz, Mary Bridge Children's Hosp and Health Ctr, Tacoma, WA; Margaret Trost, Univ of Southern California, Los Angeles, CA; Stephanie A. Yee-Guardino, The Permanente Medical Group, Inc., Sacramento, CA

Background: Tropospheric winds from northeastern China have been linked to fluctuations in Kawasaki disease (KD) cases in Japan. These winds may carry aerosols that trigger KD in genetically susceptible children. We investigated whether reduced numbers of KD cases were linked to large scale circulation patterns affecting the U.S. West Coast.

Methods: KD cases with either date of onset of fever or date of hospitalization (PHIS, Pediatric Health Information System) were obtained from 5 sites from Seattle to San Diego from 1995-2014. Six days were subtracted from date of hospitalization to approximate date of onset. For each site, periods from December-March were identified for which there were no KD cases for an interval of ≥10 days, called “KD dry spells”. Daily NCEP-NCAR atmospheric Reanalysis 700hPa height anomalies were used to represent the atmospheric circulation.

Results: From 27-48 dry spells were defined for each site. Composites of atmospheric circulation from Day -20 to Day +10 relative to first day of a dry spell were created for each study site. The atmospheric circulation preceding the KD dry spell featured a higher than normal pressure center (results in weakened onshore flow) either offshore over the North Pacific or directly over the site. The circulation anomalies were statistically significant, and unlikely to have occurred by chance. The dry spell pattern intensified and persisted over several days. The strongest anomalous atmospheric circulation (and associated blocked wind flow) occurred between Day -6 to -1 relative to the start of the dry spell. A similar pattern was shared by 4 of the 5 sites. One site featured strong high pressure anomalies > 6 days before the KD dry spells, but only a weak anomaly in the Day -6 to-1 interval preceding the dry spell.

Conclusion: This analysis reinforces results from previous studies of KD case fluctuations in Japan wherein anomalous KD activity was associated with particular wind flow patterns. The circulation patterns associated with the West Coast KD “dry spells” suggest that reduced wind flow from the North Pacific results in reduced KD occurrences. These results support the hypothesis that a KD agent is transported by winds, possibly from a shared source region with transport of the agent across the Pacific.


005
Update of 2011-2014 Kawasaki Disease Surveillance in Emilia Romagna, a Northern region of Italy.

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We updated our regional database for KD patients from 2011 to 2014 to investigate differences in epidemiological, clinical and outcome data between 2011-2014 pts and those diagnosed between 2000-2010 in Emilia Romagna. We had 77 KD patients during last 4 years ( vs 81 pts during 2000-2010), mean age at diagnosis 40 months+ 36.4 (vs 31.2 mths ), 10% were younger than 6 months at diagnosis (vs 14%), male were 60% (vs 59%). Seasonality was as follows: spring 27% (vs 33%), winter 25% (vs 28%), autumn 25% (vs 26%), summer 23% (vs 14%). Clinical presentation was complete in 69% (vs 74%),
incomplete in 30% (vs 26%), atypical 1% (vs 0%). IVIG responder were 77% (vs 67%), non responders 16% (vs 12%), late treatment 2% (vs 12% P 0.002), not treated with IVIG 5% (vs 9%). 18/77 pts (vs 7 of 2000-2010, P 0.004) had alteration of ALT (v > 45 U/l) and AST (v > 55 U/l) and among those with transaminases alteration 8% (vs 4 pts) had cholestasis. Coronary arteries anomalies (CAA) were present in 15% (9% ectasia and 6% (vs 2%) aneurysms (mean age 12.6 months, 2 pts non responders to standard therapy, 1 pts with late treatment, 1 pts not treated, and 1 pts well treated. The 2 patients who developed giant aneurysms were both non responder to standard therapy, 1 pts had associated cholestasis.

Conclusion: during the last four years we observed an higher number of diagnosis of KD than 2000-2010; incomplete and atypical cases, and non-responder pts were more frequent but we noted a decreased of pts not treated or delayed treated; more cases of cholestasis associated to KD and an increased number of patients with aneurysms.


006 Coronary Artery Involvement In Children With Kawasaki Disease In A Northern Region Of Italy In 13 Years

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Objective: to evaluate the incidence of coronary anomalies (CAA) and risk factors for coronary involvement in children with KD from 2000 through 2013 in Emilia-Romagna.

Design: an 11-centers retrospective study was conducted using data from 132 patients diagnosed with KD.

Results: during the acute phase, CAA developed in 13/132 pts (9.8%): 2 pts had isolated ectasia of right coronary artery (RCA), 10 pts had ectasia of left anterior descending CA (LAD), 1 pt had aneurysm of LAD, 1 pt had ectasia of circonflex CA (CX). During the subacute phase 14/117 pts (11.9%) presented CAA: 3 had aneurysm of LAD, 1 had aneurysm of LAD and RCA, 1 had isolated ectasia of RCA, 9 had ectasia of LAD. During the convalescent phase CAA were detected in 18/83 pts (21%); 3 had aneurysm of LAD and RCA, 2 isolated aneurysm of LAD, 12 ectasia of LAD. Out of 6 aneurysms detected in the convalescent phase developed in the subacute stage. Univariate analyses identified WBC and RBC in the subacute phase, and PLT in chronic phase as predictors of chronic CAA (respectively p 0.04, 0.013 and 0.002). A multivariate logistic regression analysis revealed that only PLT of the chronic stage was predictor for chronic CAA. ROC curve for PLT identified a value superior to 652000/mm3 to be the cut off value for CAA, with an 72% sensitivity and 87% specificity. Incomplete or atypical clinical presentation was correlated with CAA (p 0.02). Younger age (< 1 yr) at diagnosis, seasonal distribution, IVIG responsivness, race, elevation of ALT, percentage of neutrophil, hemoglobin, CRP and ESR, albumin and sodium were not correlated with risk for CAL.

Conclusions: atypical/incomplete clinical presentation, higher WBC and RBC in the subacute phase and PLT of the convalescent phase were predictors of CAA in our region, while blood exams of the acute stage, IVIG responsivness, sex and younger age were not.


007 French observatory of Kawasaki disease in adults: 24 observations.

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Introduction
Kawasaki disease (KD) is a vasculitis that occurs mostly among children and exceptionally in adults. We report data from a French observatory of adult KD.

Patients and methods:
Adult patients diagnosed with KD in 16 French centers were included. Patients were classified as complete KD or incomplete KD according to RIKDC or probable KD.

Results:
We included 24 patients with a median age of 29 years (22-39) and a sex ratio (M/F) 2.42. 12 complete KD, 9 incomplete KD and 3 probable KD without any other cause. Time to diagnosis was 13 days (10-20.5). Main events were: fever (100%), extremities changes (21/24, 87.5%), rash (22/24, 92%), conjunctivitis (16/24, 66%), cheilitis (15/24, 63%), strawberry tongue (11/24, 46%), adenopathy (10/24, 42%), cardiac abnormalities (11/24, 46%), cardiogenic shock (n = 1), myo-pericarditis (n = 3) and left heart failure (n = 1).

Median CRP was 228mg/L (166-311), SGOT: 68 IU/L (51-139), SGPT: 125 IU/L (69-190), platelets 372 G/L (209-630) and leukocytes 16 G/L (8.3-20).

Cardiac involvement was researched in 23 patients (96%) by achieving: echocardiography (20/24), coronary scanners (6/24), coronary angiography (5/24), cardiac MRI (2/24) and stress tests (2/24).

An arteritic vascular disease was found in 11 patients (46%): coronary aneurysms (8/24, 33%), coronary arteritis (10/24; 42%) and peripheral arteritis (2/24, 8.3%) with acute lower limb ischemia (1/24, 4.2%) and splenic infarction (1/24, 4.2%).

Patients received: intravenous immunoglobulin (17/24, 71%); aspirin (21/24, 88%).

After 6 months, it persisted 5 aneurysm (20.8%). Complications noticed during the last follow-up were: heart failure (1/24, 4.3%), aneurysm (3/24, 12.5%).

Conclusion:
The adult KD is a rare disease that can have bad prognosis in short or long term and leave irreversible damage. The high rate of cardiac complication could be due to the long diagnosis delay, the absence of the gold standard treatment in 30% of cases or a selectional bias due to the difficulty to diagnose this disease in adulthood.


008
Kawasaki disease in the Maghreb community in Quebec

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Background: The real incidence of Kawasaki disease (KD) in the Maghreb countries (Morocco, Algeria, and Tunisia) is unknown. It is estimated low according to the literature. However, the number of Magrebi children living in Quebec (Qc) affected by KD seems important. We sought to determine the incidence of KD among Magrebi children in Qc, Canada, and to study its epidemiological and clinical features.
and to clarify possible risk factors related or superimposed to their immigration.

Methods: A retrospective study of KD in Maghrebi children living in Qc (n=24) (1996-2013), compared to reports from Fes, Morocco (n=23) a doctoral thesis published in 2010 (2001-2009) and from Tunisia (n=31) collected in five university hospitals with four from the Great Tunis and one from Nabeul city (1996-2013). There are no reports available from Algeria. The "country of origin" specific population in the Province of Qc was obtained from Statistics Canada.

Results: The annualized incidence rate (AIR) of KD among Maghrebi children in Qc was 9.58/100,000 children under 5 years (Standard-Denominator (SD)). This is 6 times higher in Qc (5.57/SD and 19.02/SD among Tunisian and Moroccan descents) vs Tunisia (Nabeul Governorate) and Morocco (Fes) (0.95/SD and 3.15/SD). Personal and family history of allergy were significantly higher in Qc 42% (10/24) and 75% (18/24), respectively, whereas these features were reported near 0% in both reports from Morocco and Tunisia. The prevalence of incomplete KD criteria was relatively high in the 3 series 46% (11/24) in Qc vs 43% (10/23) and 35% (11/31); (p=NS). Diagnosis was late (gt day 10 of fever) in 1/24 (4%) in Qc vs 7/23 (30%) in Morocco and 11/31 (35%) in Tunisia; (p 0.01). IVIG were administered in the acute phase to all patients in Qc, 5/23 in Morocco and 28/31 in Tunisia. However coronary complications were more common in Qc 42% (10/24) vs 22% (5/23) vs 19% (6/31) (p=0.02). Aneurysms were significantly associated with the incomplete form in the 3 groups (p=0.01).

Conclusions: The observed AIR of KD in the Maghrebi community in Qc is higher than the countries of origin where underdiagnosis is possible. Atopy may still be a risk factor in Qc. The coronary artery disease seems linked not only to therapeutic delay but also to the underlying terrain.

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009 The Japan Environment and Children's Study and Kawasaki disease

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 [Background] The Japan Environment and Children's Study (JECS) is a nation-wide birth cohort study involving 100,000 parent-child pairs that was conducted by the Japanese Ministry of the Environment. This study was started in 2011 to evaluate the effect of various environmental factors on children's health and development. Health outcomes and exposure measurements will continue until the participating children become 13 years old.

 [Method] Exposure to environmental factors was assessed by chemical analyses of bio-specimens (blood, cord blood, urine, breast milk, and hair), household environmental measurements, and computational simulations using monitoring data, as well as questionnaires. The JECS's priority outcomes include reproduction/pregnancy complications, congenital anomalies, neuropsychiatric disorders, immune system disorders, including Kawasaki disease (KD), and metabolic/endocrine system disorders. Genetic factors, socioeconomic status, history of infection, and lifestyle factors were also examined as covariates and potential confounders.

 [Results] Some of the questionnaires for children under 2 years old have already been collected. The numbers of patients with KD according to age were as follows: 14/71,133 (0.02%) between 0-6 months old, 102/51,351 (0.2%) between 6-12 months old, 71/34,595 (0.21%) between 12-18 months old, and 20/20,995 (0.1%) between 18-24 months old. According to these results, the estimated incidence of KD in children younger than 2 years old could reach more than 0.5%, but this number may increase after further collection of questionnaires. We also conducted a secondary survey regarding KD patients, including family history, clinical symptoms, laboratory data, treatment, and outcome.

 [Conclusion] Recently, similar birth cohorts to JECS were already initiated in many countries, but this is the first large-scale birth cohort focusing KD. The results of this cohort may shed new light on the environmental pathogenesis of KD.

010
Effect of coincident infections in acute Kawasaki disease

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We investigated prevalence of coincident infections in acute Kawasaki disease (KD) to know the possible effects of infections on diagnosis of KD, clinical course, therapy decision and coronary outcomes. Single center consecutive 344 KD patients hospitalized in our institution, between January 2009 and December 2013 were retrospectively analyzed. Patients those were positive for bacterial culture, rapid antigen tests or elevated levels of pathogen specific antibodies were counted as KD patients with infection. Pathogen unproven patients those presented with apparent respiratory or gastrointestinal symptoms regarding infections were also counted as KD patients not to underestimate number of patients with suspected infections. Overall, 125 KD patients were grouped as KD patients with infection (Group1). Group1 included 125 patients with 73 upper respiratory tract infection, 21 bronchitis, 7 pneumonia, 3 acute otitis media and 21 gastroenterocolitis, respectively. Remaining 219 KD patients were grouped as KD without infection (Group2). Appropriate antibiotic or antiviral treatments were done for each pathogen proven infection. Distribution of age and sex, day of admission, diagnosis and treatment, prevalence of initial treatment regimen and rate of additional therapy, duration of fever, laboratory findings except serum albumin value, and coronary outcomes were similar between the groups. We showed that presence of coincident infections have no effects on clinical course, treatment decision and coronary outcomes on KD.


012
Wind Patterns are not Associated with Kawasaki Disease in Canada

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Introduction: Previous wind pattern studies have suggested that the etiologic and/or triggering agent for Kawasaki disease (KD) originates from Central Asia and that westward tropospheric winds are associated with the incidence pattern in Japan. This hypothesis has not been formally tested elsewhere. Should it be correct, it follows that incidence patterns should be similarly associated with North/North-West winds in Canada.

Methods: We queried the Canadian hospital discharge database (Canadian Institute for Health Information) for hospital admissions associated with a discharge diagnosis of KD from 2004 through 2011; only acute admissions were included. Hourly weather data, including wind direction, was obtained from 9 weather stations across Canada situated closest to clusters of cases. The number of new KD admissions per day and per weather station was calculated. Wind direction was divided in 8 different quadrants covering 45° regions starting with 0°. A Poisson regression model for count data, adjusted for repeated measures (9 measures per day) was used to determine whether wind patterns were associated with incident cases. A number of separate models were tested using theoretical incubation periods of 0, 7, 14 or 21 days.

Results: A total of 3363 KD cases were assigned to one of 26,283 time/space periods for which wind direction was available. Wind direction was not associated with incidence patterns in any of the 4 incubation models: incubation time 0 day (global wind pattern effect chi-square: 4.28, p=0.75). 7 days (chi-square: 5.08, p=0.65), 14 days (chi-square: 7.32, p=0.29) or 21 days (chi-square: 4.74, p=0.69). Focusing on North/North-West wind patterns also failed to show a significant association in all models: incubation time 0 day (+0.0021 (0.0151) cases/day, p=0.89), 7 days (-0.0071 (0.0142) cases/day, p=0.62), 14 days (+0.0009 (0.0148) cases/day, p=0.95) or 21 days (+0.0073 (0.0156) cases/day, p=0.64). Results were similar when stratifying Eastern vs. Western Canada and when each weather station was...
Elevated Atmospheric Levels of Environmental Allergens Might be Associated with Decreased Risk of an Immunologic Reaction to an Etiologic Trigger in Kawasaki Disease

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Introduction: There is considerable interest in identifying potential etiologic and/or triggering agents for the severe immune response associated with Kawasaki disease (KD). The presence of environmental allergens might modulate the odds of triggering such a response despite those allergens not being direct etiologic agents.

Methods: We queried the Canadian hospital discharge database (Canadian Institute for Health Information) for hospital admissions associated with a discharge diagnosis of KD in 2011 in the Greater Toronto Area. Atmospheric levels of pollens (35 species), spores (24 species) and fungi (27 species) were measured by Aerobiology Research Laboratories (Nepean, Ontario). A number of separate models were tested using theoretical incubation periods of 0, 7, 14 or 21 days. Correlation between KD cases and atmospheric levels of environmental allergens were assessed in linear regression models.

Results: n=145 patients with KD were included. The highest levels of environmental allergens were in summer months. Overall atmospheric pollens levels were not associated with the KD cases (total pollen count r=0.04, p=0.54); there was no consistent pattern of association with specific pollens. However, higher levels of spores were associated with a decreased prevalence of KD for all spore species (r=-0.23, p<0.001). Associations were observed for 6 of 19 specific species detected (p<0.001), including leptosphaeria, ascospores, oospore, coprinus/coprinellus, basidiospores, and uredinales. The same pattern was observed for all fungi species (r=-0.17, p=0.009). Associations were observed for 5 of 26 specific fungal species (p=0.002), including alternaria, cladosporium, epicoccum, fusarium, and fungi imperfecti. There were no discernable patterns regarding a potential incubation period.

Conclusions: High levels of environmental allergens, particularly fungus and spores, were associated with lower incidence of KD. These results suggest that environmental allergens, even if they are not etiologic agents for KD, might modulate the threshold necessary for the actual etiologic/triggering agent. Atmospheric levels of environmental allergens might be partly responsible for the KD seasonality patterns observed in Canada.

Epidemiology of Kawasaki Disease in Canada (2004-2011)

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Introduction: We have previously documented in consecutive triennial systematic surveillances a rise in the incidence of KD in Ontario, Canada between 1995 and 2004 followed by a stabilization at 24-26 cases per 100,000 children <5 year old per year between 2004 and 2009. Previous studies have been limited to the province of Ontario; we sought to determine the incidence of KD across Canada and by province.

Methods: We queried the Canadian hospital discharge database (Canadian Institute for Health Information) for hospital admissions associated with a discharge diagnosis of KD (either primary or secondary) between 2004 and 2011. Multiple admissions for a given patient were not counted as separate incident cases unless >2 months from the original admission
and associated with IVIG treatment. Denominators were derived from population data from the 2001, 2006 and 2011 Censuses.

**Results:** The annual incidence of KD during the study period was 21.9, 6.8 and 1.1 cases per 100,000 children <5 years, 5-9 years and 10-14 years old, respectively (4,340 cases total). Stratification by region showed the lowest incidence to be in Saskatchewan (11.8/100,000 children <5 year old), followed by Manitoba (17.3), Alberta (17.7), Quebec (18.1), British Columbia (20.6), Atlantic Provinces (22.5) and finally Ontario (27.5, similar to that noted on previous systematic surveillances). The incidence remained stable over the study period, confirming the plateau reached in the previous systematic Ontario surveillance between 2004-2009. An increased incidence was noted for children <5 years old, male gender and winter months. There was a moderate correlation between proportion of the provincial population of Asian descent and KD incidence (r=0.58). Coronary artery aneurysms affected 5.8% of patients, and 1.9% experienced major cardiac complications or had cardiac interventions.

**Conclusions:** The previous increase in the incidence of KD has plateaued, indicating that the true annual incidence fluctuates between 20-22 and 24-27 cases per 100,000 children <5 years for Canada as a whole, and 24-27 cases for the province of Ontario. Differences in annual incidence observed between provinces remain to be explained, but may reflect racial, genetic or environmental factors.

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**015 Multicenter Kawasaki Disease Study In Children Of Argentina**

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**INTRODUCTION:** Kawasaki disease (KD) is a vasculitis that affects vessels of small and medium caliber.

**OBJECTIVES:** 1 Determine clinical and epidemiology of KD in children in 22 pediatric referral centers in Argentina. 2 Identify risk factors for coronary complications (CC).

**MATERIAL AND METHODS:** A retrospective and analytical study from 01/01/2010 to 31/12/2013. Variables: age, sex, heart rate (HR), clinic features, erythrocyte sedimentation rate (ESR), C reactive protein (CRP), leukocytes (Gb), neutrophils, hemoglobin (Hb) and CC. Color Doppler echocardiography: acute phase and 4-6 weeks.

**RESULTS:** Subjects: 191, age (Md) 29 months (R: 2-144). Ratio v / m: 1.8 / 1. Clinical: fever 100% (191/191) more frequent and adenopatía: 57% (110/191) less frequent. CC: 15.7% (30/191). Mortality: 0.52% (1/191 cases). Increased risk of CC: leukocytosis> 20,000 / mm3 Odds ratio (OR) = 4.235 (95% CI 1704-10529). Hematocrít <30, OR = 6.042. (95% CI 2163-11814) p <0.0002; Hb <10 OR = 5.056 (95% CI 2163-11814) p 100 mm / 1h OR = 3.725 (95% CI 1642-8447) p 100 mg / dl OR =
6.417. (95% CI 2441-16869) p <0.0002 and other heart affections. OR = 7.964. (95% CI 2459-25794) p <0.0010. Children from the West of the country have 2.7 times greater risk of CC compared to the rest.

CONCLUSIONS: Increased frequency in males. Increased risk of CHD in subjects from western Argentina. Low mortality. Increased risk of CC: low hematocrit and hemoglobin; leukocytes, neutrophils, ESR, CRP, FC, high, Presence of other heart alterations and more days of fever at the time of establishing of treatment.

Risk factors for coronary involvement

<table>
<thead>
<tr>
<th>Age (MD)</th>
<th>Days of fever (MD)</th>
<th>FC (MD)</th>
<th>VSG (MD)</th>
<th>OR (MD)</th>
<th>Hem (MD)</th>
<th>Ab (MD)</th>
<th>Neutropenia (MD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group 1: Without CC</td>
<td>29.5</td>
<td>6.81</td>
<td>110</td>
<td>68.59 mm/h</td>
<td>117.71 mg/dl</td>
<td>33.01</td>
<td>10.97</td>
</tr>
<tr>
<td>Group 2: With CC</td>
<td>27</td>
<td>9.17</td>
<td>130</td>
<td>93.34 mm/h</td>
<td>112.73 mg/dl</td>
<td>30.65</td>
<td>9.92</td>
</tr>
</tbody>
</table>


016
A Clinical Study Of Older Children With Kawasaki Disease

Yukako Nagamori, Kitasato Univ Sch of Med, Kanagawa, Japan; Yoshihito Ogihara, Kayoko Sato, Ebina General Hosp, Kanagawa, Japan; Takesuke Ebato, Kitasato Univ Sch of Med, Kanagawa, Japan; Kiyotaka Otani, Shinya Nakamura, Sagamihara Cooperation Hosp, Kanagawa, Japan; Kastunori Minoura, Ebina General Hosp, Kanagawa, Japan; Shohei Ogata, Masahiro Ishii, Kitasato Univ Sch of Med, Kanagawa, Japan

Background: Kawasaki disease (KD) patients exhibiting a disease onset past infancy are likely to receive a delayed diagnosis, as it takes time for all major symptoms to manifest and the disease also includes many non-typical features. Most general pediatricians and infectious disease specialists may not consider KD in the differential diagnosis among schoolchildren.

Objective: To examine the clinical features of KD in patients with school-age onset.

Methods: Among a total of 650 patients who received a diagnosis of KD in groups Department of pediatrics, Kitasato University School of Medicine, Sagamihara Cooperation Hospital and Ebina General Hospital over the seven-year period from April 2007 to March 2014, we investigated schoolchildren 7 years of age or older. Using the patients’ medical records, we retrospectively assessed data for sex, age, duration of illness, symptoms, treatment effectiveness and coronary artery lesions.

Results: Fourteen (2.2%) schoolchildren were identified (male: n=7, 50%). The median age was 8 years (oldest age: 12 years). The incomplete type was diagnosed in 4 cases (29%), and the typical type was diagnosed in 10 cases (71%). The median duration of illness was 5 days (range: 3-12 days). Five patients (36%) were diagnosed with lymphadenitis at the initial diagnosis. Two patients with Mycoplasma pneumonia and acute appendicitis received a delayed diagnosis of KD. Their symptoms included gastrointestinal symptoms, joint pain with headaches and muscle pain. Nine patients (64%) exhibited membranous desquamation. Two of these patients displayed swelling of the hands and feet at diagnosis. All 14 patients were first treated with intravenous immunoglobulin therapy (IVIG: 2 g/kg); only one patient was resistant. Two patients (14%) were diagnosed with transient coronary artery dilatation; however, no patients had coronary aneurysms. Conclusions: KD with a school-age onset is rare; however, the incidence of cardiovascular complications in such cases has been reported to be high. Therefore, providing an early diagnosis and appropriate therapy is necessary. Physicians should consider the possibility of KD in school-age children who present with a persistent fever.


017
Environmental Epidemiology of Kawasaki Disease
**ABSTRACTS**

**Poster Abstract Presentations**

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**Sunita O’Shea**, Cedric Manlhiot, Michael Labelle, Heming Bai, Bailey Bernknopf, Nita Chahal, Catherine S. Birken, Brian W. McCrindle, The Hosp for Sick Children, Toronto, ON, Canada

**Background:** The etiology of Kawasaki disease (KD) is commonly described as an exaggerated immune response to an environmental or infectious trigger in developmentally, immunologically and genetically susceptible children. The trigger for KD has not yet been identified.

**Methods:** Patients with newly diagnosed KD (n=73) were enrolled within 6 weeks of KD diagnosis. Control subjects (n=65) were enrolled during pediatric annual visits and from friends of enrolled KD patients. All participants completed an extensive questionnaire about medical history, family and environment. Geographic localisation software characterized the participants’ neighborhoods. A hypothetical scenario was used for control patients to simulate similar recall bias to that of the KD patients.

**Results:** There were no differences in age, gender, allergies, child and family medical history or recent vaccination. Children with KD were more likely to be unwell prior to KD symptom onset than controls, including fever, stomach pain, lethargy, jaundice, loss of appetite and irritability, but not infectious disease symptoms (16% vs. 21%, p=0.49). Infectious symptomatology developed concurrently to classic KD symptoms. Children with KD had less exposure to environmental allergens and were more likely to be exposed to chemical irritants.

**Conclusions:** The presence of symptoms for up to 1 month before onset of KD may suggest that a preceding illness/environmental agents may alter barriers to entry/exposure or prime an immunologic reaction to an etiologic trigger. Children with fewer allergen/infectious exposures and chronic chemical exposure may be immunologically more susceptible.

<table>
<thead>
<tr>
<th></th>
<th>KD patients</th>
<th>Controls</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Asthma origin</td>
<td>10%</td>
<td>11%</td>
<td>0.01</td>
</tr>
<tr>
<td>Clinical signs, symptoms and infections exposure</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Child being unwell 4-11 days prior to symptoms onset</td>
<td>43%</td>
<td>29%</td>
<td>0.04</td>
</tr>
<tr>
<td>Child being unwell 1-7 days prior to symptoms onset</td>
<td>50%</td>
<td>39%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Household member ill 2-4 weeks before KD symptoms onset</td>
<td>25%</td>
<td>8%</td>
<td>0.01</td>
</tr>
<tr>
<td>Respiratory symptoms after onset of KD symptoms</td>
<td>25%</td>
<td>6%</td>
<td>0.004</td>
</tr>
<tr>
<td>Diarrheal symptoms after onset of KD symptoms</td>
<td>36%</td>
<td>5%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Joint and muscle pain after onset of KD symptoms</td>
<td>60%</td>
<td>11%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Exposure to environmental allergens in daily life</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Activities with other children -3 days/week</td>
<td>27%</td>
<td>38%</td>
<td>0.02</td>
</tr>
<tr>
<td>Neighborhood with low tree density</td>
<td>35%</td>
<td>15%</td>
<td>0.01</td>
</tr>
<tr>
<td>Have household pets</td>
<td>35%</td>
<td>57%</td>
<td>0.01</td>
</tr>
<tr>
<td>Exposure to chemical irritants</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recently constructed housing (&lt;10 years old)</td>
<td>48%</td>
<td>16%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Living near industrial area</td>
<td>44%</td>
<td>22%</td>
<td>0.007</td>
</tr>
<tr>
<td>Family use aerosols in the home</td>
<td>44%</td>
<td>27%</td>
<td>0.05</td>
</tr>
<tr>
<td>Family use chemical fertilizer on their lawn</td>
<td>38%</td>
<td>17%</td>
<td>0.01</td>
</tr>
</tbody>
</table>

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**S. O’Shea:** None. **C. Manlhiot:** None. **M. Labelle:** None. **H. Bai:** None. **B. Bernknopf:** None. **N. Chahal:** None. **C.S. Birken:** None. **B.W. McCrindle:** None.

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**018 Seasonal Characteristic Of Kawasaki Disease With The Onset At The Different Seasons**

**Yukie Ozeki**, Fumiya Yamada, Tsuyoshi Kishimoto, Saitama Inst of Public Health, Saitama, Japan; Yosikazu Nakamura, Dept of Public Health, Jichi Medical Univ, Tochigi, Japan

**Background**

Kawasaki disease (KD) has been diagnosed in more than 60 countries. Seasonal trend of the patients with KD is observed in many countries. Little is known about the difference between the patient groups in the term of high incidence.

**Objective**

The aim of this study was to characterize the two patient groups during the winter and summer seasons in Japan.

**Methods**

Epidemiologic characteristics were compared between January and July, through the 22th nationwide survey included patients who visited hospitals during 2011-2012. The proportions of survey items were observed by age-adjustment.

**Results**

The total number of patients during 2011-12 was 26,691, the number of patients was 2812 in January and 2302 in July, and the male/female ratio was 1.4, respectively. The patients <3 years accounted for 66% of each group (1854/2812, 1530/2302). The proportion of <8 months of age was 13.0% (365/2812) in January, 17.8% (409/2302) in July, that of 15 months to 3 years was 38.8% (1092/2812), and 33.5% (771/2302). Concurrency with the diagnostic guidelines was examined, the typical
cases in July were 1.6% lower than in January, and the suspected cases were 1.3% higher than in January. The suspected cases of less than 4 principle symptoms had 5.3% higher than in January. The treatment cases with γ-globulin started within 5 days of illness were 2.2% less than in July. The cases of cardiac sequelae (giant aneurysm, aneurysm, dilatation, and stenosis) were 0.3% higher than in July. The cases of serum albumin concentration less than 3.2g/dL were 3.6% higher than in July. The percentage of occurrence cardiac sequelae in this class was 9.5% higher than in July.

Discussion
The difference in age distribution in the two patient groups diagnosed in January and July was observed. The symptom had a slight difference, too. These result do not contradict a hypothesis that onset of KD is concerned with plural infections with different seasonal trend and targeting for the specific age. The association between low levels of serum albumin and cardiac sequelae has been known. The association between this class and the patients in the specific season will be clear in future epidemiologic study.

Conclusion
This study clarified part of the characteristic of the patient diagnosed in the different seasons.

Y. Ozeki: None. F. Yamada: None. T. Kishimoto: None. Y. Nakamura: None.

019
Epidemiologic Surveillance of Kawasaki Disease in Manitoba and Northwestern Ontario 2000-2010

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Objective: The purpose of this study is to determine the incidence of persistent coronary artery sequelae due to KD between the First Nation/Metis (FN/M) and non First Nation children (n-FN) in the province of Manitoba and Northwestern Ontario, Canada.

Methods: This is a 10-year (2000-2010) retrospective chart review study of all patients < 18 years of age identified with KD and persistent coronary artery aneurysms. The data was obtained from the Children’s Hospital of Winnipeg medical records and the Electronic Echocardiography data based at the Variety Heart Centre.

Results: A total of 103 children and adolescents with KD and with at least 3 echocardiography studies were enrolled. Complete or incomplete presentation of KD was determined according to the fulfillment for the disease classic criteria on diagnosis. Age at diagnosis ranged between 2 months to 4 years (median 0.5 years) with 2 patients diagnosed during their early infancy (age< 90 days). The median follow up period was 4 years (1.3 to 6.3 years). Persistent coronary artery aneurysms were detected in 10 children (M/F ratio 3:1). Nine (9) of the studied subjects account for the FN/M children group and the remaining 1 is of Asian origin. We observed no n-FN children with permanent cardiac sequelae secondary to KD.

Conclusion: There is a significantly higher occurrence of permanent coronary artery lesions due to KD among the FN/M children in the province of Manitoba and Northwestern Ontario. However, this study does not imply direct association of any risk factor, which might be related with our findings. Socio-environmental or even genetic factors might contribute to these findings. Nevertheless, these speculations are beyond the scope of this study. We suggest that a strategy of early, diagnosis and treatment of KD based on the latest AHA guidelines, when we deal with patients of these ethnic/racial groups, should be implemented.


020
Kawasaki Disease In France: Incomplete Forms Are Frequent And Associated With A High Frequency Of Cardiac Complications

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Marseille, France; Jean-Baptiste Armengaud, Trouseau Hosp, Paris, France; Armelle Arnoux, Laure Coutard, URC Bicêtre Hosp, Le Krenlim Bicêtre, France; Isabelle Koné-Paut, Bicêtre Hosp, Le Krenlim Bicêtre, France; Kawanet Group

KD is the main vasculitis affecting children < 5 years and the leading cause of acquired heart disease in children. Its epidemiology is few reported in France. Even if IVIG is still the standard treatment; the management of patients at risk for cardiac complications may change toward reinforced (and new) therapeutic approaches. Kawanet is a clinical and biological data repository aimed to define the epidemiological characteristics of KD in France.

Methods: Institutional physicians received information on a national registry for KD. All patients suspected with KD and seen since 2011 were eligible to enter the study. An eCRF was implemented in a web database. The included patients without the AHA international criteria were reviewed by an experts' committee.

Results: 468 cases were entered by 84 physicians from 65 centers. The AHA classification gave: 280 complete KD, and 73 incomplete KD. An expert consensus classified 48 other patients as probable leading to 401 patients considered as KD (M229/F72). 67 were excluded (incomplete data or doubtful). The median age at diagnosis was 3.1y (2m-14y). Their ethnical backgrounds were: European Caucasian 67%, Eastern Caucasian/North African 15%, afro-Caribbean 13%, Asian 4% and mixed ancestry 1%. The clinical symptoms were (%): conjunctivitis 84, cheilitis 82, diffuse exanthema 74, modification of the extremities 73, oral erythema 66, cervical adenopathy 52, raspberry tongue 49, seat erythema 26, perineal desquamation 18 and BCG erythema 5. The cardiac complications were: coronary dilatation 30%, pericarditis 15%, coronary aneurysm 4%, and myocarditis 3% (1 death). 392/401 (98%) patients received IVIG, 64 (21%) and 5 required 2 and 3 courses. The mean treatment delay was 6 days. The factors associated with the coronary abnormalities were: male gender (p=0.01), young KD onset age (p=0.03), and resistance to IVIG (p=0.03).

Conclusion: KD diagnosis remains challenging and overdiagnosis represents at least 10% of cases in this registry. Incomplete forms of KD account for 37% and are associated with coronary dilatation/aneurysm (34%; p<0.01) and a high rate of IVIG resistance. Unlike previous studies, our population is very mixed with 28% of children from the Middle East and Africa, in whom KD is still few reported.


022
The Incidence and Outcome of Kawasaki Shock Syndrome:2003-2013

Sara Kristen Sexson Tejtel, Andrea A Ramirez, Thomas Seery, Amy Liou, Debra Canter, Marietta DeGuzman, Caroly A Altman, Texas Childrens Hosp/ Baylor Coll of Med, Houston, TX

Kawasaki disease (KD) is the leading cause of acquired heart disease in children with a subset presenting in shock. We sought to describe the incidence and outcomes of KD shock in the US.

Methods
The Pediatric Health Information Systems (PHIS), 1/2004-12/2013, dataset including all hospitalizations at 44 of the largest freestanding children's hospitals in the US was used. We assumed KD shock patients were admitted to the ICU.

Results
KD admissions included 16,417 patients, 1,179 requiring ICU care, KD shock, with an annual incidence of 8 - 13%, Figure 1. Among KD shock admissions (versus non-ICU KD), the length of stay (10 vs 4 days, P<0.001) and mortality (10 vs 1 death) is higher in the shock group. The rate of coronary artery (CA) changes during initial admission for KD shock was higher than non-shock, Figure 2 (P<0.001).

Conclusions
KD shock may not be an uncommon presentation given 8-13% of KD admissions required ICU care. KD shock patients are more likely to have complications including coronary artery changes, mechanical ventilation, ECMO, and longer hospitalizations than non-ICU admissions.
Trends in Kawasaki Disease Incidence - 2004-2014

Sara Kristen Sexson Tejtel, Andrea A Ramirez, Amy Liou, Thomas Seery, Debra Canter, Marietta DeGuzman, Carolyn Altman, Texas Childrens Hosp/ Baylor Coll of Med, Houston, TX

Background

Kawasaki disease is the leading cause of acquired heart disease in children in the US. While it remains a rare disease, the purpose of this study is to evaluate the incidence of KD

Methods

To evaluate our hypothesis we used the Pediatric Health Information Systems (PHIS), 2004-2013, including all discharges at 44 of the largest freestanding children’s hospitals in the US.

Results

Between 2004-2013, there were 16,417 hospitalizations for KD, 10,388 (61%) were male. The race of patients admitted with KD showed 5276 (31%) Caucasian, 2370 (14%) African American, 1586 (9.3%) Other, and 941 (5.5%) Asian. The average length of stay was 3.9 days. The number of patients with KD increased annually for the past decade, Figure 1. The largest proportion of the increase was from those children between 1 and 5 years of age, Figure 2.

Most children were only hospitalized once (14,231, 84%) however some children required subsequent hospitalization (1,291, 8%).

Conclusions

There has been a steady increase in the number of admissions per year for Kawasaki disease predominately for those patients ages 1-5 years.
ABSTRACTS
Poster Abstract Presentations (continued)

Background. Kawasaki disease (KD) is an acute febrile illness characterized by systemic vasculitis. Recurrences of KD (defined as at least three clinical signs of KD in addition to fever \( \geq 5 \) days), presenting \( \geq 14 \) days after the return to baseline from the index episode is reported in approximately 3-4% of all cases in Japan.

Objective. To assess the frequency and determined the risk factors associated with recurrences of KD in patients treated at the Instituto Nacional de Pediatría in Mexico City.

Material and Methods. An observational, comparative, retrospective and case-control study of all patients diagnosed with recurrent KD in our Institution from August 1995 and May 2014 was performed. The clinical presentation, laboratory results, treatment used and coronary artery abnormalities in the recurrent-KD and non-recurrent KD groups were analyzed and compared.

Results. We included 371 patients with KD diagnosed at our institution; we had 19 recurrences of KD (5.1%), 16 patients had one recurrence, 1 patient had 2 recurrences and 1 patient had 3 recurrences of KD. 17 cases or our cases were male (89.4%) with mean age at diagnosis of the first episode of 31.63 ± 36.40 months and with a median of 16 months of the new event after the initial episode (1 to 60 mo.). In bivariate analysis, male gender (\( p < 0.037 \)), central nervous system manifestations in the acute phase of KD (\( p < 0.053 \)) and coronary aneurysms at diagnosis (\( p < 0.05 \)) showed statistical significance. There were no factors associated with recurrence in a multivariate analysis.

Conclusions. This is a very small series of KD with a slightly increased rate of recurrence compared with the rate of recurrences reported in the literature. But to allow an early recognition of a new event, a previous history of KD should be considered to initiate treatment and to achieve better outcomes in the recurrent cases.

G. Soricia-ramirez: None. L.M. Garrido-garcia: None.

025 Incidence rate of recurrent Kawasaki disease in Japan (2003-2012)

Daisuke Sudo, Ooshima Prefecture Hosp, Amami, Japan; Yosikazu Nakamura, Jichi Medical Univ, Shimotsuke, Japan

To investigate the incidence of recurrent Kawasaki disease, data of nationwide surveys of Kawasaki disease in Japan from January 2003 (18th survey) to December 2012 (22th survey) are analyzed. Our group previously reported the incidence rate of recurrent Kawasaki disease (Nakamura et al., 1994 and Hirata et al., 2001). In the current study, 104,751 patients with 498,388.9 person-years are observed to calculate the rate of recurrence. The incidence rate of recurrence is 4.14 per 1,000 person-years, with a high incidence within the 12 months from the first episode. The observed person-year categorized by some variables is calculated, such as sex, age at first episode, period of time after the initial episode, presence of cardiac sequelae in the acute (within 2 months) and late (after 2 months) stage, exposure to intravenous gamma globulin (IVGG) therapy, presence of additional IVGG administration, and exposure to steroid therapy. Using those data, incidence rate of recurrent Kawasaki disease and incidence rate ratio are calculated according to such variables, and potential risk factors for recurrence of Kawasaki disease are discussed.

D. Sudo: None. Y. Nakamura: None.

026 Kawasaki Disease With Down Syndrome:low Risk For Ivig Resistance And Coronary Artery Abnormalities

Shinichi Takatsuki, Toho university Omori medical center, Tokyo, Japan; Masato Yokozawa, Hokkaido Medical center for child health and rehabilitation, Hokkaido, Japan; Masae Ono, Tokyo Teishin Univ hospital, Tokyo, Japan; Masako Fujiiwara, Horoyuki Ida, Jikei Univ hospital, Tokyo, Japan; Hideki Motomura, Horoyuki Moriuchi, Nagasaki Univ, Nagasaki, Japan; Mio Taketazu, Junichi Oki, Asahikawa-Koisei General hospital, Hokkaido, Japan; Shigeaki Nonoyama, Natl Defense Medical college, Tokyo, Japan; Tatsuya Kawano, Kenji Ihara, Oita Univ hospital, Oita, Japan; Sachiko Kido, Hoego Prefectural Kobe Children’s hospital, Hyogo, Japan; Junko Shiono, Ibaragi Children’s hospital, Ibaragi, Japan; Shiro Tsuchiya, Soka Municipal hospital, Saitama, Japan; Keiji Tsuchiya, Japan Red Cross Medical center, Tokyo, Japan; Teruhumi Goushi, Nakatsu Municipal hospital, Osaka, Japan; Shuhei Ogata, Masahiro Ishii, Kitazato Univ
Background: Japanese nationwide survey reported that Down syndrome (DS) is less-frequently occurring comorbidity in Kawasaki disease (KD). Thus, no studies have focused treatment response and risk for coronary artery abnormalities (CAAs) in KD with DS. The aim of this study was to evaluate clinical manifestations, treatment response and incidence of CAAs in KD with DS.

Methods: We retrospectively reviewed the medical records of KD with DS from 2005 through 2012. Data were collected according to survey questionnaires from 16 hospitals.

Results: The response rate was 80% and the survey questionnaires from 16 KD patients (11 boys and 5 girls) with DS were collected. Age at diagnosis was 3 years (8 months to 12 years). Eight children (50%) were diagnosed incomplete KD. Five children had previous history of repaired congenital heart disease (AVSD 2, VSD+ASD 1, ASD 2, PDA 1). Of all, 8 children were classified as high risk group based on Kobayashi score. Twelve children received IVIG and 3 children were treated with only high dose aspirin. All 15 children were responded to initial treatment. In the remaining one girl with incomplete KD, the clinical symptoms spontaneously resolved. CAAs were not detected by echocardiography during follow-up.

Conclusions: All DS children with KD were responded to initial IVIG or aspirin therapy despite the high risk of IVIG resistance and none of children had CAAs. Therefore, our finding suggested DS is not a risk factor for IVIG resistance and developing CAAs in KD.


027
Elevated Soluble Interleukin 2 Is A Risk Of Treatment Resistance And Coronary Artery Abnormalities In Kawasaki Disease

Shinichi Takatsuki, Junko Takebe, Kazuyuki Naoi, Satoshi Ikahara, Tomotaka Nakayama, Hiroyuki Matsuura, Toshisuke Morita, Tsutomu Saji, Toho university Omori medical center, Tokyo, Japan

Background and objective: Soluble ST2 (sST2), an interleukin (IL)-1 receptor family member, has been identified as a novel biomarker for cardiac stress. Although sST2 were reported to be elevated in acute Kawasaki disease (KD) and correlated with cardiac diastolic dysfunction, relation between sST2 levels and treatment resistance and risk of coronary artery abnormalities (CAAs) is not studied. The aim of this study is to evaluate clinical utility of sST2 in acute KD.

Methods: We measured serum sST2 from 54 children (median age; 22 months, 29 boys and 26 girls) with acute KD before and after initial treatment, 10 febrile controls (FC) (median age; 14 months) and 2 healthy controls (HC). Using Kobayashi score from RAISE study, patients were divided into high (>score 5) and low risk group (score 4) for IVIG resistance.

Results: Serum sST2 in KD significantly elevated compared with FC and HC (median; KD vs FC 0.81 vs 0.25 ng/ml, p<0.05, KD vs HC 0.81 vs 0.12 ng/ml, respectively, p<0.05). Compared with sST2 levels before treatment, sST2 decreased at 4 days after initial therapy, but it was not significant (median 0.81 vs 0.67 ng/ml). Statistically significant differences were observed in sST2 between high risk group and low risk group (median; 1.80 vs 0.54 ng/ml, respectively, p<0.05). Additionally, sST2 levels in non-responders to initial treatment were significantly higher than those in responders (median; 1.65 vs 0.64 ng/ml, respectively, p<0.05). There were no significant correlations between sST2 level at diagnosis and plasma brain natriuretic peptide (r = -0.05), C-reactive protein (r = 0.04), and AST (r = 0.07). Overall, 4 children (7%) had CAAs at 4 weeks of illness.

Conclusions: Elevated sST2 levels at diagnosis were not significantly different between children with and without CAAs, median sST2 levels in children without CAAs (1.68 vs 0.79 ng/ml, respectively, p=0.07). At 4 days after initial therapy, median sST2 levels decreased in children without CAAs (0.79 vs 0.65, p=0.1), whereas median sST2 levels
increased in children with CAAs (1.68 vs 1.70, p=0.9).

Conclusions: Elevated sST2 may be a potential risk factor of initial treatment resistance and developing CAAs in acute KD.


028
African American Race is Not Protective Against Coronary Artery Involvement in Kawasaki Disease

Emily P Williams, Emory Univ Sch of Med, Atlanta, GA; Michael S Kelleman, Emory Univ, Atlanta, GA; William T Mahle, Emory Univ Sch of Med, Atlanta, GA

It has been previously reported that African American race may be protective against coronary artery aneurysm development in Kawasaki Disease (KD). We aimed to test this with our own cohort of KD patients from a large pediatric cardiology practice. Data from 250 subjects diagnosed with KD and followed as outpatients with surveillance echocardiography over a two-year period were analyzed. Twelve patients were excluded due to incomplete records or an unconfirmed diagnosis. Race designated by parent was recorded. Charts were reviewed for any coronary involvement (ectasia or aneurysm) and coronary Z-score greater than 2.5 at the time of diagnosis and at subsequent follow-up visits. Odds ratios were calculated comparing each racial group to others for any coronary involvement and for coronary Z-score > 2.5. Of 238 included patients, 44.5% were African American, 37.4% were non-Hispanic white, 10.5% were Hispanic, and 7.6% identified with other racial designations. Approximately 21.9% of African American patients had any coronary involvement and 9.5% had a coronary Z-score > 2.5. Of 238 included patients, 44.5% were African American, 37.4% were non-Hispanic white, 10.5% were Hispanic, and 7.6% identified with other racial designations. Approximately 21.9% of African American patients had any coronary involvement and 9.5% had a coronary Z-score > 2.5. Approximately 21.4% of non-Hispanic whites had any coronary involvement and 13.5% of non-Hispanic whites had a coronary Z-score > 2.5. Twenty-eight percent of patients that identified with other racial designations, 38.9% had coronary involvement and 22.2% had a coronary Z-score > 2.5. No statistically significant odds ratios were identified. Relative to reference group (non-Hispanic whites) African American patients had nearly identical rates of 1) any coronary involvement, or 2) coronary Z-score > 2.5. KD occurs commonly in African-American children. Given equal risk for late coronary sequelae vigilance and strict adherence to consensus guidelines is essential.

E.P. Williams: None. M.S. Kelleman: None. W.T. Mahle: None.

029
The Clinical Risk Factors of Intravenous Immunoglobulin Resistance and Coronary Artery Lesion of Kawasaki Disease: Retrospective Analysis of 602 Cases

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Introduction
The incidence of Kawasaki disease (KD) in China is increasing for years. The current coronary artery lesion (CAL) incidence is 5-10% in KD with intravenous immunoglobulin (IVIG) treatment. And the 10-20% KD patients still exhibit IVIG resistance. However, little clinical evidence on the occurrence of either CAL or IVIG resistance for big KD sample study in China during the past decade.

Objective
In order to find clinical risk factors of CAL and IVIG resistance of KD in China.

Methods
We retrospectively analyzed the clinical manifestations, laboratory results, treatment and complications of cardiac vascular of 602 KD cases from 2007 to 2012 admitted at Shanghai Children's Hospital. The SAS 9.2 edition was used for statistical analysis. The mean ± standard deviation or the median were used for measurements. Case numbers and percentages were used for the count number. The t-test and the Mann-Whitney test were both used for mean comparisons. Single factor and multi-factor logistic regression analyses were used to analyze the risk factors.

Results
1. The KD gender male to female ratio was 1.85: 1. The KD median age was 2.0 years old (one month to 11.7 years old). 20.1% cases (121 of 602) exhibited CAL. There was no difference of CAL incidence between the gender (p=0.09). 2. The incidence of bright red cracked lips
(p=0.001), peeling of the skin of the toes (p=0.021) and perianal skin peeling (p=0.031) are less in group with CAL. 3. Among the 602 cases, there were 525 cases that were sensitive to IVIG therapy. Among the 26 IVIG resistance cases, there were 9 cases with CAL with an incidence of 34.6%, which was higher than the IVIG sensitive group (p=0.05). 4. ESR (p=0.014), CRP (p=0.017), PLT (p=0.003) and Hb (p=0.032) were much higher in the IVIG resistance group than the IVIG sensitive group, even though the IVIG resistance group started the IVIG treatment earlier (p=0.003). 5. Logistic regression analysis was conducted to show that GPT≥80IU/L was the independent risk factor of IVIG resistance, risk ratio was 2.945 (p=0.012).

Conclusion
This research suggests that risk factors of clinical evidence for IVIG resistance and CAL in KD.

Key words
Kawasaki disease, intravenous immunoglobulin, coronary artery lesion


030
Are Man-made Pollutants Originating From China, Central Asia One Of The Windborne Mystery Infections Of Kawasaki Disease Carried Across The Pacific?

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Kawasaki disease (KD) is an acute febrile illness predominately affecting children (75-80%) that is classified as an autoimmune vasculitis of small- to medium-sized arteries. KD is generally self-limited, although serious cardiac lesions develop in 25-30% of cases. Despite over four decades of extensive international investigation, no cause of KD has been confirmed. Significantly higher rates of concurrent viral infections were recently observed in patients during acute KD, while another study found significantly greater risk of early hospitalization for bacterial infections before KD onset. Several recent large investigations appear to confirm that patients are significantly more likely to develop asthma or common allergies such as acute rhinitis and atopic dermatitis both before and after KD. Seasonal shifts in large-scale wind currents originating from heavily polluted regions in China and Central Asia are significantly associated with the occurrence of KD cases in Japan, Hawaii, and San Diego. Recently, it appears that these authors discovered that marked candida pollution from the soil of heavy agricultural and industrial areas in Northeastern China is significantly associated with the occurrence of KD in Japan. There is extensive precedent for trans-ocean wind transport of industrial pollutants, including across the Pacific. China now accounts for more than 50% of the world's total anthropogenic emissions and is responsible for 20-29% of total air pollution in the United States, particularly as a result of its rapid industrialization and heavy reliance upon coal-fired power plants. Significantly higher consumption of seafood contaminated with methylmercury, PCBs, and dioxins may account for the disproportionate rates of KD in East Asian populations. In Japan, the appearance of KD during the 1950s and 1960s coincides with outbreaks of Minamata disease during this same period, which resulted from an unprecedented increase in mercury pollution and the contamination of seafood. Lastly, industrialization and subsequent pre- and postnatal exposure to various irritants are significantly associated with the development of asthma and common allergies during early childhood, which suggests a potential common link to KD that deserves scrutiny.

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031
Acute Febrile Acrodynia (1781-1966): Historical Cases Of Kawasaki Disease Before Kawasaki?

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Infantile acrodynia is a mercurial reaction that can mimic the complete clinical picture of Kawasaki disease (KD), and is therefore considered a differential diagnosis for KD. Before the 1950s, acrodynia affected 1 in 500 children in industrialized nations. The recently formed pediatric community was fascinated by
Kawasaki disease (KD) is characterized by development of an autoimmune vasculitis and potential coronary artery lesions (CAL). Patients present with significantly marked expression of various immune cells and the inflammatory cells that they produce, recruit, or secrete, particularly cytokines. Concurrently, regulatory immune cells that suppress immune and inflammatory cells are significantly reduced in KD, particularly regulatory T cells (Tregs) such as CD4+CD25+FOXP3+ Tregs. Therefore, the clinical picture results from an unchecked, marked increase of immune and inflammatory cells infiltrating passed activated endothelial cells and into the vascular wall. This appears to largely be a consequence of amplified cell signaling via the Ca2+/NFAT pathway in KD, which is involved in targeted gene expression. As a result, we hypothesized that epigenetic control of gene expression through histone modifications may play a leading role in development of KD, its complications, and recovery. A previous study found significant DNA hypomethylation of CpG sites for the SOCS1 gene in KD patients (n=32), which was higher in patients without CAL. We conducted a preliminary study to widely examine epigenetic changes in DNA methylation of CpG sites before and after IVIG treatment in KD patients (n=9) using age-matched febrile controls (n=8). Our results demonstrated ≥10% differences in DNA methylation rates for 67 genes in KD patients, in addition to 10 genes with ≥15% methylation difference. Larger studies are required to accurately determine the role of epigenomic changes in KD development, in addition to investigations of the methylation reactions which

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032
Improper Histone Modification Of Gene Expression In Kawasaki Disease May Influence Both Its Development And Outcome

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033
A Meta-analysis Of Three Genome-wide Association Studies Identifies A Novel Susceptibility Locus For Kawasaki Disease.

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Background
Although genome-wide association studies (GWAS) have conclusively identified several susceptibility genes / loci for Kawasaki disease (KD), a large part of the genetic etiology of this disease have not been unraveled and, above all, its marked predilection for East Asian populations have not been explained.

Objective
To identify genetic variants commonly associated with KD in the East Asian populations, we conducted a meta-analysis of three GWASes from Japan, Korea and Taiwan.

Methods
In the GWAS analyses, we genotyped 6322 subjects (1236 cases and 5086 controls) using either Illumina 550K or Affymetrix SNP 6.0 platforms and then imputed untyped genotypes using Impute2 or minimac software with 1000 Genomes Project's East Asian population (JPT, CHB and CHS) reference haplotype data. We then performed a meta-analysis using a weighted-average method with inverse-variance weights and selected representative SNPs in 49 top associated loci, which were then genotyped in 4798 independent subjects (2151 cases and 2747 controls). Finally, we combined the data for the three GWASes and follow up studies in a meta-analysis.

Results
SNPs within previously identified susceptibility loci showed significant association in the meta-analysis of the GWASes (ITPKC: rs28493229, P...
Poster Abstract Presentations (continued)

= 3.07 x 10-9; CASP3: rs2720377, P = 2.66 x 10-9; BLK: rs2736340, P = 1.23 x 10-16; CD40: rs1883832, P = 1.76 x 10-8; HLA class2: rs189914842, P = 4.57 x 10-11). In a meta-analysis of the three GWASes and follow-up studies, we observed a genome-wide significant level of association at a SNP in a chromosomal region different from the six known loci (P = 6.49 x 10-9).

Conclusion
The meta-analysis of three GWASes and follow-up studies successfully identified a new SNP significantly associated with KD. Further investigation of the region where the SNP is located toward specification of the susceptibility gene, the responsible variant, as well as its effect on gene function is warranted.

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034
Genome-wide Association Study Identified New Susceptibility Loci To Coronary Artery Aneurysm-related In Kawasaki Disease

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Kawasaki disease (KD) is an acute systemic vasculitis syndrome that predominantly affects children younger than 5 years of age, and may causes serious, sometimes life-threatening, cardiac sequela associated with coronary artery aneurysm (CAA). To identify genetic variants that confers a highly increased risk of coronary artery aneurysm-related in Kawasaki disease. In this study, we carried out genome-wide association study (GWAS) in a Korean children population including 102 CAA-related KD cases and 126 controls. Fifteen genetic loci were found to be significantly correlated with KD risk (P<1.0X10(-7)). Our case-control study revealed that rs4236089 C allele in chloride intracellular channel 5 (CLIC5) gene at 6p21.1 was significantly associated with KD patients with CAA (odds ratio (OR)=4.6, P=7.53X10(-7)). These findings suggest that the CLIC5 gene may play a crucial role in CAA development pathway of KD.


035
Common Variants in the CRP Promoter are Associated with a High C-reactive Protein Level in Kawasaki Disease

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Kawasaki disease (KD) is an acute self-limiting form of vasculitis that afflicts infants and children and manifests as fever and signs of mucocutaneous inflammation. Children with KD show various laboratory inflammatory abnormalities, such as elevations in their white blood cell (WBC) count, C-reactive protein (CRP) level, and erythrocyte sedimentation rate (ESR). We here performed a genome-wide association study (GWAS) of 178 KD patients to identify the genetic loci that influence 10 important KD laboratory markers: WBC count, neutrophil count, platelet count, CRP, ESR, hemoglobin (Hb), aspartate aminotransferase (AST), alanine aminotransferase (ALT), albumin, and total protein. A total of 165 loci passed our arbitrary stage 1 threshold for replication (p < 1 x 10^-5). Of these, only 2 SNPs (rs12068753 and
rs4786091) demonstrated a significant association with the CRP level in replication study of 473 KD patients ($p < 0.05$). The SNP located at the CRP locus (rs12068753) demonstrated the most significant association with CRP in KD patients ($\beta = 4.73$ and $p = 1.20 \times 10^{-6}$ according to the stage 1 GWAS; $\beta = 3.65$ and $p = 1.35 \times 10^{-8}$ according to the replication study; $\beta = 3.97$ and $p = 1.11 \times 10^{-13}$ according to combined analysis) and explained 8.1% of the phenotypic variation observed. However, this SNP did not demonstrate any significant association with CRP in the general population ($\beta = 0.37$ and $p = 0.1732$) and only explained 0.1% of the phenotypic variation in this instance. Furthermore, rs12068753 did not affect the development of coronary artery lesions or intravenous immunoglobulin resistance in KD patients. These results indicate that common variants in the CRP promoter can play an important role in the CRP levels in KD.


036

**FCGR2A Promoter Methylation and Risks for IVIG Unresponsiveness in Kawasaki Disease**

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Kawasaki disease (KD) is characterized by pediatric systemic vasculitis of an unknown cause and the Fc Fragment of IgG, Low Affinity IIa, Receptor (FCGR2A) gene was reported to involve in increasing susceptibility of KD. Because DNA methylation is one of the epigenetic mechanisms that control gene expression, we hypothesized that methylation status of CpG islands in FCGR2A promoter predisposes an individual to Kawasaki disease. We recruited 36 KD patients and 24 healthy subjects with informed consents. And eleven potential methylation loci within the targeted promoter region (chr1:161474603-161475102) of Fc Fragment of IgG, Low Affinity IIa, Receptor were selected for investigation. Methylation at the CpG sites G, H and J displayed a strongly associations with KD, whereas CpG sites B,C,E,F,H,J and K were found to be correlated with non-responsive to IVIG treatment. In addition, CpG sites G, J and K were predicted as the significant transcription factor binding site for NF-kB, Myc-Max and SP2 respectively.

Our study reports a significant association between the promoter methylation of FCGR2A, susceptibility of Kawasaki disease and therapeutic outcomes of IVIG treatment. The methylation levels of CpG sites of FCGR2A gene promoter may be an important marker for optimizing IVIG therapy.

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development, whereas low serum albumin concentration is an independent risk factor for IVIG non-responsiveness. Recently, we are re-analyzing the clinical data of all collected KD patients to evaluate the effect of age, gender, family history status, recurrence status, KD types on clinical features of KD. In addition, in our previous genome-wide association studies (GWAS) using Affymetrix SNP array 6.0 in 186 Korean KD patients and 600 healthy controls, we identified a Kawasaki disease susceptibility locus at 1p31. We also identified significant associations of coronary artery aneurysm with a variant located in KCNN2 gene and common variants in CRP gene promoter with the increased CRP levels in KD patients. Furthermore, to identify new KD susceptibility and subphenotype loci, we are performing another GWAS using Illumina Human Omni1 SNP chip with approximately 300 KD cases containing 16 cases with family history, 46 cases with recurrence, 119 cases with IVIG non-responsiveness, 52 cases with CALs (diameter >5mm). Multiple subsets of KD cases will be very useful to detect loci associated with the subphenotypes of KD in GWAS data analysis. We also performed DNA microarray analysis to determine differential gene expression by in vitro immunoglobulin treatment using patient-derived B cell lines (IVIG-responders vs. IVIG-non-responders). However, we could not find any difference between B cell lines. Furthermore, a pilot study of exome sequencing of 12 KD cases was not successful in identifying causal KD susceptibility genes.


038
Variations in ORAI1 gene associated with Kawasaki disease

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Kawasaki disease (KD; MIM611775) is a systemic vasculitis syndrome with unknown etiology which predominantly affects infants and children. Recent findings of susceptibility genes for KD have suggested up-regulation of Ca2+/NFAT pathway as one of the main pathophysiological processes in KD. In this study, we focused on ORAI1, a gene for a channel involved in store operated Ca2+ entry located on 12q24 where positive linkage signal was seen in our previous sib pair study of KD, and conducted a genetic association study. By re-sequencing 17.4kb of ORAI1 region for 94 subjects, we identified 37 variants with minor allele frequencies larger than 0.05. After selecting 9 tagging SNPs which represent 37 variants we performed an association study using 730 KD cases and 1315 controls. As a result, one tagging SNP located within exon2 showed nominal association (rs3741596; OR = 1.19, 95%CI 1.02~1.40, P = 0.028). The same trend of association was observed in an independent case control panel (1813 KD cases and 1097 controls, OR=1.22, 95% CI 1.06-1.40, P = 0.0056) and a significant P value was observed in a meta-analysis (OR = 1.21, 95%CI 1.09~1.34, P = 0.00041). Furthermore, we also found a rare 6 base-pair insertion polymorphism located on 12q24 which cause elongation of proline repeat within N-terminal cytoplasmic domain of the ORAI1 protein was overrepresented in KD cases (rs78448924; OR = 3.91, 95%CI 1.30~11.80, P=0.010). These data indicate altered ORAI1 function confers susceptibility of KD and further studies are needed to elucidate ORAI1 associated mechanisms in KD.

Objective We studied microbiome of throat swab, rectal swab, and venous blood obtained from patients with Kawasaki disease (KD) to determine whether bacterial nuclei are detectable in circulating blood of KD patients and whether the microbial composition resembles to that of oral cavity or gut.

Methods We initially studied 7 patients (4 males and 3 females, 20-59 months) and obtained swabs and blood samples before IVIG treatment (day 2-8) to prepare DNA and cDNA library. Next, we studied 14 patients (8 males and 6 females, 2-47 months) and prepared blood cDNA library before IVIG treatment (day 2-8) and before discharge (day 10-15). Samples were sequenced by Illumina HiSeq2000 and the results were analyzed using MePIC for human genome subtraction and megablast search, followed by taxonomic analysis with MEGAN viewer.

Results The number of sequences homologous to bacterial genome per swab sample obtained from DNA or cDNA libraries varied 20,000~4,700,000 or 500,000~2,400,000, respectively. In most of the throat samples, the sequences were classified in descending order of phyla, Firmicutes > Proteobacteria > Bacteroidetes > Actinobacteria. In rectal samples, Proteobacteria and Bacteroidetes were more abundantly and Firmicutes was less abundantly represented than throat samples. The total number of sequences per blood sample was 30,000,000~70,000,000 and 99.0~99.9% of them were homologous to human genome. The number of sequences homologous to bacterial genome per DNA or cDNA library was 221-286 or 125-593, respectively. In blood samples, the frequencies of phyla were

arranged in descending order, Proteobacteria = Actinobacteria > Firmicutes >> Bacteroides. The sequences homologous to Burkholderia, Streptococcus and Neisseria, the indigenous bacteria in the oral cavity, were present in most of the patients. Among them, the abundance of Streptococcus was significantly (p=0.03) reduced in the cDNA libraries during convalescence.

Conclusion A variety of sequences homologous to bacterial genome were detected from the venous blood obtained from KD patients during the acute as well as the convalescent phase. Further study is necessary to investigate the specificity and the characteristics of these sequences in patients with KD.


040
A Prospective Study on the Association of Kawasaki Disease and Mycoplasma pneumoniae Infection

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Objective: The etiology of Kawasaki disease (KD) remains unknown, and several infectious agents have been proposed as the etiology of KD. There have been some studies, stating that KD and Mycoplasma pneumoniae (M. pneumoniae) infection are linked. So authors performed a prospective study to elucidate whether there is an association between KD and M. pneumoniae infection.

Subjects and Methods: Subjects are 36 patients with KD who admitted to Bundang Jesaeng General Hospital from January 2013 through August 2014. Patients were assigned to the M. pneumoniae group and the control group according to anti-mycoplasmal IgM antibody (AMA) titers. Clinical features, laboratory findings, courses and outcomes were compared between two groups.

Results: AMA were positive or indeterminate in 11 patients (30.6%; M. pneumoniae group) and were negative in 25 patients (69.4%; control group). There were no significant differences between two groups in age and sex distributions, duration of fever, laboratory findings (WBC counts, ESR, CRP, AST, ALT, bilirubin), chest X-ray findings, and echocardiographic abnormalities (coronary arterial lesion, pericardial effusion, valvular regurgitation, LV dysfunction).

AMA titers were rechecked in 6 patients, of whom 5 (83.3%) showed decreased titers and 1 (16.7%) showed an increased titer. All of patients were treated successfully with intravenous immunoglobulin and oral aspirin.

Conclusion: Although AMA was detected in some patients with KD, it did not affect clinical features, laboratory findings, courses and outcomes of KD. In most cases AMA titers were decreased in the second examinations, so authors think that M. pneumoniae infection was a previous infection rather than a concurrent infection in some patients with KD and it did not act as a causative agent of KD.

J. Choi: None. M. Cha: None.

041
Evidence Against Mycoplasma pneumoniae as An Etiologic Agent of Kawasaki Disease

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Background: The etiology of Kawasaki Disease (KD) remains unknown. The majority of KD patients present with a history of, or concurrent respiratory symptoms. Isolated case reports of Mycoplasma pneumoniae (Mp) associated with KD have been reported. Since Mp can cause mucous membrane disease (eye and mouth lesions), rash, and fevers, it remains a possible etiological agent for KD.

Objective: To evaluate the prevalence of Mp identified in the upper respiratory tract of patients admitted with a diagnosis of KD.

Methods: All KD patients admitted to Children's Hospital Colorado (CHCO) over a 14 month period (Feb 2013 - Mar 2014) who had a nasopharyngeal wash (NPW) submitted for diagnostic testing were included in the study. Mp PCR was performed using the Film Array Respiratory Panel (BioFire Diagnostics, Salt Lake City, UT).
Lake, City, UT). Furthermore, a CDC investigated pediatric outbreak of Mp in our community afforded the opportunity to investigate an epidemiological association between Mp and KD by comparing the incidence of KD to the incidence of Mp positive respiratory samples from Jan 2013 - May 2014.

Results: Forty-seven (65%) of 72 KD patients had a NPW submitted and tested for Mp. None of these 47 patients tested positive for Mp. During 2013 - 2014 there was no correlation between the overall incidence of Mp positive respiratory samples and the incidence of KD.

Conclusions: Our data do not support the hypothesis that Mp is an etiological agent of KD. Although unlikely, this study does not exclude the possibility that another Mycoplasma species could be involved in the pathogenesis of KD.


042 Simultaneous development of Kawasaki Disease associated with adenovirus infection in identical twins

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Background: The cause of Kawasaki disease (KD) remains unknown. However, many studies have suggested that specific genetic factors and some infectious agents could be associated with the onset of KD. Human adenovirus (AdV) infection is one of the triggering events in KD. We experienced identical twins who sequentially developed KD in conjunction with AdV infection.

Patients: The patients were 4-year-old identical twin boys. The elder brother developed a high fever and was diagnosed with AdV infection by an immunochromatographic kit for AdV (IC-kit). He was transferred to our institute after persistence of fever for 7 days. On admission, he already fulfilled all of the diagnostic criteria of KD. The laboratory data were as follows: WBC, 9700/µl; CRP, 2.42 mg/dl; IFN-γ, 99.8 pg/ml; and TNF-α, 10.9 pg/ml. He received intravenous immunoglobulin (IVIG) and aspirin, and responded well without coronary artery abnormalities. The younger brother, who was also IC-kit-positive, was hospitalized on the same day as his elder brother after persistence of fever for 3 days. The data on admission were as follows: WBC, 12,600/µl; CRP, 5.54 mg/dl; IFN-γ, 105.0 pg/ml; and TNF-α, 33.6 pg/ml. Although he developed all of the KD symptoms by the 4th day, his fever spontaneously subsided on the 6th day without IVIG or aspirin. He developed dilation of the coronary artery on the 10th day at the left circumflex artery bifurcation area. This disappeared after 3 months with antiplatelet therapy. AdV type 3 (AdV3) DNA was detected in both of the patients’ stool samples by PCR, and AdV3 was isolated from the younger brother’s stool sample. Moreover, serum neutralizing antibody to AdV3 was greatly elevated in both of the patients.

Discussion: Identical twins who simultaneously develop KD are rare. Both of the twin brothers were infected with AdV3 immediately before they developed symptoms of KD. The combined condition of genetic susceptibility and an infection could be an essential trigger in development of KD.


043 Real Time Polymerase Chain Reaction Assays For Detection Of Respiratory Viruses In Kawasaki Disease Patients

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Purpose: Respiratory symptoms are frequently observed in children with Kawasaki disease (KD) during the acute phase. The association rate of KD with antecedent respiratory illness has been reported to range from 56 to 83%. Clinical and epidemiologic features of KD support an infectious cause, but the etiology remains unknown. We investigated the association of respiratory viruses in children with KD using multiplex reverse transcriptase-polymerase chain reaction (RT-PCR).

Methods: 138 KD patients were enrolled from January 2010 to June 2013. Two study groups (Group 1; n=94, KD without respiratory symptoms, Group 2; n=44, KD with respiratory symptoms) were compared with a control group (Group 3; n=5, febrile patients with respiratory symptoms).
symptoms). Laboratory data were obtained from each patient including complete blood count (CBC), erythrocyte sedimentation rate (ESR), platelet count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total protein, albumin, C-reactive protein (CRP), NT-pro brain natriuretic peptide (BNP). Echocardiographic measurements were compared between the three groups. RT-PCR was performed using nasopharyngeal secretion to screen for the presence of 14 viruses (corona virus, parainfluenza virus 1, 2 and 3, influenza A and B, respiratory syncytial virus A and B, rhino virus A, B and C, metapneumo virus, adenovirus, and bocavirus) in groups 2 and 3.

**Results:** The rate of KD with respiratory symptoms was 17.5%. The duration of fever was significantly longer and coronary artery diameter was significantly larger in group 2 than in group 1. Coronary artery diameter, CRP, platelet count, ALT, and NT-pro BNP were significantly higher and albumin lower in group 2 compared with group 3.

Detection rate of adenovirus was 55.0% in group 2 and 28.6% in group 3.

**Conclusion:** A positive RT-PCR for respiratory viruses may be helpful to elucidate the specific virus in KD patients with respiratory symptoms. NT-proBNP is a very important diagnostic tool in differentiating KD from other febrile viral respiratory infection.

Y. Hong: None. S. Lee: None. H. Choi: None. J. Kwon: None. H. Kim: None. S. Son: None.

044

**Uveitis As An Important Ocular Sign To Help Early Diagnosis In Kawasaki Disease**

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**Purpose:** Atypical or incomplete Kawasaki disease (KD) frequently leads to delay in diagnosis and treatment. Delayed diagnosis is associated with increased risk of coronary artery aneurysm. Anterior uveitis peaks about a week after the onset of fever. The purpose of this study was to assess the differences in laboratorial findings including echocardiographic measurements, clinical characteristics such as duration of fever and treatment responses between KD patients with and without uveitis.

**Materials and Methods:** 106 KD patients were studied from January 2008 to June 2013. Study group (n=28, KD with uveitis) was compared with control group (n=78, KD without uveitis). Laboratory data were obtained from each patients including complete blood count (CBC), erythrocyte sedimentation rate (ESR), platelet count, alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum total protein, albumin, C-reactive protein (CRP), brain natriuretic peptide (BNP). Echocardiographic measurement and intravenous immunoglobulin responses were compared between two groups.

**Result:** The incidence of uveitis was 26.4%. Neutrophil counts were higher in the uveitis group compared with the control group (64.3±15.8×103/mm3 vs. 54.4±19.3×103/mm3). The age of patients was higher in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months).

**Result:** The incidence of uveitis was 26.4%. Neutrophil counts were higher in the uveitis group compared with the control group (64.3±15.8×103/mm3 vs. 54.4±19.3×103/mm3). The age of patients was higher in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months). ESR (43.3±27.2 mm/hr vs. 30.8±24.6 mm/hr) and CRP (8.1±6.1 mg/dL vs. 7.9±10.7 mg/dL) were slightly increased in the uveitis group compared with the control group (40.5±21.4 months vs. 33.4±29.3 months).

**Conclusion:** Uveitis is the one of the important ocular signs to diagnose incomplete KD. It is significantly associated with the patient’s age and neutrophil count but not with the other laboratory measurements, coronary arterial complication or treatment responses between the two groups.

Y. Hong: None. H. Choi: None. H. Kim: None. S. Sohn: None.

045

**Incomplete Kawasaki Disease followed by Systemic Onset Juvenile Idiopathic Arthritis**
ABSTRACTS
Poster Abstract Presentations (continued)

Jeong-hyun Jo, Na-yeon Kim, Eell Ryoo, Gachon Univ Gil Medical Ctr, Incheon, Korea, Republic of

Incomplete Kawasaki disease (KD) is second most common systemic vasculitis presented with persistent fever in childhood. Systemic onset juvenile idiopathic arthritis (SoJIA) is a rare rheumatic arthritis characterized with spiking fever for more than 6 weeks with prominent painful joint swelling. KD may trigger or prodrome of SoJIA. Both diseases have overlapping clinical features and laboratory findings including fever, rash, lymphadenitis, thrombocytosis, arthralgia and coronary artery dilation so that they could hardly be distinguished. We present 4 years old girl and 30 months old girl who presented with persistent fever, rash and arthralgia. They were initially diagnosed with incomplete KD and treated with intravenous immunoglobulin and steroids. Spiking fever and painful swelling of bilateral knee joints were noticed after 25 days and 40 days of illness. They were diagnosed with SoJIA followed by incomplete KD and treated with intravenous immunoglobulin and steroids. Neither coronary complication nor joint complication was noticed. Careful follow up is needed for patients with KD and arthralgia.

J. Jo: None. N. Kim: None. E. Ryoo: None.

046 Effect Of Infliximab And Plasma Exchange Therapy On Activated Monocytes/macrophages In Kawasaki Disease Intractable To IVIG.

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[Background]
Kawasaki disease (KD) is a generalized vasculitis of unknown etiology that occurs predominantly in infant and children. KD has been reported as one of the cytokine-induced disease. The monocyte / macrophage is thought to the subject of proinflammatory cytokines sources. It has been reported that IVIG therapy in KD normalizes the increased numbers of activated CD14 + CD16 + monocyte / macrophage. We examined the effect of the infliximab (IFX) and plasma exchange (PE) therapy on the peripheral blood cells, especially the monocyte / macrophage in KD intractable to intravenous immunoglobulin (IVIG).

[Patients]
We studied 9 patients with KD intractable to IVIG (2g/kg/dose), seven with IFX therapy (5mg/kg/dose), four with PE therapy (including two patients of refractory to IFX therapy), who were seen at our hospital. The median age and body weight were 3.3 years (range, 0.5 to 5.5 years) and 13.0kg (range, 6.1 to 20.3kg), respectively. White blood cell count and differentiation were compared before with after the treatment.

[Results]
IFX group: White blood cell count was significantly decreased to 11640 ± 3509 from 14141 ± 4673/µl. The neutrophil count was decreased and the lymphocyte count was increased. Both the counts were normalized. CD14 + monocyte / macrophage count (normal value: 339 ± 91/µl) was significantly decreased to 488 ± 195 from 999 ± 528/µl. Especially, the activated CD14 + CD16 + monocyte / macrophage count (normal value: 35 ± 18/µl) was significantly decreased to 69 ± 45 from 176 ± 164/µl.

PE group: White blood cell count was decreased to 10683 ± 4665 from 16810 ± 2527/µl. Neutrophil count was decreased, but the lymphocyte count was no changed. CD14 + monocytes / macrophage count was decreased to 401 ± 278 from 1402 ± 1286/µl. The activated CD14 + CD16 + monocyte / macrophage count was decreased to 24 ± 9 from 243 ± 364/µl.

[Conclusion]
In KD intractable to IVIG, the CD14 + CD16 + monocyte / macrophage count which involved in the pathogenesis of KD.


047 Expression of Galectin-3 in the Myocardium and Arterial Walls of Kawasaki Disease Patients

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Adriana H Tremoulet, Univ of California, San Diego, La Jolla, CA; John B Gordon, San Diego Cardiac Ctr and Sharp Memorial Hosp, San Diego, CA; Lori B Daniels, Jane C Burns, Univ of California, San Diego, La Jolla, CA

Abstract:
Although coronary artery aneurysms are the most significant complication of Kawasaki Disease (KD), histologic examination has revealed myocarditis and myocardial fibrosis (MF) in most cases. Galectin-3 (Gal-3) is a matricellular protein that plays a multifunctional role in inflammation, fibrosis, and cell differentiation. It is a prognostic indicator of heart failure and cardiovascular events. Gal-3 plays a role in adhesion and migration of inflammatory and fibroblastic cells. We previously reported that plasma Gal-3 levels were elevated in acute pediatric KD and adult KD with giant aneurysms (GA). We postulated that Gal-3 may be involved in both acute inflammation and convalescent fibrosis in KD.

Methods:
Conventional H&E staining, Trichrome staining and immunohistochemical analysis for Gal-3 were performed on 1 acute stage KD subject and 10 convalescent stage KD hearts including 6 from subjects with GA and 4 from subjects without aneurysms who died of non-cardiovascular causes.

Results:
In the acute KD myocardium, round inflammatory cells were seen infiltrating the myocardium and positive staining for Gal-3 was noted. In the myocardium of convalescent KD with GA, widespread cardiomyocyte degeneration and necrosis with extensive bridging fibrosis were observed but inflammatory cells were not detected; spindle-shaped cells expressing Gal-3 in the cytoplasm were observed between cardiomyocytes. Myocardial fibrosis and Gal-3 expression were not observed in the myocardium of KD subjects without aneurysms. In the acute KD coronary arteries, Gal-3 positive inflammatory cells were observed in all layers, and the intima was already thickened by illness day 7. Destruction of the internal elastic lamina and intimal thickening with Gal-3-positive spindle-shaped cells were observed in coronary and systemic arteries of convalescent KD subjects.

Conclusion:
Gal-3 expression was related to inflammation in acute KD and tissue fibrosis in late convalescent KD with GA. Elevated levels of Gal-3 should raise concern for MF in KD patients with GA. However, in KD without aneurysms, myocardial fibrosis and Gal-3 expression were not observed; therefore myocarditis in KD patients with normal coronary arteries may improve without progression to MF.


048
Small Arteritis is the Basic Pathology of Kawasaki Disease

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Introduction: Pathologic processes of two features in Kawasaki disease (KD) have not been elucidated. The one is the preponderance of aneurysms in the main coronary artery. The other is the discontinuity in the process of the vasculitis between those of microvessels and small arteries, and those of medium-sized to large arteries.

Hypothesis: We assessed the hypothesis that arteritis of the vasa vasorum, which we described for the first time, plays a key role in the preponderance of aneurysms in the main coronary artery in KD. METHODS: We examined the relationship between patient age at onset of KD and the distance ratio of the aneurysm in the left main coronary artery (LMCA) to clarify the role of arteritis of the coronary vasa vasorum, originated from the atrial and ventricular branches of the peripheral coronary artery, in the ischemia at the media of LMCA. The distance ratio Y was defined as D1/D2 × 100, where D1 and D2 are the distances from the left coronary ostium to the proximal point of the aneurysm and to the bifurcation into the left anterior descending and left circumflex artery, respectively. We then studied the relations between cardiogenic shock and extracardiac aneurysm, and coronary aneurysm in our cases and those of literatures.

Results: The mean distance ratio of 56 aneurysms correlated with age, similar to the development of the coronary vasa vasorum: Y = 49.75383 - 3.3739X, P = 0.002987, R = 0.356.
Cardiogenic shock which indicates severe interstitial myocarditis and severe arteritis of the coronary vasa vasorum occurs in the 1st week of the illness and is followed by aneurysm formation in LMCA. Extracardiac aneurysm due to severe arteritis of its vasa vasorum associates with severe arteritis of the coronary vasa vasorum originated from the aorta which may induce dilatation at the proximal portion of LMCA. Thus, aneurysm in LMCA complicated with extracardiac aneurysm reveals its proximal extension. In conclusion, these findings may contribute to understand morphogenesis and to investigate the treatment on KD.


049
Kawasaki Disease With Tsutsugamushi Disease: A Case Report

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Background: Clinical and epidemiologic features suggest infectious agents as a possible cause of Kawasaki disease; however, the etiology of Kawasaki disease still remains unknown. A number of microorganisms were hypothesized as an etiology of the illness. This is the first reported case of Kawasaki disease with tsutsugamushi disease.

Case presentation: We report the case of a 4-year-old boy who presented with fever of 7 days duration and skin rash and bilateral conjunctival injection. He had a history of visiting a rural area with his grandmother. On admission, he had fever of 39.4 °C. His heart rate was 90/minute and his blood pressure was 90/60 mmHg. His pharynx was slightly injected and there was red lip. His neck was swollen with cervical lymphadenitis. He had erythematous macular rash on her trunk. Examination of his skin revealed an eschar on penile base of right scrotum. His laboratory results showed WBC 4,720/mm³, 42% polymorphonuclear leucocytes, 39% lymphocytes, hemoglobin 10.3 g/dL, platelet count 148,000/mm³, CRP 3.23mg/dl, pro-BNP 316.5 pg/ml. The respiratory viruses using a multiplex real-time-PCR kit (Adenovirus, Influenza A, Influenza B, Metapneumovirus, Rhino A virus, Respiratory syncytial virus, Parainfluenza ) were all negative. Mycoplasma pneumonia IgM was negative. R.tsutsugamushi Ab was positive. Echocardiographic findings 1 day after admission was mild dilatation of LCA (RCA=1.8mm, LCA=3mm). He was treated on oral roxithromycin for presumptive diagnosis of tsutsugamushi disease along with clinical features of Kawasaki disease which resolved after therapy with intravenous immune globulin and aspirin. Over the next 48 hours, he became afebrile and his rash improved. He was placed on low-dose aspirin for 8 weeks. His echocardiogram were within normal limit (RCA=1.9mm, LCA=2.7mm) at 2 months after the onset of his illness.

Conclusion: This case report suggests that Kawasaki disease can rarely occur concurrently or immediately after a rickettsial illness such as tsutsugamushi disease.

M. Song: None.

051
Kawasaki disease in a patient with Acute Myeloid Leukemia and Candida infection

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Though the causative agent of Kawasaki disease (KD) remains unclear, an infectious agent is thought to trigger the disease. KD has been described associated with immunodeficiency disorders including HIV. We report a patient with Acute Myeloid Leukemia (AML) who developed KD in an early course of the disease. A 4 year-old boy was diagnosed as AML and received treatment with daunorubicin, etoposide and Ara-C. Eleven days later he started presenting fever, diarrhea and abdominal pain. A diagnosis of neutropenic colitis was made and treatment with vancomycin and cefepime was started. He continued having fever and polymorphic eruption was added, with prominent perineal erythema. Later he presented redness of the lips, hands and feet edema, erythema in the palms and soles and conjunctival erythema. The diagnosis of KD was established and treatment with IVIG and low-dose prednisone was administered. Echocardiogram revealed left coronary aneurysm and pericardial effusion. Abdominal-ultrasound showed gallbladder hydrops. Candida grew in blood culture and treatment with amphotericin-B was started. Akita et al. reported one previous case of leukemia associated with KD. As the previous reported case, our case developed the disease
in the induction therapy for the AML. Interestingly, infection with Candida was documented in our patient. Administration of Candida cell Wall-antigens induced KD-like coronary vasculitis in mice. *C. abicans* colonizes the intestinal tract and causes invasive deep micosis in an immune-compromised host. Beta-glucan from the fungus stimulates the host immune system inducing an inflammatory response. Sampling campaigns over Japan during the KD season detected major differences in the microbiota of the tropospheric aerosols, with the unexpected finding of the Candida species as the dominant fungus from aloft samples (54% of all fungal strains). These results, provide support for the feasibility of a windborne pathogen. A fungal toxin could be pursued as a possible etiologic agent of KD. To our knowledge this is the second case of KD associated with leukemia. Chemotherapy-induced immunosuppression could have a role in the genesis of KD in our patient and possibly triggered by a Candida infection.


052 The Gut Microbiome Alters Susceptibility to Coronary Inflammation in Kawasaki Disease

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The gut microbiome has been shown to have immunomodulatory capabilities, and changes in the composition of the microbiome have altered the pathogenesis of inflammatory diseases. In this study, we sought to investigate the effects of the microbiome on the pathogenesis of Kawasaki Disease (KD) using the Lactobacillus cell wall extract (LCWE)-induced coronary arteritis model. Using qPCR on mouse fecal samples, we quantified bacterial communities through the 16S rRNA gene. Animals originating from the same supplier where housed in two independent facilities. There were marked elevations in Bacteroides, Bifidobacteria, Lactobacillus and segmented filamentous bacteria (SFB) and decrease in Clostridia in Facility A compared to Facility B. The transition to the newer Facility B resulted in a reduction in disease induction by LCWE to 26% (25/95), compared to 50% (35/70) at Facility A. Addition of antibiotics to the drinking water to deplete the microbiome reduced disease incidence to 40% (2/5) of mice housed at Facility A compared to 100% (5/5) of untreated mice, suggesting that components of the microbiome are necessary to exacerbate inflammation. To address whether the gut microbiome was sufficient to support disease susceptibility, the cecal contents of the susceptible mice at A were gavaged into the less susceptible mice at B. Recipients of the cecal contents from Facility A had an increased disease incidence of 91% (10/11) compared to 60% (6/10) in control mice which received cecal contents from mice housed in Facility B. We also report elevated levels of IL-17 in the serum of SFB-colonized mice. SFB, known to exacerbate several models of autoimmunity, was completely absent in mice housed at Facility B. Interestingly Th17 and its associated cytokine IL-17 have been associated with acute KD, but its role in pathogenesis remains unclear. Th17 cells have been implicated in autoimmunity, and are also important players in gut homeostasis. Our data provide evidence for the role of the gut microbiome in modulating the immunopathogenesis of KD, pointing to the important interactions of commensal and pathogenic factors as determinants of disease.

R.S.M. Yeung: None. D. Chan: None. T.T. Duong: None.

053 Tenascin-C Expression in Cardiovascular Lesion of Kawasaki disease.

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[Background] Tenascin-C (TN-C) is an extracellular matrix that is closely associated with tissue remodeling and inflammation. It is expressed under pathological condition such as myocarditis, myocardial infarction, atherosclerosis and aneurysm. However, examination of TN-C expression in Kawasaki disease (KD) has not been yet performed.

[Materials and methods] The tissue samples of myocardium and coronary arteries were obtained from 25 autopsy cases of KD (age: 3
months to 20 years old, sex: 18 males and 7 females, duration of the illness: 6 days to 17 years). Histological findings of the myocardium and coronary artery were analyzed and correlated with TN-C expression by immunohistochemistry.

[Results] 1) Myocardium: Myocarditis was observed in 8 KD patients who died within 33 days after the onset. On the other hand, chronic persistent myocarditis and post-inflammatory myocardial fibrosis were not seen in the patients who died after 33th day of the disease. Myocardial infarction was observed in 9 patients who died in the convalescent and remote phases of KD. Expression of TN-C in the myocardium corresponded to the area with inflammatory cell infiltration and granulation tissue. The degree of expression correlated with the severity of the inflammation.

2) Coronary artery: Intense TN-C expression was observed at the site of active inflammation of coronary arteries in acute stage. Regarding convalescent period (27 to 57 days after the onset) when the inflammation began to disappear, the TN-C expression still remained in the intima and media but weakened in the adventitia and surrounding connective tissue. In remote phase, TN-C expression was limited to the neovascular vessels in the thickened intima and recanalized vessels.

[Conclusion] The results of this histological study demonstrate that TN-C may be a useful biomarker for indicating in KD cardiovascular lesions.


054 The Correlation Between IgE And The Level Of Interleukin-21 In Kawasaki Disease

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Purpose: It has been reported that serum level of immunoglobulin E (IgE) is increased in patients with Kawasaki disease (KD) after acute phase. However the exact mechanism of increasing IgE is yet to be revealed. We investigated whether the interleukin-21 (IL-21) could be related with the high IgE in KD. Instead of IL-4, IL-21 was focused in this study because it has been reported that its level is increased in various autoimmune vasculitis.

Methods: From June 2008 to June 2010, 49 patients with KD admitted in Wonju Severance Christian Hospital and 13 controls with high fever due to unknown infection who had no history of KD were included in this study. The sera from patients and controls were collected and checked in terms of immunoglobulin E (Chemiluminescent method, Siemens, Munich, Germany) and IL-21 (ELISA, eBioscience, San Diego, USA).

Results: The median age of patients with KD was 3 years of age (range: 0.4-10) and that of controls was 7 years of age (range: 1-12). The group of patients with KD was composed of 39 complete KD and 10 incomplete KD. Among patients with KD, 10 patients had coronary arterial dilatation (CAD) and 39 patients had no coronary complications. The median value of IL-21 in patients with KD was significantly increased as 466 pg/mL (range: 0-1544) while that value in controls was <62.5 pg/mL (range: 0-825 pg/mL) (P < 0.01). We could not find the significant correlation between the serum level of IgE and that of IL-21 in patients with KD (Spearman R=0.2, P = 0.08) though 30% of patients with KD showed increased IgE more than 100 IU/mL. In addition, our data showed no significant difference between CAD group and non CAD group in terms of serum IL-21.

Conclusion: Our data showed firstly that IL-21 is increased in patients with KD. There was no significant correlation between high IgE and the level of IL-21.

H. Lee: None.

055 Histological And Rheological Evaluation At Coronary Artery Lesions In Patients With Kawasaki Disease Within 2 Years From Onset

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[Background] Some paper reported that intravascular ultrasound (IVUS)- virtual histology (VH) showed atherogenesis in the evolution of coronary artery lesions (CAL) in young adults long after Kawasaki disease (KD). However, there is no report about those findings during early phase of KD. [Purpose] We perform coronary intimal histologic evaluation by IVUS-VH for KD patients with CAL within two years from onset. Furthermore, we calculate shear stress in the target site and examine whether
rheological potential affects to vascular histological change after KD [Subjects and Methods] IVUS-VH was performed in 12 Japanese KD patients (median age, 5.1 years) during 2 years after onset of KD (median, 10.2 months). All these patients had giant aneurysm in another branches. We investigated 20 coronary branches including 10 sites of small aneurysm (s-AN), 10 sites of regressed s-AN, and 20 sites of normal segment. Each of the 4 plaque components was assigned a respective color and defined as follows: fibrous area (green); fibro-fatty area (yellow); necrotic core area (red); and dense calcium area (white). Moreover, we measured average coronary peak flow velocity by Flow wire and calculated shear stress in each site. [Results] 10 sites of s-AN showed prominent endothelial hypertrophy with fibrous and/or fibro-fatty plaques. In 7 sites of these 10 sites, dense calcium and necrotic core localized which indicates early phase of atherosclerosis. 10 sites of regressed s-AN had circumferential endothelial hypertrophy occupying mainly fibrous and/or fibro-fatty plaques composition. In 8 sites of these regressed 10 sites, dense calcium and necrotic core locally existed. On the other hand, normal segment in 20 sites had no plaque in 19 sites and trivial plaque in 1 site. Moreover, shear stress in all evaluated VH sites were within normal limit, which shows rheological potential doesn’t affect to vascular remodeling in such coronary artery lesions. [Conclusions] IVUS-VH study revealed that initial atherosclerotic findings locally existed not only at small aneurysm site but also at regressed site. Therefore, careful further investigation to vascular remodeling in KD patients with CAL including regressed s-AN will be need.

W. Makoto: None.

056 Increased Neutrophil Counts and Serum Transforming Growth Factor-beta 1 Levels in an Infant With Autoimmune Neutropenia Who Recovered From Kawasaki Disease

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Kawasaki disease (KD) is an acute, febrile, and systemic vasculitis that primarily occurs in infants and young children. Although the etiology is unknown, it is considered that abnormal activation of monocytes/macrophages but not lymphocytes could occur during the acute phase of KD. Neutrophils may have a pivotal role in the pathogenesis of KD as well as the formation of coronary artery lesions (CAL). Primary autoimmune neutropenia (AIN) is a common form of chronic benign neutropenias of childhood. AIN, occurring in infancy, is characterised by persistent severe neutropenia (<500/µL of absolute neutrophil counts [ANC]), detection of the autoantibodies against neutrophil-specific antigens, and 95% of resolution before 4 years of age. There has been only one report on a patient with AIN who developed severe KD after the administration of granulocyte colony-stimulating factor. Here, we describe a 21-month-old female with AIN who developed full-blown KD on severe neutropenia remained. Single dose intravenous immunoglobulin led to a prompt response with defervescence. During the convalescent phase of KD, the patient showed a rapid increase and the following recovery of ANC in concert with the elevated levels of serum transforming growth factor-beta 1, that is one of the representative immunoregulatory cytokines. During hospitalization, echocardiography indicated no evidence of CAL. The pathophysiology of KD and the resolution of autoimmunity were discussed with special reference to the cytokine profiles.


057 Costimulation Mediated T-cell Survival Exacerbates Kawasaki Disease

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Introduction: Kawasaki Disease (KD) is a multi-system vasculitis leading to coronary artery damage. Previous work has shown that co-stimulatory signals can rescue a subset of superantigen (SAg) reactive T-cells from apoptosis and one of the major pathways responsible for delivery of this co-stimulatory signal is CD28 signaling on T-cells. Lactobacillus casei cell wall extract (LCWE) contains a SAg among its active ingredients, leading to induction of coronary arteritis in mice that closely resembles human KD.

Methods: Flow cytometry was used to measure the expression of pro-survival molecules and markers of apoptosis. In vivo studies were performed with C57BL/6 mice (4-5 weeks) injected i.p. with either LCWE, or LCWE and anti-4-1BB or Isotype control antibody. Cardiac tissue isolated, processed, stained and scored as per protocol. Gene expression analysis in KD patients was performed using the Illumina HumanHT-12v4.

Results: Despite the fact that SAg-activated T-cells undergo apoptosis and are deleted, T-cells persist and are central to ongoing inflammation in affected arteries. Stimulation of CD28 leads to upregulation of pro-survival molecules cFLIP and BCLxL and reduction of caspase 3-annexinV double positive cells (markers of apoptosis) after SAg-stimulation, as detected by flow cytometry. In animals co-injected with anti-4-1BB (co-stimulation agonist), the incidence of coronary arteritis was dramatically increased to 94% compared to 54% with LCWE alone. Analysis of gene expression profile from 171 children with KD show elevated levels of molecules specific to the CD28 signaling cascade through Grb2, and VAV1 leading to the upregulation of Rac1 and CDC42, together with upregulation of pro-survival molecules cFLIP, MCL1 and NAIP. Interestingly, increased expression of cell survival molecules was associated with IVIG failure, with statistically significant elevation of NAIP and CDC42 and a trend towards increased expression for cFLIP and MCL, in IVIG non-responders compared to responders.

Conclusions: Enhanced co-stimulation contributes to T-cell survival after SAg-stimulation leading to persistent coronary artery inflammation and poor treatment response in KD.


058 Magnetographic Recognition Of Abnormal Depolarization And Repolarization In Patients With Coronary Artery Lesions Caused By Kawasaki Disease

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[Background]Noninvasive recognition of abnormalities of depolarization (DE) and repolarization (RE) in patients with coronary artery disease is difficult.

[Purpose]Our aim was to identify abnormalities of DE and RE in patients with coronary artery lesions (CAL) due to Kawasaki disease (KD) using magnetocardiography (MCG).

[Methods]We evaluated sixty one pts (48 males and 13 females) with CAL due to KD, The age at MCG ranged from 11 months to 38 years (median 15 years). Eleven pts had had previous myocardial infarction (MI), and 22 pts had had at least an occlusion of a major coronary artery branch. MCG was performed at rest with a multichannel superconducting quantum interference device system. The integral value was computed for each channel and isointegral maps were constructed during DE and RE. We analyzed abnormalities of DE and RE depending on occlusion of coronary arteries (OC) or a history of MI. Univariate analysis was performed on respective factors for DE and RE.

[Results]In the MI group, the number of abnormal DE and RE, abnormal DE and abnormal RE were 3 , 1 and 3, respectively. In OC group, the number of abnormalities of DE and RE was 2, and abnormality of RE was 9. In the non-OC group, the number of abnormal DE and RE was 2, and abnormal RE was 5. The factor of MI was significantly related on abnormality of DE and RE (p<0.05). On the other hand, the factor of OC was significantly related to abnormality of RE (p<0.05).

[Conclusion]Although symptomatic coronary occlusion affects both DE and RE, occlusion of coronary artery only affects RE. MCG is useful to detect changes in DE and RE.
**Poster Abstract Presentations (continued)**

**059**

**New findings implicated in Coronary calcification in Chronic phase Kawasaki disease**

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**Background**

Kawasaki disease (KD) is a systemic vasculitis prevalent in infants and sometimes complicates coronary artery lesions (CALs). It has been well known that CALs gradually develop endothelial dysfunction, post-inflammatory atherosclerotic changes, and finally coronary calcification. It has been also reported, recently, that vascular calcification is an active cell-driven process characterized by osteogenic differentiation of vascular smooth muscle cells, relating to the chronic inflammation and oxidative stress. In this study, in KD, we evaluated the possible implication of significant calcification prevalent in CALs to the long-term prognosis.

**Methods**

We included 42 patients with a history of KD (age: 18.3±6.7 year-old). The breakdown was 17 patients without CALs and 25 with CALs: 12 without calcification and 13 with calcification on multi-detector computed tomography. We measured %FMD as an endothelial function marker and hs-CRPs as an inflammatory marker, serum hydroperoxide and urinary 8-OHdG as oxidative stress markers, and the bone mineral density (BMD). Patients in CALs(-) group took no medicine and those in CALs(+) group were under antiplatelet and/or anticoagulant therapy, particularly, those with calcification were additionally administrated statin or ARB.

**Results**

Values of %FMD in CALs(+) group were significantly lower compared with those in CALs(-) (p<0.05), and values in those with calcification were still lower than those without calcification (p<0.05). Values of hs-CRPs in CALs(+) group were significantly lower than those in CALs (p<0.05). 8-OHdG values as oxidative stress marker in CALs(+) group were significantly lower than those in CALs(-) (p<0.05). The BMD in CALs(+) group tended to be lower compared with the age-matched reference values (88.9±7.0% of normal).

**Conclusions**

In KD chronic stage, the decreased %FMD may be an essential condition to occur coronary calcification. Decreased BMD in patients with coronary calcification suggested the possible existence of the skeletal and the vascular system in KD, similar to the mechanism of common vascular calcification.


**060**

**FcR⁺CD4⁺ T Cells as a Specific Subset of IL-17-producing Cells Controlled by BATF/IRF8: Novel Insights Into Etiology of Kawasaki Disease**

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Kawasaki disease (KD) is an acute vasculitis primarily involved coronary arteries of infants and children. Although more than 40 years have passed since the first description of the disease, its etiology remains unclear. Circulating interleukin 17 is increased in the acute stage of KD and expressed in the damaged coronary arterial wall from autopsies of children after KD. The aim of this study was to elucidate the involvement of IL-17 in the pathogenesis of KD.

In this study, we identified a specific subset of CD4⁺ T cell expressing Fc receptor which existed high percentage in acute stage of KD than in recover stage. In addition, FcR⁺CD4⁺ T cell in acute stage expressed higher level of IL-17 than in recover stage.

Therefore, we suggest this IL-17-producing FcR⁺CD4⁺ T cell may be a critical regulator of immunity in Kawasaki disease. In order to investigate the detail mechanism that FcR⁺CD4⁺ T cell subset expressed higher amount of IL-17 in KD, we isolated FcR⁺CD4⁺ and FcR⁺CD4⁺ T cells from adult healthy donors and stimulated with anti-CD3/CD28 beads only. We found that FcR⁺CD4⁺ T cells produced much higher IL-17 than FcR⁺CD4⁺ T cells without the need of Th17-differentiation cytokine. Furthermore, FcR⁺CD4⁺ T cells expressed higher IL-17-related transcriptional activator, BATF and lower level of transcriptional repress, IRF8 than FcR⁻CD4⁺ T cells.
cells. Knockdown of BATF and IRF8 could reduce and increase IL-17 production, respectively. These findings define BATF and IRF8 as the intrinsic transcriptional regulators in IL-17 production from FcR⁺CD4⁺ T cells. Collectively, our results suggest that IL-17-producing FcR⁺CD4⁺ T cells are the novel subset of IL-17-producing cells and important pathogenic immune cells in KD. Inhibition of IL-17 production from FcR⁺CD4⁺ T cells has great potential to be as a therapeutic strategy for Kawasaki disease and other FcR⁺CD4⁺ T cell-driven autoimmune diseases.

C. Chang: None. T. Ko: None. C. Chen: None. J. Wu: None. Y. Chen: None.

061 Anti-inflammatory Effect Of Resveratrol In Human Coronary Arterial Endothelial Cells Via Autophagy: Implication For The Treatment Of Kawasaki Disease

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Kawasaki disease (KD) is an acute febrile vasculitis of childhood and is the leading cause of acquired heart disease in children in the developed world. If untreated, KD can result in coronary aneurysms in 25% of patients, who are at risk of myocardial infarction, sudden death, and congestive heart failure. Despite the success, 10-20% of children will have persistent or recrudescent fever after their first infusion of IVIG. These patients are at increased risk of developing coronary artery abnormalities. Additional therapies should be explored to decrease the incidence of coronary arteritis complication and improve the prognosis in Kawasaki disease. Induced autophagy with resveratrol confers cardioprotection during ischemia and reperfusion in rats. KD is associated with elevated production of inflammatory cytokines, causing damage to the coronary arteries. Serum TNF-alpha levels are elevated in KD, which was supposed to activate the endothelial cells. As a result, adhesion molecules such as intercellular adhesion molecule-1 (ICAM-1) and vascular cellular adhesion molecule-1 (VCAM-1) are expressed in the endothelial cells, and leucocytes adhere firmly to endothelial cells. The leucocytes then damage the endothelial cells and smooth muscle cells and cause vasculitis. In this study, we examined the anti-inflammatory effects of resveratrol on TNF-alpha-induced adhesion molecule expression (VCAM-1 and ICAM-1) and cytokine production (interleukin (IL)-1beta, IL-6 and IL-8) in HCAECs. Pretreatment with resveratrol significantly inhibited TNF-alpha-induced adhesion molecules and cytokines production in HCAECs via the activation of autophagy. Our results suggest that adjunctive resveratrol therapy may modulate the inflammatory response during KD vasculitis and explore the role of autophagy in the pathogenesis of the complication and the promising therapy.

F. Huang: None. H. Kuo: None. H. Yu: None.

062 Functional mechanism of cyclosporin A therapy for immunoglobulin-resistant Kawasaki disease

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Background: We have reported that cyclosporin A (CsA) therapy may be a promising and safe option for patients with Kawasaki disease (KD) resistant to initial and additional intravenous immunoglobulin (IVIG). Up to now, it has been considered that CsA exerts effects on the intracellular phosphatase calcineurin, and subsequently inhibits activation of nuclear factor of activated T cells (NFAT). However, the functional mechanism of CsA therapy in KD patients has remained unclear.

Methods: The KD patients enrolled in this study were treated with CsA between April 2012 and December 2013. In accordance with our treatment protocol, KD patients are initially treated with IVIG and aspirin. If there is no response, a further course of IVIG is given, and if there is no response to this additional IVIG, the patients are treated with CsA. Peripheral blood samples were obtained just before and after the initial course of IVIG, additional IVIG, and CsA therapy. To evaluate the NFAT pathway and
**Poster Abstract Presentations (continued)**

activation of the Janus kinase (JAK)-signal transducer and activator of transcription (STAT) pathway, we examined the gene expression of cytokines and intracellular signal transducers using real-time RT-PCR and phospho-STAT3 (pSTAT3) and STAT5 (pSTAT5) using flow cytometry.

Results:
Thirty-six KD patients were divided into three groups: responsive to initial IVIG (n=19), responsive to additional IVIG (n=7), and treated with CsA group (n=10). In the CsA group, expression of mRNAs for interleukin (IL)-2, NFATc1 and NFATc2 was significantly increased, whereas that for STAT3, 5A, 5B was decreased after CsA treatment; on the other hand, the MFI of pSTAT3 (CD3+ T cell) and pSTAT3 (CD16b+ granulocyte) was decreased after CsA treatment. In the group responsive to initial IVIG, the expression of mRNAs for IL-2, NFATc1 and NFATc2 was significantly increased, whereas that for STAT3, 5A, 5B was decreased after IVIG treatment; on the other hand, the MFI of pSTAT3 (CD3+ T cell) and pSTAT3 (CD16b+ granulocyte) was decreased, and that of pSTAT5 (CD16b+ granulocyte) was increased, after IVIG.

Conclusion:
In patients with refractory KD, CsA exerts effects on the activity of the NFAT and JAK-STAT pathways. However, our results suggest that in patients with immunoglobulin-resistant KD, CsA may act through a mechanism other than the NFAT pathway.

**N. Kakimoto**: None. **H. Suzuki**: None. **T. Suenaga**: None. **T. Takeuchi**: None. **S. Shibuta**: None. **J. Abe**: None. **N. Yoshikawa**: None.

**063**
**Evaluation Of The Immune Dynamics Of Kawasaki Disease :For Opting Timing for Vaccination**

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Background;
We investigated immune function in Kawasaki disease patients during the acute phase, 1 month after onset, 6 months after onset and 9 months after onset.

Methods;
All patients treated with 2g/kg of Intravenous immunoglobulin (single IVIG) or 4g/kg of IVIG(additional IVIG). We enrolled 18 KD patients (age,4 to 90 months). IgG,IgM,IgA,IgD,B-cell surface immunoglobulin(Sm-Ig),CD3,CD4,CD8,CD20,CD56 were measured using flow cytometry; the lymphocyte transformation test(LTT) was also performed. In addition, migration of IVIG antibodies was assessed, and measles, rubella, mumps, and chickenpox antibodies were investigated using enzyme immunoassay(EIA).

Results:
IgG at 1 month after KD onset was significantly higher than before IVIG treatment. In addition, the number of lymphocytes at 1 month after KD onset was higher than before IVIG treatment. The values for Sm-Ig IgM, Sm-Ig IgD, Sm-Ig κ, and Sm-Ig λ before IVIG treatment was higher than those at 1 month after KD onset. In addition, The values for CD8 before IVIG treatment was higher than those at 1 month after KD onset. The values for CD3,CD4 before IVIG treatment was lower than those at 1 month after KD onset. The values for CD8 was higher at 1 month after KD onset. The levels of measles, rubella, mumps, and chickenpox antibodies were positive at 1 month after single IVIG treatment and these antibodies were negative at 6 months after single IVIG treatment. The levels of measles, rubella, mumps, and chickenpox antibodies were positive at 1 month after additional IVIG treatment. These antibodies were still positive in some of patient at 6 month after additional IVIG treatment.

Conclusions:
Abnormal immune function at KD onset may improve at 1 month after KD onset. We can vaccinate children at least 2 month after KD onset. However it is recommended that live vaccines be deferred for at least 6 months following treatment with single IVIG ,and 9 months following treatment with additional IVIG.
ABSTRACTS (continued)


064
Correlation Of The Platelet Count With Immunoglobulin G, M, And A Levels In The Early Convalescent Stage Of Kawasaki Disease

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Background: The clinical course of Kawasaki disease (KD), which is self-limiting and immune-mediated, is controlled by the host’s immune system. The incidence of incomplete KD is increasing in Korea. We evaluate the changes in the platelet count and immunoglobulin (Ig) levels (IgG, IgM, IgA, and IgE) during hospitalization and the relationships among these parameters.

Methods: We examined the platelet count and levels of the four above-mentioned Igs twice at presentation and at discharge (mean of 6.2 days apart) in 43 patients with complete KD who received intravenous Ig at 2 g/kg. The relationships across all parameters were evaluated.

Results: The mean patient age was 29.9 ± 16.4 months, and there were 28 male and 15 female patients. The mean platelet count and IgG, IgM, IgA, and IgE levels at presentation and at discharge were 366 ± 92 and 548 ± 135 ×10³/µL, 718 ± 317 and 2433 ± 426 mg/dL, 63 ± 57 and 98 ± 79 mg/dL, and 69 ± 70 and 57 ± 64 IU/mL, respectively. The values of these parameters were correlated with the time of examination from fever onset, in comparing three groups with fever duration of the <5 days, the 5–10 days, and the 11–16 days (Nonparametric Kruskal Wallis test and Dunn's method for each post-hoc pairwise test). A correlation was also noted in the degree of increase calculated at the two time points between the platelet count and IgG (P = 0.002), IgM (P = 0.01) or IgA level (P = 0.002), respectively (Spearman correlation coefficient).

Conclusions: The platelet count and Ig levels (IgG, IgM, and IgA) increased in the early convalescent stage of KD and were correlated with each other. This finding suggests that the host’s immune/repair system is involved in recovery from KD and may help to differentiate KD, especially incomplete KD, from other KD-like diseases if these phenomena do not occur in other diseases.

K. Lee: None.

065
T cell Differentiation in Human Kawasaki Disease and a Murine Model of Coronary Arteritis

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The role of T cell differentiation in the immunopathogenesis of Kawasaki disease (KD) remains unclear. The aim of this study is to elucidate the role of T cell subsets in coronary artery lesion (CAL) of KD. Peripheral blood was obtained in 10 patients with acute KD before and 1 week after intravenous gamma-immunoglobulin (IVIG) treatment and in 20 patients with past history of KD for more than 5–20 years. Meanwhile, induction of coronary arteritis was performed on wild type BALB/c mice by Lactobacillus casei cell wall extract (LCWE). Human peripheral blood leukocytes were analyzed by using flow cytometric analysis and murine hearts were examined for immunofluorescence study and for RNA expression levels.

RESULTS: Compared to the febrile controls, KD patients prior to IVIG treatment had increased percentage of CD3+/CD4+/interferon-γ+ (Th1, Th1) cells and CD3+/CD4+/interleukin-17A+ (Th17) cells (mean ± SD, 1.36% ± 1.39% and 0.51% ± 0.25%, respectively) among Th cells (CD3+/CD4+). Both increases declined after IVIG treatment (0.71% ± 0.74% and 0.33% ± 0.18%) despite no statistically difference by Mann-Whitney test. None of these 10 acute KD patients developed CAL after IVIG treatment. However, patients with previous KD and definite CALs (n = 11) seemed to have higher percentage of Th17 cells (0.50% ± 0.25% versus 0.35% ± 0.23%) but similar level of Th1 cells (0.93% ± 0.51% versus 1.05% ± 0.64%) when compared to those without CAL (n = 9). Murine cardiac tissues displayed the presence of Th1 (double-stained with CD3 and T-bet) and Th17 cells (double-stained with CD3 and RORγt) during days 7 and 14 after LCWE treatment but not in PBS-treated mice. Compatible with these, cardiac mRNA levels showed both increased
levels of IFN-γ and IL17A mRNA in LCWE-treated mice.
CONCLUSIONS: Our initial data suggests that specific T cell differentiation into Th1 and Th17 cells occurred in both human KD and mice stimulated with LCWE. IVIG treatment was associated with the recovery of such T cell differentiation. However, the clinical application to predict IVIG responsiveness and future CAL development by such increase in the peripheral Th17 remains unclear. Further studies to elucidate the detailed immune regulation of these T subsets on CAL are warrant by using this LCWE murine model.


066
High-dose IgG Completely Inhibited TNF-α-induced, But Not IL-1β-induced, G-CSF Expression By Human Coronary Artery Endothelial Cells

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High-dose intravenous IgG (IVIG) is a well-established standard therapy for Kawasaki Diseases (KD) that effectively reduces both systemic inflammation and the risk of developing coronary artery aneurysms, in approximately 80% of KD. However, some patients do not respond to IVIG and the cause of their unresponsiveness remains unclear. We previously reported that high-dose IgG specifically and completely inhibited accelerated expression of KD-related cytokines, including G-CSF, by human coronary artery endothelial cells (HCAEC) in response to TNF-α. The suppression of these cytokine genes correlated closely with functional inhibition of a transcription factor, C/EBPδ. Here we show that IL-1β-induced expression of the KD-related cytokines by HCAEC was never inhibited by high-dose IgG treatment. Furthermore, although TNF-α-induced C/EBPδ activities, as measured by gel shift assay, were completely inhibited after high-dose IgG treatment, those induced by IL-1β were not inhibited at all. Our findings suggest that C/EBPδ may play a pivotal role in the clinical effectiveness of IVIG in patients with KD. Greater understanding of the precise underlying mechanisms of IVIG on coronary artery endothelial cells may contribute to the development of novel therapeutic strategies for current IVIG-resistant patients with KD.


067
Peroral Administration Of Extract Of Candida Albicans Induce Kawasaki Disease-like Vasculitis In Mice

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[Background] The cause of Kawasaki disease (KD) has been still unknown though the intestinal flora was reported as one of the candidate etiology of KD. Candida is known as one of the intestinal flora. Intraperitoneal injection of Candida albicans water-soluble fractions (CAWS) that compose of polysaccharide of cell wall of the yeast can induce systemic vasculitis in mice. It is evaluated as animal model of Kawasaki disease vasculitis because this experimental vasculitis is similar to those observed in KD patients. However it is uncertain whether or not oral administration of CAWS can induce vasculitis in mice.
[Aim] The present study aimed to elucidate whether or not oral administration of CAWS can induce vasculitis.
[Materials and methods] Mice, DBA/2, male, 4 weeks of age were used. CAWS suspended in PBS was administered perorally to mice for 28 consecutive days. As a priming agent, 20 micrograms of LPS was injected to mice intraperitoneally before administration of CAWS. Experimental groups are as follows. Group-I : Peroral administration of 800 micrograms of CAWS with LPS, Group-II: Peroral administration of 800 micrograms of CAWS without LPS, Group-III : Peroral administration of 250 micrograms of CAWS with LPS. Mice injected CAWS intraperitoneally (conventional procedure) were used as control group. Vasculitis was evaluated by routine histological
techniques. This study conformed with regulations of position of the American Heart Association on research animal use and Toho University’s Animal Ethics Committee.

[Result] The incidence of vasculitis in each group were as follows: Group-I: 1/6, Group-II: 0/6, Group-III: 1/6, Control: 3/3. Dense infiltration of neutrophils and macrophages was observed in coronary artery and/or aortic root. Severity of inflammatory cell infiltration and extent of the lesion in Group-I and Group-III were milder and smaller than those of control.

[Conclusion] Present study revealed that peroral administration of CAWS could induce vasculitis in mice though the incidence of vasculitis was lower than that of control. This model is considered to be useful to clarify the relation between intestinal immunity and vasculitis. We should clarify the mechanism that oral administration of CAWS induced vasculitis.


068
Echocardiographic Evaluation of the Kawasaki Disease Mouse Model

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Background: Mouse echocardiography is an established, non-invasive method to evaluate experimental cardiovascular disease. The murine Kawasaki disease (KD) model demonstrates aortic and coronary artery inflammation by histology. The clinical relevance of these pathological changes has not been confirmed. In children, KD involves coronary artery abnormalities visualized by echocardiography. However, echocardiography has not been previously applied to the mouse KD model. We hypothesized that coronary vasculitis caused the lactobacillus casei cell wall extract (LCE) causes abnormalities detectable by echo.

Methods: Male mice (ages 3-4 months) were injected with LCE or vehicle. Sedated echos were performed with a VisualSonics Vevo 2100 system. Twelve mice (8 LCE and 4 vehicle) had pre-injection echos followed by serial studies for 6-10 weeks. Evaluations were blinded to treatment group. 2-D measurements were taken at consistent locations in the arteries. Aortic regurgitation was rated based on clinical criteria. Histology was evaluated at 6 weeks post-LCE.

Results: Mild aortic regurgitation (AR) was present in 6 of 8 mice injected with LCE starting at 1 week post-injection. No AR was present at baseline or vehicle injected mice. LCE mice showed increased aortic root diameter at 6 weeks compared to baseline (1.78mm±0.01 vs 1.52±0.02, p<0.05). Overall left coronary artery dimensions were not changed from baseline at 6 weeks post-LCE, but coronary imaging was difficult. One mouse had a diffusely enlarged left coronary system and severely diminished left ventricular function at 10 weeks post-LCE. Histology findings were present in all LCE-injected mice including aortic valvulitis, myointimal proliferation and a single case of infarction.

Conclusion: The most prominent echo findings in the mouse KD model are severe aortitis with dilation and valvular regurgitation. These features could serve as non-invasive experimental measurements. Coronary dilation was a rare finding; however the coronaries are difficult to evaluate in mice. Overall, the mouse KD model demonstrates greater aortic pathology than found in human KD. Further studies are underway to evaluate additional non-invasive measurements such as vascular strain.

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Introduction: Although etiology of Kawasaki disease (KD) remains elusive, a line of recent experimental studies implies that some kinds of infectious stimuli are implicate in the vasculitis through uncontrolled innate immune systems such as pattern recognition receptor (PPR)-mediated inflammatory signaling. It has already known that Candida albicans water-soluble fraction (CAWS) inducing KD-like vasculitis in mice function through PRP. Furthermore, it is reported that proline-rich tyrosine kinase (Pyk2), which is molecule involved in the PRPs-dependent signaling pathways, plays an important role in activation of NF-κB. Therefore, we investigated a possible relevance of Pyk2 in the pathogenesis of KD.

Methods: Pyk2-knock out (Pyk2-KO) and wild-type C57BL/6 mice (WT) were administered CAWS to induce KD-like vasculitis. Extension of the experimental vasculitis was immunohistochemically determined with anti-MPO antibody. CAWS-stimulated NF-κB activation was evaluated by quantifying nuclear translocation of NF-κB p65 subunit in peritoneal macrophages isolated from PYK2-KO and wild-type mice in vitro. Cytokines and chemokines across each mice were compared by cytokine array.

Results: Pyk2-KO mice didn’t show any apparent defective phenotype. While marked inflammation was observed in the aortic root of CAWS-treated WT mice, such vasculitis was barely detected in CAWS-treated Pyk2-KO mice. CAWS-induced NF-κB activation was also less observed in macrophages from Pyk2-KO mice. There were differences in some cytokines and chemokines production between mice.

Conclusion: We speculate that Pyk2 is involved in the pathogenesis of KD. Pyk2 might be a potential therapeutic target for KD.


070
Trial of Ulinastatin treatment for murine model of Kawasaki Disease

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Recently, we reported that the initial Ulinastatin (UTI) therapy combined with intravenous immunoglobulin (IVIG) reduced the proportion of patients with Kawasaki disease requiring additional rescue treatment and the occurrence of coronary artery lesions as compared with IVIG alone (Circulation. 2011;124(25):2822-2828.). However, there have been no reports that histologically examined the therapeutic effects of UTI. In the present study, to investigate the histological efficacy of UTI, we administered UTI in a vasculitis murine model, resembling Kawasaki disease. Four-week-old male mice DBA/2 were intraperitoneally administered Candida albicans water soluble extract (CAWS) for 5 days and were treated either with UTI, IVIG, or a combination of UTI and IVIG. Further, we examined the plasma levels of neutrophil elastase and cytokines and evaluated histopathological features.

Neutrophil elastase, TNF-α, IL-6, IP-10, and MIG significantly increased in the CAWS-treated mice. Large amount of elastase-positive neutrophils infiltrated in the coronary tissue. In addition, the infiltration of elastase-positive neutrophils was reduced in the pathological tissue of the UTI treatment group. Neutrophil elastase is strongly involved in the destruction of the elastic plate and smooth muscle layer. There is a possibility that destruction of the vascular structures can be suppressed by decreasing the elastase-positive neutrophils infiltration in the UTI treatment group.


071
Abdominal Aorta Dilatation and Aneurysm in Kawasaki Disease Vasculitis Mouse Model: Role of IL-1 Signaling

Daiko Wakita, Youngho Lee, Kenichi Shimada, Shuang Chen, Timothy R Crother, Ceders-Sinai
ABSTRACTS

**Poster Abstract Presentations (continued)**

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Background: Kawasaki disease (KD) is the most common cause of acute systemic vasculitis and acquired cardiac disease among US children. KD causes coronary artery aneurysms in up to 25% of untreated patients, and less frequently aneurysms in other systemic arteries including the abdominal aorta. Lactobacillus casei cell wall extract (LCWE)-induced KD mouse model mimics histopathologically the coronary artery lesions seen in KD patients.

Objective: To evaluate the development of abdominal aorta dilatation and aneurysm in KD mouse model and investigate the role of IL-1 signaling.

Methods and Results: We investigated the incidence and progression of abdominal aorta aneurysm (AAA) and dilatation in the KD model at 1, 2, 5 weeks. Over 80% of the mice developed significant dilation of abdominal aorta at 2 wks with progressively greater dilatation at 5 wks, with greater severity in males. KD mice showed fusiform and saccular AAA, which were always below the renal artery. Immunohistochemistry showed significant intimal proliferation, massive myofibroblastic proliferation that breaks the elastin layer, infiltration of large numbers of neutrophils and macrophages into the media and adventitia. IL-1R- or IL-1beta-deficient mice were completely protected from the KD associated abdominal aorta dilatation and AAA. IL-1R antagonist (Anakinra) significantly prevented the abdominal aorta dilatation and AAA (in addition to blocking coronary arteritis) in the KD mice.

Conclusions: We report a new model of AAA and aortic dilatation in the LCWE-induced KD mouse model. These studies suggest that in children with KD the incidence of abdominal aortic dilatation and AAA maybe higher than currently appreciated, thus requiring prospective studies to determine the frequency of these vascular complications. Our findings also demonstrate that IL-1 plays an important role in development of LCWE-induced abdominal aortic lesions and blockade of IL-1 signaling may be a promising therapeutic target not only for KD vasculitis and coronary arteritis, but also for abdominal aorta dilatation and AAA associated with the disease.


072

**Chest X-ray as an Additional Diagnostic Tool in Kawasaki Disease**

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Background: Diagnosis of Kawasaki disease (KD) is sometimes doubtful. Chest x-ray examination is easily available and relatively not expensive. However, its role in the diagnosis of Kawasaki disease according to some studies, is not significant. So far we have no data from Indonesia.

Objective: To know the chest x-ray patterns in acute KD patients.

Methods: We studied chest x-ray films of KD children at acute stage from January 2003 till July 2013 which were taken consecutively in 5 hospitals. All cases were treated by the author. All films were seen and confirmed by radiologists.

Results: We analyzed chest x-ray films (antero-posterior view) of 503 KD patients at acute stage, age ranging from 33 days to 16 years. The results were that 335 (67%) of them showed abnormalities, of which almost all showed infiltrates in bilateral lung fields especially in perihilar and paracardial regions. Only one case showed lobar pneumonia pattern and another with pleural effusion. Only 31 (10.8%) patients with chest x-ray abnormalities clinically showed respiratory signs and symptoms such as cough and running nose.

Conclusion: It is concluded that the presence of pulmonary infiltrates in chest x-ray may be of value in supporting the diagnosis of KD, especially in doubtful or incomplete cases.

Keywords: Kawasaki disease, chest X ray.

N. Advani: None. L. Alim Santoso: None.

073

**A Case Of Fatal Kawasaki Disease Associated With Fulminant Myocarditis**

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Shinji Yamamoto, Keiko Tanaka, Wakaba Morinobu, Seikeikai Hosp, Sakai, Osaka, Japan; Yoshio Ohta, Dept of Pathology and Lab medicine, Kindai Univ Faculty of Med, Ikoma, Nara, Japan

Introduction
Acute phase Kawasaki disease (KD) is often associated with myocarditis. In most cases, such myocarditis is self-limiting. Fulminant myocarditis is rare as a cause of death for acute KD. We report a case of fatal KD associated with fulminant myocarditis.

Case
A 4-year-old boy presented high fever and consulted family doctors for the second successive day. Although he received antibiotics, high fever persisted. He consulted to our hospital on the 4th day of illness. At the initial visit, conjunctival congestion, redness of pharyngeal and lip, bilateral cervical lymphadenitis and erythema on neck, palms and abdomen were observed. Initial laboratory data were shown as follows: WBC count 20,800 / µL, CRP 14.18 mg / dL. He was hospitalized with the diagnosis of acute febrile disease including KD. At first he was prescribed acetylsalicyclic acid and intravenous infusion of antibiotics, however high fever still persisted. On the 6th day of illness, immunoglobulin (IG) and prednisolone were administered intravenously because he was anticipated to be refractory to IG. On echocardiography, left ventricular contraction was normal. There were no findings of coronary artery abnormalities or pericardial effusion. After the first administration of IVIG, high fever persisted. Inflammatory markers on blood examination exacerbated. Laboratory data on the 8th day of illness were as follows: WBC 23,500 / µL, CRP 14.18 mg / dL, CPK 1,451 IU / L (MB 2%). Therefore, we added the second IVIG, steroid pulse therapy and urinastatine. On the next day (9th day), however, he suddenly suffered from cardiopulmonary arrest and deceased.

Pathological findings revealed scattered myocardial necrosis on both ventricles. The CD 3, CD 8 positive T lymphocytes were infiltrated around myocytes. There were no findings of coronary artery aneurysms or thromboembolisms. These findings were compatible with fulminant myocarditis.

Discussion
Recent advances in therapy for acute KD significantly reduce coronary artery lesions and subsequent mortality. However, clinical feature of KD has a lot of variety. Although fulminant myocarditis associated with KD in early acute phase is extremely rare, we should prepare for refractory KD and its abrupt change.


074 Coronary Artery Lesions in Children with Kawasaki's Disease: A 10-Year Follow-up in Moscow

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Background: Kawasaki's disease (KD) is an acute systemic vasculitis in childhood. Lesion in the coronary arteries (CA) causes an acute or chronic ischemia, myocardial infarction and sudden death.

Materials and Methods: The study included 189 children with KD for the period of 9 years (2004 - 2013). The age of the patients at the time of the acute stage of the disease was 1 month - 12 years 8 months . Boys and girls ratio was 1.8:1. 92% of the children were ill at the age of up to 5 years. Mean follow-up period was 15,8 months. We performed coronary angiography by CT scan in 14 children and by catheter in 9 children in CCVS. Echo was done in all 189 children.

Results: Aneurysms of CA were found in 59 (31.2%) patients according to echocardiography data. The frequency of aneurysm formation in children first year of life was higher than in children older than 1 year (41.3% and 29.3%). 92% of the children were ill at the age of up to 5 years. Mean follow-up period was 15,8 months. Thirty eight (20%) patients had multiple aneurysms. Small aneurysms with a diameter less than 5 mm were found in 16.4% of patients, average (5 - 8 mm) - in 9%, giant (greater than 8 mm) - in 5.8% of patients. Transient CA ectasia was diagnosed in 13.2% of children.
Sensitivity of echocardiography in diagnosis of CA aneurysms was 88.5% in comparison with MSCT coronary angiography, specificity - 92.3%. Mean aneurysms' diameter measured by ECHO was 7.1 ± 3.3 mm, while CT contrast study revealed 7.3 ± 3.1 mm (p> 0.05). We found an involution of 40.2% of aneurysms during follow-up.

Thrombi were found in 8 of 11 patients with giant aneurysms by echocardiography. Five thrombi disappeared after conservative therapy, two increased and occluded the RCA. CA stenosis greater than 75% was revealed in 2 patients with giant aneurysms in 2 years 7 months and in 3.5 months after manifestation of KD by using coronary arteriography.

Conclusion: Kawasaki's disease is a frequent cause of aneurysms, thrombosis and stenosis in coronary arteries in early childhood. Giant aneurysms often predispose to occlusion of the CA. Echocardiography is a highly specific and sensitive method for the visualization of CA aneurysms and thrombi. Other methods are useful when distinguishing stenosis and thrombosis in small CA is required.

O. Bockeria: None. G. Lyskina: None. O. Shirinskaya: None. A. Satyukova: None. N. Gagarina: None.

075
High Sensitivity C Reactive Protein in Adolescent and Young Adult Patients with Kawasaki Disease Late After Onset

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Background.
In children with history of Kawasaki disease (KD), low grade inflammation was ever reported to be associated with persistent coronary artery lesions (CAL). However, this issue had rarely been checked in adolescents and young adults (10-25 years old).

Methods and Results.
The study cohort was comprised of 104 subjects: 22 KD patients with angiography-confirmed CAL, which persisted at an average of 12.5 years after onset of KD, 38 KD patients with regressed aneurysms, 44 KD patients without any coronary complications from the disease onset and 31 age-matched (18.7 ± 1.88 years old) healthy controls. Plasma levels of high-sensitivity C reactive protein (hs-CRP) were measured for all participants with a commercially available high-sensitivity method (Immuliite, Simens, USA). Plasma levels of hs-CRP were significantly higher in KD patients, regardless of the severity of coronary artery involvement, than controls. However, there was no difference of hs-CRP level between each KD patient groups including any severity of coronary artery lesions. After adjustment for confounding factors such as body mass index, gender and levels of HDL-c, linear regression analysis showed the only independent predictor of logarithmically transformed hs-CRP levels was BMI (β=0.32, p=0.007), rather than patient grouping (p=0.126).

Conclusion.
Levels of hs-CRP are significantly higher in adolescent and young adult KD patients than age-matched controls. However, we failed to detect significant difference among patients with different severities of CAL. The results implied, in Taiwan, low grade inflammation might play a minor role on the persistence of coronary lesions in KD.


076
Clinical Usefulness Of Serum Procalcitonin Level In Kawasaki Disease Children.

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Purpose: Procalcitonin (PCT) is one of acute phase reactants such as C-reactive protein (CRP), and is likely to elevate in systemic inflammation, especially bacterial infection. As we know, the CRP level rise in the patients with high fever including Kawasaki disease (KD) and bacterial infection. So we investigated the clinical usefulness of serum PCT level in Kawasaki disease (KD), which is a systemic inflammation caused by vasculitis.

Method: From August 2013 to June 2014, a total 336 patients were studied serum PCT level during hospitalization. We enrolled 41 patients of KD, 83 patients with viral infection, and 21 patients
with bacterial infection. Result: The patients with KD had significantly higher mean age (24.4±18.1 months), mean body weight (12.1±3.9 Kg), and mean duration of fever prior to admission (4.4±1.8 days) than other patients (p<0.05). The serum PCT level, white blood cell (WBC) and platelet count, neutrophil proportion, erythrocyte sedimentation rate (ESR), and C-reactive protein (CRP) were significantly higher in KD patients than viral infection patients (p<0.05). Although not statistically significant, the serum PCT level was lower in KD patients than bacterial infection patients, whereas the CRP was higher in KD patients than bacterial infection patients. No significant difference in serum PCT level was showed between complete KD patients and incomplete KD patients. Also there was no significant difference in serum PCT level between responders to an initial intravenous immunoglobulin treatment and nonresponders. Conclusion: Serum PCT level may help to differentiate KD from viral infection, but we did not find a significant difference in PCT level between KD and bacterial infection. And the utility of PCT level as clinical marker in KD may be limited.

H. Choi: None. T. Kwon: None.

077
Association of Sodium and Coronary Arteriopathy in Acute Phase of Kawasaki Disease

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BACKGROUND:
Kawasaki disease (KD) is an immune related multisystemic inflammatory vasculitis in children, especially ensues coronary artery lesions. Several cardiovascular diseases are known to be correlated with sodium level. In this study, we examined the association between serum sodium levels and the severity of coronary artery lesion in acute phase of Kawasaki disease.

OBJECTIVE:
The purpose of this study was to determine the association of serum sodium level for predicting cardiac events in Kawasaki disease (KD) patients especially in coronary artery lesions (CALs).

METHODS:
We conducted a retrospective review of the medical records of 158 Kawasaki disease patients from June 2013 to August 2014. We devided the subjects into two groups regarding to the serum sodium level. Various laboratory tests and echocardiographic data were analyzed. Student t-tests were carried out to analyze the significance of the difference in each group.

RESULTS:
ESR, CRP, BNP, and liver enzymes were significantly greater in lower sodium group. Echocardiographic diastolic marker of mitral E and E/E' measurement were statistically different. Coronary arterial changes were significant in lower sodium group as well.

CONCLUSIONS:
The lower sodium group demonstrated significant increase of various inflammatory markers and coronary arterial lesions. The sodium level might be associated with the severity of coronary vessel and cardiac inflammation in acute phase of Kawasaki disease.


078
An Incomplete Kawasaki Disease Child With Initial Presentation Of Murmur

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Abstract: Kawasaki disease (KD) is acute vasculitis in childhood. The authors report the 12-month-old girl with initial presentation of cardiac murmur who was diagnosed incomplete KD.

Case: A 12-month-old girl with history of 3 days fever up to 38°C and upper respiratory symptoms including rhinorrhea visited a
pediatric clinic. Cardiac murmur was noticed, then she was referred to Pediatric Cardiology clinic. She had loss of appetite and her growth curve showed severely underweight of 8.4kg (less than 3p) compared to height 78cm (50~75p).

On hospital day 1, laboratory studies revealed a white blood cell (WBC) 9.4 (seg 73%, Lym 23%) x 10^3/μL, hemoglobin concentration (Hb) of 5.5 g/dL with hematocrit (Hct) 21%, platelet count 426,000/μL. And laboratory results included ESR 2mm/hr, C-reactive protein 0.05mg/L, AST/ALT 31/19 IU/L, Ferritine 13 ng/mL, TIBC 510ug/dL, Transferrin Saturation Index 2.5% and MCV 50.4fl, MCH 13.4pg, MCHC 26.5g/dL.

She had grade II-III/VI end-systolic & early diastolic murmur. The echocardiography showed left main coronary artery dilatation and pericardial effusion.

Based on diagnosis of incomplete Kawasaki disease and iron deficiency anemia, she treated with IVIG (IV gamma globulin), acetylsalicyclic acid, packed RBC transfusion and supplement of oral iron. On hospital day 2, repeat laboratory studies revealeed Hb 6.5 g/dL, and the murmur decreased rapidly. 6 days later Hb was 9.3 g/dL.

Pro-BNP was 352 pg/ml on hospital day 1 and repeat studies revealed 978 pg/ml on hospital day 2, 84pg/ml on hospital day 8.

The patient was discharged 8 days after admission (on day 11 of her illness) without fever.

After 1 month of discharge, she had gained weight to 10.5kg and laboratory study results Hb 11.0 g/dL.

The authors report one child presenting with heart murmur under incomplete Kawasaki disease.


079
Is Harada Score a Useful Tool in Mexican Childrens with Kawasaki Disease?

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Background/Purpose
In developed countries Kawasaki disease (KD) is the most common cause of acquired heart disease in childhood. Haradascore is one of the most used predictive tool for coronary arteries aneurysms (CAA) development in KD. The aim of the study is to describe clinical data, treatment, and to assess the Harada score in Mexican patients with KD.

Methods
We retrospectively indentified all patients evaluated at Hospital Infantil de Mexico Federico Gómez during a 6-year period between 2008 and 2014. We reviewed demographic, clinical, laboratory, echocardiographic, and treatment data; and Harada scores were derived to evaluate efficacy in predicting risk for CAA.

Results
In our Institution 34 cases were reported during the study period, 16 (47.1%) males, and median age of 36 (8 - 120) months. Incomplete KD was diagnosed in 6 (17.6%) cases with no significant differences in demographic data, but with a lower accuracy in establishing diagnosis at admission compared with complete presentations (100% vs 66.7%, P = 0.027). Most of the patients (76.5%) received at least one antibiotic prior to admission to our Hospital.

Patients presented with history of 6 (4 - 16) days with fever and conjunctivitis. Significant differences were observed between complete and incomplete presentations regarding oral changes (100% vs 66.7%, P = .027), strawberry tongue (92.9% vs 33.3%, P = .004), pharyngitis (100% vs 33.3%, P < .001), and rash (71.4% vs 16.7%, P = .021). No significant differences were observed in laboratory results. Seven (20.6%) echocardiograms were reported with CAA, one of them found valve insufficiency, and none identified effusion. Harada score was positive in 23 (67.6%) patients, with high sensitivity (85.7%) and low specificity (37%), OR 1.36 (CI95% 0.89 - 2.06, P = .384).

In total, 32 (94.1%) patients received intravenous immunoglobulin (IVIG). Retreatment with IVIG was given in 3 (8.8%) and steroid treatment in 1 (2.9%) patient. All of the patients received aspirin.

Conclusions
This study revealed a high incidence of CAA in our population, added to lack of suspicion and antibiotic overuse. As in Japanese and US population, Harada score is a good screening tool to identify risk for CAA development in Mexican patients.
Correlation of N-terminal pro-BNP Release with Myocardial Involvement in Acute Kawasaki Disease

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N-terminal pro-BNP (NT-proBNP) is elevated at the onset of Kawasaki Disease (KD). This is based on the hypothesis of immune myocardial inflammation. We sought to study the relationship between NT-proBNP and cardiac function in KD.

Parameters of myocardial involvement determined by ECG (PR and QTc intervals, QT dispersion, R-T axis) and by echocardiogram (systole and diastole) were correlated with levels of NT-proBNP in the acute (1 week), sub-acute (2-3 months) and chronic (6 months to 1 year) phases of KD. KD patients were compared to a febrile group. KD patients were further subdivided into 2 groups according to the levels of NT-proBNP; normal NT-proBNP (NT-proBNP Z-score < 2), or elevated NT-proBNP (Z-score ≥ 2).

There were 56 subjects (14 controls, 19 KD-1 and 23 KD-2 patients), with similar age at assessment (3.8±4.3 vs. 3.3±2.3 years-old, p=0.609). Myocardial contractility was significantly lower in KD patients in the acute phase with an ejection fraction of 57.4±7.5% compared to CTL 61.9±6.5%; p=0.049). Myocardial dysfunction was more significant in KD with high NT-proBNP compared to those with normal NT-proBNP, (shortening fraction Z-score of -1.6±1.5 versus -0.5±1.5; p=0.025) QTc interval was longer in KD compared to febrile CRT 412.3±21.0 mS vs. 390.6±14.6 mS, respectively; p=0.009). In contrast, there were no significant differences for left ventricular mass index (p=0.935) or LV end-diastolic diameter (p=0.565). Likewise, there were no significant differences for the PR interval (p=0.344), QT dispersion (p=0.288) or R-T axis (p=0.577). Otherwise, there was a significant correlation between coronary artery involvement (CA z-score ≥ 2.5) and the likelihood of lower LV ejection fraction (p=0.049) and higher NT-proBNP z-score (p=0.043), but no correlation with normalized LV shortening fraction (p=0.16) or QTc (p=0.14). The anomalous findings disappear in the sub-acute phase. On the other hand, a lengthening of QTc interval in the acute phase, irrespective of NT-proBNP status, resolves after 2-3 months.

In acute KD, there is a reduction in myocardial function, to a higher extent in cases with elevated NT-proBNP. This correlates with coronary artery involvement. KD patients with elevated NT-proBNP z-score may warrant careful follow-up.

A. Fournier: None. L. Desjardins: None. N. Dahdah: None.
ABSTRACTS

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Treatment show significant difference between the groups stratified on the requirement of post-IVIG therapy. In the stratification based on acute CAL- AST, ALT, Albumin and Sodium show significant difference between the groups.

[Conclusion] We suggest that ratio of neutrophil, total-bilirubin, AST, ALT, Albumin, Sodium, C-reaction protein, D-dimmer and time to first treatment are predictive factors of resistance to single IVIG therapy. Similarly, levels of AST, ALT, Albumin and Sodium are predictive factors of acute coronary artery lesions in Kawasaki disease.

K. Goto: None.

082
Web-based Coronary Evaluation of KD Children in Taiwan

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Background
Z-score system for coronary diameters of Taiwanese children was developed in the October of 2013. We started web-based service since 2014. This study was aimed to evaluate the demographics of users and patients. The distribution of analyzed results (Z-score) were also reported.

Methods
We set the questionnaire at the website: www.tspo.org.tw/service/Z_score.asp. The questions listed in the questionnaire included (1) age of users and patients, (2) are users medical personals or parents? and (3) are the analyzed coronary diameters from measurements at the acute phase? (4) Are users willing to let us collect the above information?

Results
Since the beginning of 2014, 850 times of using the coronary Z-score calculator were recorded. 155 times of approach are due to evaluation of coronary changes before IVIG. Of the 155 times of analyses, coronary dilatation (Z≧+2.5) was noted in 12.4% of LMCA, 3.5% of LAD and 7.96% of RCA. Dilatation of at least one coronary arteries occupied 18% of all. 86% of users were medical personals and only 7.2% were parents.

Conclusions
This is the first time that web-based coronary evaluation in Taiwan was reported. Relatively small percentages of users were parents. That means we should put greater efforts to let such friendly tool known to the public.


083
Usefulness of Serum Immunoglobulin G Levels Calculated in the Acute Phase of Kawasaki disease

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Background: Intravenous gamma-globulin treatment (IVGG) is an established therapy for acute phase Kawasaki disease (KD). Since a lot of studies have already testified that the efficacy of IVGG is dose-dependent, a single large dose of IVGG has been accepted as a standard treatment of KD. Some reports described the increasing rate of serum Immunoglobulin G (IgG) after IVGG would have a relationship with efficacy of IVGG. It should, therefore, be very important to compass trends of serum IgG levels in each in KD patient. However, it is unable to frequently measure values of serum IgG in KD patients from the standpoint of medical expenses. If we can estimate IgG levels in KD patients from routine biochemical data without additional costs, that is very helpful to assess inflammatory status in acute phase of KD.

Aim to this study: We hypothesized that serum levels of IgG in acute phase of KD patients could be extrapolated by serum values of total protein (TP) and albumin (Alb), and, we tried to establish a simple formula to estimate serum levels of IgG.

Materials and methods: We enrolled 42 KD cases (27 ± 21 month, Male 24/Female 18) that were treated in Saga University Hospital, Japan from April of 2010 to August of 2014. All cases met the diagnostic criteria of KD. They were initially treated with IVGG and aspirin or flurbiprofen. 12 patients (28.6%) needed additional treatments such as steroid and cyclosporine A. In this study, we examined relations before and after treatments of serum TP and Alb and IgG in serum of them and tried to establish a simple formula to estimate serum
levels of IgG in acute phase of KD. For statistical analysis, we used paired t-test.
Results: We found that values obtained by subtracting serum values of IgG and Alb from TP were almost constant through acute phase in each KD patient, regardless of differences in clinical course and therapies. Therefore, we could estimate serum IgG values, once we checked levels of TP, Alb and IgG before treatment. Calculated IgG values were lineally correlated with values of directly measured IgG (P<0.0001, r=0.90). From this finding, we would assess the course of IgG levels during acute phase of KD patients correctly.
Conclusion: By estimation of IgG levels, we can grasp inflammatory status of KD and make appropriate therapeutic plans.

C. Iida: None. A. Iwanaga: None. K. Tashiro: None.

084
The Circulating MicroRNA Study for Children with Acute stage of Kawasaki disease

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Background: Kawasaki disease (KD) is a systemic vasculitis syndrome related to immune dysregulation. MicroRNAs (miRNAs) can regulate the expression of protein-coding genes, and have been used as a biomarker for the diagnosis of various diseases. This study was designed to identify plasma miRNAs changed in patients with acute stage of KD and to identify candidate miRNAs.
Methods: A total of ten children, ranged from 9 months to 5 years old, with acute stage of KD were enrolled. The profiles of plasma miRNAs were analyzed by miRNA arrays. The miRNAs of interest identified by array were confirmed by reverse transcription-quantitative PCR (qRT-PCR).
Results: In comparison with the convalescent stage, plasma miR-10a (ten of ten) and miR-155 (eight of ten) were significantly down-regulated during the acute stage of KD. Pathway analysis of the combinatorial effects of these two miRNAs (Diana miRPath) indicated the genes involved in the T-cell receptor signaling pathway (p.=4.541392e-05) and the Toll-like receptor signaling pathway (p.=0.0001528698) that were highly co-regulated by these two miRNAs.
Conclusions: This is the first report of uncovering circulating miRNAs involved in patients with acute stage of KD. The results of this study indicated that the miRNAs might play a crucial role in the immune dysregulation of acute KD. Further studies and more KD patients should be investigated to elucidate the roles and as biomarkers of these miRNAs for early diagnosis of acute KD.
Keywords: Biomarker, Children, Kawasaki Disease, MicroRNAs


085
Early Detection of Kawasaki Disease in Infants

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Background and Objective: This study was aimed to investigate clinical characteristics of infantile Kawasaki disease (KD), and to evaluate early diagnostic features of KD in febrile infants.
Subjects and Methods: We retrospectively reviewed the medical records of 66 patients with KD who were admitted to Dongguk University Gyeongju Hospital, between January 2010 and August 2014. The clinical, laboratory data between infants and children were analyzed. And the clinical and laboratory data of infantile KD patients were compared with 18 infants who were admitted for other acute febrile disease during same period as above.
Results: A total of 66 patients were identified; 21(31.8%) were infants; 45(68.2%) were > 1 year old children. Incomplete KD was much more common in infants (n=15, 71.4%) than in children group (n=14, 31.1%) (P = 0.002). The infants group was characterized by significantly higher rates of inflammatory changes at the Bacille Calmette-Guerin (BCG) inoculation site (P<0.001), but lower rates of changes in the cervical lymphadenopathy (P=0.005), conjunctival injection (P=0.047). The serum levels of hemoglobin were lower (P<0.001), and platelet (P=0.029), C-reactive protein (P=0.042), N-terminal pro-brain natriuretic peptide (NT-
ABSTRACTS
Poster Abstract Presentations (continued)

proBNP) (P=0.042) was higher in the infants group significantly. Pyuria was also significantly higher in the infants group (P=0.017). Between infants with KD and with other acute febrile diseases, there were significantly higher serum levels of ESR (P<0.001), CRP (P=0.009) and NT-proBNP (P=0.002) in the infantile KD.

Conclusion: Because incomplete KD was much more in infants, the diagnosis of infantile KD can be difficult. The BCGitis and higher level of NT-proBNP can help to early diagnosis of incomplete KD in infants, and may be a good predictor of KD in acute febrile infants combined with other acute phase reactants.


086
Pentraxin 3 Can Be A Candidate For Biomarker Of Kawasaki Disease

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Background: Kawasaki disease (KD) is a systemic vasculitis and the leading cause of acquired heart disease. There are some cases that show unresponsiveness to initial intravenous immunoglobulin (IVIG) and require addition treatment. High incidence of coronary artery lesions (CAL) is seen in unresponsive cases. Pentraxin 3 (PTX3) is produced at the site of vascular inflammation, and used as a new biomarker for vasculitis. The aim of this study is to explore the application of PTX3 in KD.

Methods: 128 patients with KD are enrolled. Blood samples are collected at before IVIG and 1, 3, 6 month later from the onset of KD. PTX3 values are compared with IVIG unresponsive scoring system by Kobayashi et al. (Circulation, 2006).

Results: Mean values of PTX3 before IVIG and 1, 3, 6 month were respectively 25.1*, 7.1*, 3.8, 3.6 ng/ml (asterisk shows statistical significance with age-matched control: 3.6). Mean values of PTX3 in unresponsiveness (n=20) and responsiveness (n=108) at before IVIG and 1, 3, 6 month were 46.8* vs. 20.9, 9.1* vs. 6.7, 4.2 vs. 3.7, 3.9 vs. 3.5 ng/ml (asterisk shows statistical significance between two groups). There is statistical positive correlation between PTX3 and score points by Kobayashi et al. (r=0.602, p=0.000). According to the statistical analysis, the area under the ROC curve (AUC) was 0.87 and sensitivity and specificity of PTX3 as IVIG unresponsiveness prediction were 90 and 81 %, if cut off value was set as 28 ng/ml. Conclusions: 1. vasculitis continues at least 1 month after onset of disease. 2. PTX3 can be a candidate biomarker for prediction of unresponsiveness in patients with KD.


087
Urinary LDH activities in patients with Kawasaki disease

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Background: Kawasaki disease (KD) is a systemic vasculitis with unknown origin. KD patients often have leukocytes in urine as well as urinary tract infection (UTI). The aim of this study is to evaluate urinary LDH and its isozyme, which is useful in diagnosis with UTI, in patients with KD.

Patients and methods: 158 patients with KD (including 4 with incomplete KD) and 52 patients with febrile sickness were enrolled as control group in this study. Urine samples were obtained at least one point.

Results: Total level of urinary LDH in patients with KD was significantly higher than that in
control group. Urinary LDH level in the acute phase was significantly higher than that with convalescent phase in patients with KD. Urinary LDH isozyme showed predominant elevations of LDH1 and LDH2. Some patients showed the elevation of urinary LDH level before the clinical criteria of KD were fulfilled. There was no correlation between urinary LDH concentration and pyuria.

Conclusion: The levels of LDH isozyme (LDH4 and LDH5) in urine is known to increase in patients with acute upper urinary tract infection, while the level of its isozyme (LDH1 and LDH2) increased in acute phase of KD. The elevated levels of total urinary LDH and its isozyme (LDH1 and LDH2) may be useful for early diagnosis of KD and also for diagnosis of incomplete KD.


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Pentraxin 3 in Coronary Artery Lesions in Kawasaki Disease

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Although vascular inflammation is an important feature of Kawasaki disease (KD), the usefulness of local inflammatory markers as biomarkers for KD is unknown. Pentraxin 3 (PTX3), soluble lectin-like oxidized low density lipoprotein receptor 1 (sLOX-1) and matrix metalloproteinase-9 (MMP-9) are biomarkers of inflammation of vascular components. Objective: We tested whether plasma concentrations of PTX3, sLOX-1 or MMP-9 would be a useful biomarker for detecting high risk patient of coronary artery aneurysm (CAA) in KD and compared with serum level of interleukin-6 (IL-6) and IL-18. The ability of the assays to identify KD patients at risk for CAA was analyzed. Methods: PTX3, sLOX-1, MPP-9, IL-6 and IL-18 concentrations of 50 KD patients at different four clinical points were analyzed. Point A represented on admission; B, pre-IVIG; A+B, before IVIG; C, after IVIG; D, after fever resolution. Each concentration was compared with the rate of occurrence of CAA and IVIG unresponsiveness. Results: Each value was evaluated in 50 KD patients (2 with CAA, 48 without CAA). Three patients were treated without IVIG, 17 with one course of IVIG, and six with two IVIGs, two with three IVIGs, respectively. At the points A+B, C, D means for PTX3 were; 33.4; 11.7, 9.00 ng/ml, mean for MMP-9; 34.6, 19.2, 24.2 ng/ml, mean for sLOX-1; 3.82; 2.33, 2.25 ng/ml, respectively. Levels of PTX3 (p<0.001) and MMP-9 (p<0.05) were significantly higher in before IVIG than after IVIG; whereas levels of sLOX-1, as well as those of IL-6 and IL-18 were comparable between before and after IVIG. PTX3 were well correlated with IL-6 level (R2=0.73). Both cases with extraordinary high PTX3 levels at admission of 91.8 and 65.3 ng/ml were complicated with coronary artery aneurysms, even though they were treated by three courses of IVIG. The level of plasma PTX3 was significant related with the course numbers of IVIG (p<0.05). Conclusion: Levels of PTX3 and MMP-9 appear to be associated with clinical course of KD. Levels of PTX3 were correlated with the severity of disease; how many doses of IVIG enough to resolve fever. An extraordinary high PTX3 level might be suggestive of the existence of CAA. These data suggest that PTX3 can be a candidate biomarker for prediction of unresponsiveness and CAA formation in patients with KD.


089
Reducing Overdiagnosis and Miss Rates of Kawasaki Disease at First Contact Setting

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Background: Kawasaki Disease(KD) is a challenging diagnosis at first presentation. Diagnosis relies on the 1993 American Heart
Association (AHA) criteria of ≥5 days of fever with ≥4 of the following features: mucositis, cervical lymphadenopathy, non-suppurative conjunctivitis, swollen or desquamating extremities, polymorphous rash. Many present atypically and are not easily identified by the Emergency Department (ED) physician. This leads to delays in diagnosis and treatment of KD.

Aim: To reduce miss rates and overdiagnosis in the ED through identifying early clinical predictors for KD, within and out of the AHA criteria.

Methods: Retrospective case-controlled study on patients discharged with a diagnosis of KD at KK Women’s and Children’s Hospital (KKH) from April 2007 - December 2010. Patients admitted from the ED over the same period with initial diagnoses of KD, but with discharge diagnoses that stated otherwise formed the control group. We analysed the presentation patterns in both groups. Using multivariate logistic regression, we identified significant clinical predictors of KD.

Results: The diagnostic guidelines in the ED were neither specific nor sensitive, resulting in high overdiagnosis and miss rates, respectively. Of the patients admitted with the initial diagnosis of KD, 59.2% did not have KD. 44.3% and 29.1% of KD diagnoses were missed at first visit and during reattendances respectively. Miss rates were higher in infants than in older children (≥1 year old).

In older children, lymphadenopathy (OR1.79, p=0.013), non-suppurative conjunctivitis (OR2.22; p=0.001), irritability (OR2.24, p=0.005) and age (OR0.75, p<0.0001) were early predictors for true KD. With reattendances, lymphadenopathy (OR2.23, p=0.002), conjunctivitis (OR3.02, p<0.0001), irritability (OR1.86, p=0.040) and age (OR0.75, p<0.0001) remained significant, while changes in extremities (OR1.93, p=0.008) emerges as a useful predictor. No significant predictors were found for infants.

Conclusion: ED physicians should be aware of early predictors of KD. We advocate incorporating irritability into diagnostic guidelines for older children. These measures would reduce overdiagnosis and miss rates, permitting appropriate institution of early treatment.


**090**

**Serum Kawasaki Disease-specific Microbe-associated Molecular Patterns are Derived from in Vitro and in Vivo Biofilms**

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Background: We have found that serum KD-specific molecules possess molecular structures common to microbe-associated molecular patterns (MAMPs) from several bacteria by liquid chromatography-mass spectrometry (LC-MS) analysis. In the present study, we have extensively searched for the culture conditions that reproducibly produce MAMPs common to serum KD specific molecules.

Methods: Yersinia pseudotuberculosis, spore-forming bacteria and pathogenic bacteria were obtained from KD patients. Others were purchased from American Type Culture Collection. Microbes were cultured in a variety of conditions (medium, temperature, duration, shaking and biofilm formation). For biofilm formation, a various kind of oil/butter was added to the culture medium. Extraction from in vitro samples (culture supernatants, bacteria cells, and biofilms) as well as in vivo biofilm samples (teeth, tongue, nasal cavity, or rectum) was performed with ethyl acetate. Samples were analyzed by HPLC and MS (Esquire 6000 electrospray ionization). Human coronary artery endothelial cells (HCAECs) were employed for cytokine assay. The concentrations of cytokines were measured by EC800 cell analyzer with a BD™ Cytometric Bead Array.

Results: Serum KD-specific molecules showed m/z and MS/MS fragmentation patterns almost identical to those of MAMPs obtained from the biofilms formed in vitro (Bacillus cereus, Bacillus subtilis, Yersinia pseudotuberculosis, Staphylococcus aureus) or in vivo. Not culture supernatants but biofilm extracts from these bacteria, especially cultured in the presence of butter, induced proinflammatory cytokines by HCAECs.

Conclusions: Extensive analysis by LC-MS/MS revealed that serum KD-specific molecules common to MAMPs were mostly derived from
biofilms in vitro and in vivo. This report offers novel insight into the pathogenesis of KD.


091
Useful Predictor of Responsiveness to Initial Intravenous Immunoglobulin in Kawasaki Disease

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Background and Objectives: Ten to twenty percent of children with Kawasaki disease (KD) do not respond to initial intravenous immunoglobulin (IVIG) treatment, and if untreated approximately 15% to 25% of patients with KD have complications. The aim of our study is to find more useful predictors of responsiveness to initial IVIG in KD.

Subjects and Methods: We retrospectively reviewed medical records of 91 children diagnosed with KD at Myong Ji Hospital from March 2012 to April 2014. Laboratory data obtained before and 24 to 36 hours after IVIG treatment were collected, which include hemoglobin level, white blood cell count, proportions of neutrophils, lymphocytes and eosinophils, platelet count, erythrocyte sedimentation rate, C-reactive protein (CRP), creatine kinase (CK), creatine kinase MB (CK-MB) and N-terminal pro-brain natriuretic peptide (NT-proBNP). Subjects were then divided into 2 groups, IVIG-responsive and IVIG-resistant.

Results: Among the 91 patients, 11 patients (12%) required retreatment. By univariate analysis, before-IVIG laboratory parameters of white blood cell count, % neutrophils, erythrocyte sedimentation rate, CRP, sodium, CK, CK-MB and NT-proBNP were significantly different. In the after-IVIG laboratory parameters, hemoglobin level, white blood cell count, % neutrophils, % lymphocytes, CRP, CK, CK-MB and NT-proBNP were significantly different. While the mean-differences were not statistically significant, fractional change (FC)-CRP and FC-% neutrophils showed significant difference. By multivariate analysis, FC-CRP was confirmed to be an independent predictor for initial IVIG resistance.

Conclusion: FC-CRP might be a more useful and important value for predicting initial IVIG responsiveness in KD patients than before- and after-IVIG CRP.

J. kwak: None.

092
Evaluation Of The Ascending Aorta Stiffness Following Kawasaki Disease In Comparaison With Systemic Hypertension

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Background: Kawasaki Disease (KD) is a systemic vasculitis that affects large and medium-size arteries. The coronary arteries draw most of the clinical attention whereas few studies have taken interest in involvement of other vessels. Using an imaging-based mechanical biomarker (ImBioMark), we measured the ascending aorta (AA) stiffness in pediatric KD subjects compared to healthy controls (CTL) and patients with systemic hypertension (HTN).

Methods: We evaluated AA (Fig. 1a) in 20 CTL, 12 KD subjects (4 with and 8 without CA aneurysms). 8 children with HTN represented a comparative clinical model of vascular stiffness. We measured systolic and diastolic AA strains using ImBioMark. Strain was tested for normality against height for CTL. Strain values from KD and HTN subjects were normalized (Z-score) according to height. Comparisons were performed between groups using non-parametric statistics.

Results: Systolic and diastolic pressures were normal in KD subjects (49.8±28.4 and 46.1±6.9 percentile, respectively). Age was similar between KD (9.1±5.3 yo) and HTN (9.9±5.3 yo), p=NS. Fig. 1b exhibits a strain curve computed with ImBioMark. Systolic and diastolic strain values were normally distributed against height in CTL. HTN subjects had abnormal systolic and diastolic strain values. KD subjects had normal diastolic strain, but significantly abnormal systolic strain (Fig. 2). There was no statistically significant difference in strain, based on the presence or absence of CA aneurysm.

Conclusion: Despite normal blood pressure, AA in KD exhibited reduced strain during systole.
This may reflect in situ rigidity of the AA.


093
Analysis of Serum Levels of Procalcitonin and Serum Amyloid A as Biomarkers of Intravenous immunoglobulin-resistant Kawasaki Disease

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Aim: Immune globulin is the most effective treatment of Kawasaki Disease, however, 15-20% of patients with Kawasaki disease (KD) is resistant to 2g/kg of IVIG (refractory case), and those patients are high risk for complication of coronary artery abnormalities, to detect these refractory KD before treatment of acute phase is very important to determine their treatment, but the methods to predict the refractory case is not yet established. We analyze the relation of IVIG-resistant Kawasaki disease and serum levels of procalcitonin (PCT) or serum amyloid A (SAA).

Method: 192 patients with KD were involved in this study, and 48 were IVIG-resistant cases. Refractory case was defined as patients who needed additional treatment with IVIG and/or steroid after the first treatment with total 2g/kg of IVIG. Serum levels of PCT and SAA were measured before treatment, and the relationship to clinical course was analyzed.

Result: Median level of PCT of patients with IVIG-resistant KD was 2.24 ng/ml and those with non-IVIG-resistant KD was 0.47 ng/ml, and median levels of PCT of patients with IVIG-resistant KD was significantly higher than those with non-IVIG-resistant KD (p<0.01). Median level of SAA of patients with IVIG-resistant KD was 753.6 µg/ml and those with non-IVIG-resistant KD was 635.9µg/ml and there was no significant difference. We compared the accuracy of prediction of IVIG resistant KD by PCT and SAA using receiver operating characteristic (ROC) analysis. The areas under the receiver operating characteristic curve(AUC) of PCT, SAA and CRP was 0.75, 0.57 and 0.63 respectively. For identification of IVIG-resistant patients, a cut-off point, sensitivity and specificity of PCT, SAA and CRP were as follows, 1.5 ng/ml, 77% and 61%, 444 µg/ml, 83% and 32% and 7.7 mg/dl, 73% and 59%, respectively.

Conclusion: As PCT levels of patients with IVIG-resistant Kawasaki disease were significantly higher than those with non-IVIG-resistant KD, PCT could be one of the predictor of IVIG-resistant KD.


094
Diagnostic value of D-dimer and fibrinogen degradation products In Kawasaki disease

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Background: Echocardiography remains the cornerstone of diagnosis of cardiac complications in patients with Kawasaki disease (KD), and is also useful for the diagnosis of incomplete KD (i-KD). Since echocardiographic evaluation is based on somewhat subjective assessment by pediatric cardiologists, objective diagnostic measures by which general pediatricians can screen high-risk patients or make diagnosis of i-KD are desired.

Objective: To assess D-dimer and fibrinogen degradation products (FDP) as possible markers of coronary vascular damage in KD patients.

Design/Methods: Between June 2008 and March 2014, we recruited 121 KD patients: 86 with complete KD (c-KD) treated with intravenous immunoglobulin (IVIG), 10 with c-KD treated only with aspirin (a-KD), 16 with i-KD fulfilling four major criteria, and seven with severe refractory KD (s-KD). Control patients included five with Henoch-Schonlein purpura (HSP), 15 with fibrile convulsion (FC), and 39 with pneumonia. We retrospectively checked their medical records, echocardiography, and blood test results on admission and after IVIG therapy.

Results: Peak D-dimer values (normal range <1.0 µg/ml) were significantly higher in c-KD (2.9±2.4) than in a-KD (1.1±0.7), FC (0.8±0.4).
and pneumonia (1.3±1.1) groups (p < 0.05). Peak FDP value in the c-KD group was 6.8±4.7 µg/ml (< 5.0). Peak D-dimer and FDP values were the highest in the HSP group, followed by the s-KD group, and were comparable between the i-KD and c-KD groups. D-dimer values (2.9±1.4) at post IVIG were higher than those on admission (1.8±1.1) (p < 0.0001), while there was no significant change in FDP values. There was no significant difference in D-dimer or FDP values between KD with cardiac finding(s) and without. WBC and CRP values had no correlation with those of FDP or D-dimer. Receiver operating characteristic analysis determined a cut-off value of 1.1 µg/ml for D-dimer for c-KD, with the area under the curve (AUC) 0.85, sensitivity 0.95, specificity 0.59 and probability 0.44. Similarly, a cut-off value for FDP was determined as 2.5 µg/ml with AUC 0.90, sensitivity 0.89, specificity 0.70 and probability 0.40. Conclusions: Elevated D-dimer and FDP values help assist diagnosis of i-KD, but cannot predict cardiac complications in KD patients.


095
Increased Circulating Endothelial Microparticles In The Acute Phase Of Kawasaki Disease

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Method: We enrolled 9 patients (aged 3 months to 14 years, 6 male, 3 female), 7 common febrile children and 5 healthy children. KD patients in the convalescent phase were divided into two subgroups: coronary artery lesion (CAL, n=2) and no coronary lesion (NCAL, n=7). Blood samples were collected at the time of diagnosis before the initiation of IVIG treatment, then immediately after the first IVIG infusion and at 2-4 weeks after disease onset. Samples were measured using flow cytometry. Result: The percentage counts of EMPs were 2.90±1.26% in KD children before initial treatment, which were significantly higher (P<0.005) than those of disease controls (0.12±0.13%) and healthy controls (0.09±0.08%) before initial treatment, and reached normal levels within 4 weeks (0.05±0.05%). The highest percentage count of EMPs (5.47%) was observed in the patient with CAL before initial treatment. Further, prolonged high percentage count of EMPs (3.34%) was recognized in the patient with multiple giant aneurysms at 2 weeks after onset. Conclusion: The relation between the increased levels of EMPs and the involvement of CAL may suggest that EMPs could serve as a sensitive marker of the severity of endothelial dysfunction and vasculitis in patients with KD. Although the function of EMPs has not been fully elucidated, there is evidence that it plays an important role for distinct inflammatory reactions in endothelium.

H. Nakaoka: None.

096
Changes In HDL Cholesterol During The Acute Phase of Kawasaki Disease

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To determine the correlations between changes in high-density lipoprotein cholesterol (HDL-C) and other blood variables during the acute phase of Kawasaki disease (KD), we investigated changes in the plasma level of HDL-C, serum apolipoproteins and number of peripheral blood monocytes. 26 Japanese patients with KD were subjects of this study.
Plasma HDL-C decreased during the 1st week of illness, and increased during the 2nd week. The mean levels of minimum HDL-C in KD patients treated with total intravenous immunoglobulin (IVIG) dose $\geq 4g/kg$, was significantly lower than those treated with total IVIG dose $< 4g/kg$ ($p=0.0005$). There was a strong direct correlation between minimum HDL-C in KD patients and HDL-C on 5th day of KD onset ($r=0.71$, $p < 0.0001$). Assessing the performance of plasma HDL-C on 5th day of KD onset in predicting the necessity for high-dose IVIG treatment to KD, ROCs were plotted and the AUC was 0.82. A cutoff value of 16mg/dl had a specificity of 0.82 and sensitivity of 0.80 for predicting those.

The apo A-I and A-II levels were correlated with plasma HDL-C, respectively. And the peripheral blood monocytes counts which correlated with serum levels of macrophage-colony stimulating factor, were not correlated with plasma HDL-C.

Plasma HDL-C levels during the 1st week of illness might serve as a predictor for non-responder to low-dose IVIG treatment in patients with acute KD.

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097

Resistance Values in the Limbs are Useful for Estimating the Severity of Kawasaki Disease.

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Vascular permeability is one of the characteristics of vasculitis in Kawasaki disease (KD) and is closely related to indurative edema. Evaluating indurative edema may be useful for estimating the severity of KD. Indurative edema is correlated with resistance values in the limbs. Therefore, we evaluated the efficacy of resistance values in the limbs in KD patients, as measured by a multiple-frequency bioelectrical-impedance method, for estimating the severity of KD.

Patients and Methods: In 38 patients with the acute phase of KD (before intravenous immunoglobulin treatment; IVIG), 32 with the sub-acute phase (after IVIG), and 49 controls, we measured resistance (impedance; IMP) in each child’s total body, forearm, and lower leg at frequencies of 0 and infinity (IMP-0 and IMP-$\infty$, respectively) using MLT-550N (Sekisui). Corrected Imp values (colIMP; Imp x limb’s cross-sectional area/ limb’s length) were also examined.

Results: IMP values were not different among patients with the acute and sub-acute phases of KD and controls. However, colIMP values in the forearm of patients in the acute phase of KD were significantly higher than those of controls (colIMP-0 $\Omega$cm: 197±50 vs. 164±35, $P<0.001$, colIMP-$\infty$: 151±42 vs. 125±36, $P=0.003$). These values were decreased to 181±46 $\Omega$cm for colIMP-0 and 144±44 $\Omega$cm for colIMP-$\infty$ at the sub-acute phase and were still significantly higher than those of controls. Values of colIMP in the lower leg showed similar changes to those in the forearm. The values of colIMP in the forearm of IVIG non-responders at the acute phase were higher than those of responders, but this difference was not significant.

Conclusion: Values of co-IMP in the forearm might be useful for estimating the severity of KD.

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098

Tenascin-C as a Novel Biomarker for Predicting Therapeutic Effect in Kawasaki Disease

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[Background]
In acute stage of Kawasaki disease (KD), patients who are unresponsive to initial therapy are immediately administered additional therapy to prevent the development of coronary artery abnormalities (CAAs). Although failure to respond is defined as persistent or recrudescent fever after treatment, it is difficult to recognize the presence of fever because steroids are administered with intravenous immunoglobulin (IVIG) in severe KD patients in Japan. In addition, inflammatory markers such as CRP usually decrease after initial therapy in patients who are unresponsive to initial therapy and there is no biomarker for monitoring treatment effect. Tenascin-C (TN-C) is an extracellular matrix protein specifically upregulated in response to tissue injury and inflammation.

[Methods]
We recruited 174 patients (male 102, female 72) from August 2011 to April 2014, from fourteen institutions in Japan. Serum levels of TN-C (sTN-C) were examined using ELISA before and after initial treatment. The initial treatments consisted of: 30 aspirin only, 111 IVIG + aspirin, and 33 IVIG + aspirin + prednisolone. We compared patients who responded to initial therapy (R group; n = 134) with those who did not respond (NR group; n = 40) regarding patient profile and laboratory data.

[Results]
Patients in NR group had higher % neutrophil (p = 0.004), CRP (p = 0.012) and sTN-C (p = 0.049) than in R group before treatment. After initial therapy, WBC, % neutrophil and CRP significantly decreased in both groups (p < 0.001), but sTN-C did not significantly decrease in NR group (p = 0.485). When sTN-C after initial therapy was used to predict unresponsiveness of initial therapy, sensitivity, specificity and AUC were 85%, 55%, and 0.745 respectively. Especially in patients who were administered steroids with IVIG as initial therapy, the accuracy of predictive model using sTN-C after initial therapy was high (AUC 0.812, sensitivity 71%, specificity 81%). The incidence of CAAs tends to be higher in NR group than in R group (12.5 vs. 3.7 %, p = 0.051).

[Conclusions]
TN-C is a potential biomarker in predicting the need for additional therapy. Especially in KD patients who are treated by steroids with IVIG, TN-C may be useful.


099
Retrospective Analysis of Kawasaki Disease Patients Resistant to Second Intravenous Immunoglobulin

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Objective: This retrospective analysis aimed to identify the risk factors of Kawasaki disease (KD) resistant to second intravenous immunoglobulin (IVIG) and design the score system discerning IVIG resistant patients in acute phase.

Materials and Methods: A retrospective chart review of pediatric patients admitted to Children’s Medical Center, Yokosuka General Hospital Uwamachi with the diagnosis of KD during 2011 to 2013. In total 127 patients, 116 patients received IVIG and of 92 patients were respondent for initial course of IVIG. Rest of 17 patients received second course of IVIG and of 7 patients were resistant to second course of IVIG.

Results: Logistic regression analysis showed that serum sodium concentration <131 mEq/L (odds ratio[OR]=7.43, 95% confidence interval [CI]=1.470-37.564), serum albumin concentration <3.0 g/dl (OR=7.00, 95% CI=1.109-44.195), age less than six months (OR=8.25, 95% CI=1.615-42.146), and white blood cell count <9000/µ (OR=6.29, 95% CI=1.309-30.191) were associated with risk factors of resistant to second IVIG. Designed the
score system on the basis of these four factors, we could estimate the failure to second IVIG and its accuracy was 95.3%.

Conclusion: The score system based on easy and simple clinical factors might be useful for estimating the patients resistant to second IVIG and improve those patients’ further treatment.


101 Serum Pro Brain Natriuretic Peptide (pro BNP) Levels In Children With Kawasaki Disease

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Introduction:

Brain natriuretic peptide (BNP) is a useful biomarker for diagnosing heart failure in adults and children. ProBNP, the precursor form of BNP has been shown to predict myocardial involvement in acute Kawasaki disease (KD) especially in cases of incomplete KD. As the phenotype of KD in North India is different from that in Japan and North America, this study was carried out to validate the utility of proBNP in North Indian children with KD.

Objectives: To assay the levels of proBNP in North Indian children with KD.

Methodology

Serum pro brain natriuretic peptide (pro BNP and NT-proBNP) levels were estimated in 25 children with Kawasaki disease, both during acute phase and later in convalescence. The levels were similarly assayed in an equal number of age and sex matched controls. The proBNP levels were estimated by an enzyme linked immunosorbent assay (ELISA) using the RayBio Human proBNP ELISA kit which detects both pro BNP and NT-pro BNP.

Results: Pro BNP levels were significantly elevated in children during acute phase of KD (4259±8015 pg/ml) when compared to febrile controls (407±542pg/ml) or to children in convalescent phase of KD (509±1066 pg/ml). Pro BNP levels were also higher in children with coronary abnormalities in acute phase.

Conclusions: In our experience, pro BNP is a useful biomarker for KD especially with regard to myocardial involvement. ProBNP level is markedly elevated during the acute phase in all children with KD. In children with persistent coronary artery abnormalities, the proBNP level remains elevated even during convalescence.

Future impact: ProBNP may be useful marker for children with incomplete forms of KD.


102 Midkine, A New Functional Cytokine, Increased After IVIG May Protects From Vascular Injury In Acute Kawasaki Disease

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Introduction

Midkine(MDK), found in 1988, a heparin-binding low-molecular protein, is a member of growth factors or cytokines, activated in the process of inflammatory disorders like RA, cancer development, angiogenesis and wound healing.
etc. It also acts as protecting cell apoptosis, stimulating fibrinolysis on endothelial cells, inhibiting or suppressing the development of regulatory T cells, improving myocardial dysfunction, and promoting the survival of ischemic myocardium. But, little is known in vasculitis syndrome.

Methods
Serum samples, clinical data and laboratory values from 17 patients with acute KD patients in before, 1-2 days, and 7-10 days after IVIG. Serum samples were analysed for MK concentrations by EIAl with anti-human MDK antibody.

Results:
MDK values were significantly elevated in serum from 1-2d after IVIG; mean=1291.6 ± 1119.0, compared with Pre-IVIG; mean=530.9±468.6(p<0.01), and rapidly decreased 7-10d after IVIG; mean=599.4±447.3 pg/ml(p<0.05)(healthy human cut off level; <300pg/ml). CRP is significantly correlated with MDK (r=0.45, p<0.05). MDK of 2 patient with CAA was higher than that of no CAA.

Discussions and Conclusions
Knockout mice deficient in the MDK gene poorly develop neointima when the artery is damaged by ischemic shock. Clinically, MDK increases in human carcinoma and play a central role in inflammatory pathway. It promotes the migration of inflammatory leucocytes, namely macrophages and neutrophils. Recently, it is becoming a molecular target for the treatment or prevention of inflammatory diseases.

Finally, this preliminary study suggests that MDK is a possible novel effector and may be relevant in the pathogenesis of arteritis in acute KD. IVIG may increase MDK levels and protect from inflammatory vascular damage.


103 Incomplete Kawasaki Disease - Patients With ≤ 5 Days Of Fever Successfully Treated By Antibiotics But Left With Coronary Aneurysms -

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Objective: We report four patients with incomplete Kawasaki disease (KD) successfully treated by antibiotics without intravenous immunoglobulin (IVIG) treatment with ≤ 5 days of fever but left with coronary artery lesion.

Result: The patients were 2 babies and 2 young children age ranged from 2 months to 2 years old and 9 months. They showed fever and other signs of KD, but did not fulfill diagnostic criteria.

Conclusions: This case series indicates that there are patients with incomplete KD successfully treated by antibiotics without IVIG but left with CAA. These cases must be underdiagnosed if intentional echocardiographic examination are scheduled and might be left without appropriate treatment, antithrombotic treatment. Further collection of data of these patients is indispensable.


104 Elevated Serum Cortisol Levels As A Risk Factor For Developing Coronary Artery Abnormalities In Kawasaki Disease

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Background and objectives
Endogenous cortisol (CRS) increases in a variety of inflammatory diseases and vasculitis syndrome, and recognized as a one of risk
factors of disease progression. Although only one previous study reported that CRS level is elevated in acute Kawasaki disease (KD), the predictive value of CRS in KD has not been fully investigated. The aim of this study is to evaluate whether serum CRS levels can predict initial treatment response and development of coronary artery abnormalities (CAAs) in the acute phase of KD.

Materials and Methods
A retrospective study was designed to evaluate serum CRS levels in 92 children with acute KD who were admitted between December 2011 and May 2014. The subjects consisted of 46 males and 46 females aged from 1 month to 12 years (median, 2 years). Serum CRS levels were measured before the initial treatment of IVIG. With Kobayashi score for predicting IVIG resistance, patients were divided into high (Kobayashi Score $\geq 5$) and low risk (Kobayashi Score $<5$) group. Coronary artery diameter was measured at weeks 1, 2, 4 and we calculated maximum Z-score. CAAs were defined as equal to greater than 2.5 of Z-score.

Results
Serum CRS level was 32.7µg/dl (median, 6.2 to 139µg/dl) which is higher than healthy children (5 to 25µg/dl), and significantly elevated in high risk group (median, 41.3µg/dl ) than those in low risk group (median, 27.1µg/dl, $p=0.003$). In patients with CAAs CRS level was higher than those without CAAs (Z<2.5 vs Z$\geq 2.5$, median 30.4 vs 37.3µg/dl, $p=0.052$). Additionally, 1 patient who had maximum cortisol level (139µg/dl) showed CAAs (Z-score, seg1: 9.1, seg5: 10.2 at week 4). CRP, WBC counts, and albumin level had no significant correlation with CRS.

Conclusions
We conclude that serum CRS before IVIG were significantly higher in patients with high risk group. CRS may be a potential predictor for developing CAAs.


105 Platelet-Neutrophil Aggregates play a crucial role in regulating vasculitis in Kawasaki Disease

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Objective: Circulating platelet-neutrophil aggregates play a crucial role in amplifying acute inflammation and could promote adverse effects involving vascular injury. The aim of this study was to clarify the role of platelet-neutrophil aggregates in patients with Kawasaki disease (KD).

Methods: We analyzed 40 patients with KD (30 intravenous immunoglobulin [IVIG] responders and 10 IVIG non-responders), 7 febrile patients with bacterial infections, and 9 normal volunteers. Thirty-three patients with KD were treated with IVIG alone, and remaining seven were treated with IVIG plus prednisolone. We evaluated the rate of platelet-neutrophil aggregates and measured the platelet factor 4 (PF4) and $\beta$-thromboglobulin ($\beta$-TG) levels in patients with KD.

Results: The rate of platelet-neutrophil aggregates was significantly higher in patients with KD than in both patients with bacterial infection and normal volunteers. There was a trend toward increased rate of platelet-neutrophil aggregates within 2 or 3 days after IVIG than before IVIG. The rate of platelet-neutrophil aggregates was significantly higher in patients who showed coronary artery abnormalities (CAA) than in those who showed without CAA and was correlated with PF4 and $\beta$-TG levels in patients with KD. Comparing time course analysis, the rate of platelet-neutrophil aggregates was significantly decreased in patients treated with IVIG plus prednisolone than in those treated with IVIG alone.

Conclusions: Our findings demonstrate that platelet-neutrophil aggregates play a crucial role in regulating vasculitis, and are involved in the development of CAA. Additional prednisolone treatment in the acute phase of KD might have a potential role in inhibiting amplified reciprocal inflammatory activation by suppressing platelet-neutrophil aggregates.

K. Ueno: None.

106 Utility of Ferritin as a Predictor of the Patients with Kawasaki Disease Refractory to Intravenous Immunoglobulin Therapy

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Poster Abstract Presentations (continued)

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Purpose: Several scoring systems for prediction of non-responsiveness to initial course of intravenous immunoglobulin (IVIG) therapy have been available in the patients diagnosed as Kawasaki disease (KD). However, all non-responders cannot be identified completely by these scoring systems. The aim of this study is to investigate whether ferritin can be a useful marker as a predictor of the patients with KD refractory to IVIG therapy.

Materials and Methods: This retrospective study enrolled 63 patients with KD hospitalized at Kitakyushu General Hospital during 2010 to 2013. These patients were divided into IVIG responders (n= 41) and non-responders (n=22). Serum ferritin levels and the scoring systems for prediction of non-responsiveness to initial IVIG treatment were compared between these two groups.

Results: Serum ferritin level was significantly elevated in non-responders (p=0.01). The area under the receiver-operating-characteristics curve was 0.698, and the sensitivity and specificity in more than 215 ng/ml of serum ferritin levels was 54.5% and 85.4%, respectively. Two of the three scoring systems for prediction of non-responsiveness to initial IVIG treatment were compared between these two groups.

Conclusion: Serum ferritin level can be a useful marker for the prediction of non-responsiveness to initial IVIG treatment and may be an important complementary marker to the scoring systems for prediction of non-responsiveness to initial IVIG treatment.


107 Urinary β2 Microglobulin To Creatinine Ratio As A Predictive Factor Of Intravenous Immunoglobulin Resistance

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<Introduction>
The standard dose of intravenous immunoglobulin (IVIG) as initial therapy for patients with Kawasaki disease (KD) is generally 2 g/kg. In our hospital, the initial IVIG dose for patients with KD is 1 g/kg, which is augmented according to treatment response, and therapy is changed to plasma exchange (PE) if IVIG therapy over 6 g/kg is ineffective. To date, various factors and scoring systems for predicting IVIG resistance have been reported. We evaluated consecutive urinary β2 microglobulin to creatinine ratio (β2MG/Cr) data as a possible predictive factor of IVIG therapy resistance.

<Objectives>
To clarify whether urinary β2MG/Cr is an effective predictive factor for IVIG therapy resistance.

<Methods>
We retrospectively reviewed the data of all patients with KD who underwent IVIG therapy at a dose of over 6g/kg in our hospital from January 1997 to January 2014. Patients with recurrent KD were excluded from the study. Patients were divided into two groups for analysis, those who did and did not require PE. Factors including urinary β2MG/Cr were compared across the two groups. We used the peak urinary β2MG/Cr of each patient in the course of the disease.

<Results>
There were 713 patients with KD who were treated in our hospital from January 1997 to January 2014. There were 28 patients without recurrent KD who underwent IVIG therapy over 6g/kg. IVIG was successful in 24 patients (non-PE group), and 4 patients required PE (PE group). Urinary β2MG/Cr was not measured in only one patient of the non-PE group. Urinary β2MG/Cr significantly higher in the PE group (median 119,228 µg/gCr, 69,286-234,290 µg/gCr) compared to the non-PE group (median 12,270 µg/gCr, 1,981-210,647 µg/gCr) (p=0.001, t-test). Urinary β2MG/Cr exceeded 100,000 µg/gCr in 4 % (1 of 23) of the PE group and 75
% (3 of 4) of non-PE group. There were temporarily coronary artery lesions (dilation or aneurysm) in 57 % (13 of 23) of the non-PE group and 75 % (3 of 4) of the PE group. Coronary artery lesions regressed in all patients. <Conclusion>
Our study suggests that urinary β2MG/Cr measurement is a useful non-invasive test for predicting IVIG resistance.


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New Assessment Of Comprehensive Coagulation Function Using Clot Waveform Analysis In Patients With Kawasaki Disease In The Acute Phase

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Background: Hypercoagulability for Kawasaki disease (KD) in the acute phase is known, through many reports based on the change of the individual coagulation factor. Little information on the assessment of comprehensive coagulation function of this disease is described, however. A recent developed clot waveform analysis (CWA), defines changes in light transmittance that occur during the process of clot formation, can assess comprehensive coagulation function qualitatively and quantitatively by measuring the parameters. In this study, we have investigated the clotting dynamics of acute-phase KD by CWA. Method: The subjects were 43 patients of KD with treatment of intravenous γ-globulin (IVIG), at onset ranged from 3 months to 5 years old (median 1.8 years old). Normal pooled plasma (NP) was prepared from 20 healthy individuals. Blood samples were collected at three points of time; before the IVIG administration (Pre), after 1 week of IVIG (1W), and after 1 month of IVIG (1M). Cases with anticoagulant medication were excluded. CWA was performed using MDA-II™, and parameters, clotting time (CT), maximum coagulation velocity (dT/dt,[min1]), and maximum coagulation acceleration (dT2/dt2,[min2]) were calculated from clot waveforms obtained. Values were shown as mean±SD, and the data were analyzed by paired t-tests and Pearson’s correlation. Results: The CT value (38.0±8.9 sec) in Pre on acute-phase KD was significantly prolonged compared to NP (29.8±2.4 sec, p<0.01). Both CTs in 1W and 1M were more shortened than that in Pre (p<0.01), but that in 1W was not so different from 1M. In contrast, the [min1] and [min2] (9.7±2.5, 0.83±0.16) in Pre showed ~2-fold higher levels than those in NP (5.6±0.7, 0.45±0.05). These levels were significantly decreased in 1W, followed by the return to normal levels in 1M. In Pre, the prolonged CT seemed to be low coagulation function in acute-phase KD, but higher levels of [min1] and [min2] showed the hypercoagulant state. Conclusion: These data support the paradoxical coagulation dynamics that the more developed hypercoagulability after the start of coagulation, in spite of delayed coagulation start time in acute-phase KD.


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Predictors Of Unresponsiveness To Initial Immunoglobulin In Patients With Kawasaki Disease

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Background: Recently, several studies to predict the unresponsiveness to initial intravenous immunoglobulin (IVIG) treatment during the acute phase of Kawasaki disease have been conducted. However, reported predictors are varied in those studies. The racial difference was assumed as the cause of such diversity. The aim of this study is to find predictors of unresponsiveness to initial IVIG in Korean children with Kawasaki disease. Subjects and methods: Subjects were 424 patients with Kawasaki disease who had been admitted to Asan Medical Center from January 2006 to December 2012. Demographic, clinical, and laboratory data were investigated through a review of medical records. Laboratory data before initial IVIG treatment and within 10 days after fever onset were selected. Forty one patients (9.7%) were non responders to initial IVIG treatment. Univariate and multivariate logistic regression analyses were performed to find predictors of unresponsiveness to initial IVIG treatment.
Results: Median age was 30.0 months (range 1.6-186.0 months) in IVIG-responders, and 30.9 months (range 2.9-107.8 months) in IVIG-nonresponders (P=0.819). Number of females was 156 (40.7%) and 15 (36.6%) respectively (P=0.607). No other demographic and clinical variables were different between two groups. Univariate analyses showed that neutrophil percentage (P<0.001), serum C-reactive protein (P=0.008) and total bilirubin (P<0.001) were higher, and that serum protein level (P=0.001), albumin level (P<0.001), sodium concentration (P<0.001), and chloride concentration (P=0.002) were lower in IVIG-nonresponders. Neutrophil percentage (OR 1.075, 95% confidence interval 1.027~1.125. P=0.002) and serum total bilirubin(OR 1.845, 95% interval 1.284~2.650. P=0.001) were significant predictors in Multivariate analyses.

Conclusion: The results of this study were inconsistent with the results of previously conducted studies with the same purpose in other countries. Therefore future study with more number of subjects is needed for confirmative identification of predictors of unresponsiveness to initial IVIG treatment in patients with Kawasaki disease.


110 Histologic Assessment of a Case of Likely Kawasaki Disease in 1870 London

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William Shrosbree, a 7 yo boy, died in 1870 at St. Bartholomew's Hospital in London, England, “in consequence of scarlatinal dropsy” after a 2d hospitalization. His case was cryptically reported briefly by Dr. Samuel Gee in 1871, who found 3 epicardial coronary artery (CA) aneurysms at autopsy, each containing “small recent clots, quite loose.” Two aneurysms were “pea-sized” at the apex close to the tip of the right auricular appendage, while the 3rd was the size of a “horse bean” and located in the sulcus at the posterior base of the ventricles. “Specks of atheroma” were described in the aorta “near the valves” and on the aortic cusp of the mitral valve. The heart was reported to be of normal size, and the valves were healthy. We have had the opportunity to study a limited number of CA photomicrographs of this specimen.

Overall, the vasculopathy in this case is highly compatible with our recent description of pathognomonic histologic features in 41 fatal or transplanted KD cases with severe disease (PLoS One, 2012). Of the 3 characteristic linked pathologic processes we reported, the limited number of sections do not show acute self-limiting necrotizing arteritis, which is relatively rare. Areas of subacute/chronic (SA/C) vasculitis containing barely recognizable lymphocytes, variably damaged media and prominent fibrotic adventitial fibrosis are seen. Very little of the internal and external elastic lamina could be seen in EVG and methylene blue stained sections. The most characteristic of the 3 processes, luminal myofibroblastic proliferation (LMP), is variable in prominence. The medium power magnification, H+E and methylene blue stained sections show a relatively uniform circumferential luminal layer thicker than the normal media. A higher magnification H+E section shows up to 100% LMP narrowing of the lumen involving about half the vessel, containing relatively prominent pleomorphic cells that may be myofibroblasts. The lumen in another section shows total obliteration by LMP with similar myofibroblasts and half of the media replaced by LMP.

The gross and histologic features of the CA of the child who died in 1870 in London are highly compatible with the changes noted in severe KD, suggesting that this illness was present as early as the 19th Century.


111 Identification of the agent causing Kawasaki Disease via throat swab cultures

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Kawasaki disease (KD) is a paediatric inflammatory disease and is the most common cause of acquired heart disease in children in
developed countries. The cause of KD is unknown but epidemiological data indicate that it is most likely to be an infectious agent. The clinical features of KD are consistent with either bacterial or fungal infection rather than a virus, as KD is associated with an intense inflammatory process. It has been suggested that the oral and respiratory mucosa are the primary site of infection as the initial infection in KD patients is likely to be in the mucosal surfaces of the respiratory track with prominent lymphadenopathy and oral mucous membrane inflammation. This study examines whether the agent causing KD induces disease through production of novel toxins, or inflammation inducing antigens in the supernatants of cultured bacteria isolated from KD patients and healthy controls. Throat swabs were collected from children with KD (n=14), other diseases (n=10) and healthy children (n=8), and were inoculated into growth medium, incubated and then centrifuged. The supernatants were collected and toxicity was measured by microscopic observation as well as by resazurin dye reduction of cells after growth in the presence of the KD or control supernatant. An effect of the toxins in activating inflammation was also tested by the addition of the supernatants to healthy donor peripheral blood mononuclear cells (PBMCs) and measurement of interleukin 6 production by Enzyme linked immune assay (ELISA). There was no significant difference in the reduction of cells after growth between control and KD supernatants. No difference in the production of IL-6 was observed between the three groups. Further analysis and larger sample size are required to establish whether novel toxins are present in cultured supernatants of KD patients.

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A Case With Left Ventricular Failure And Unconsciousness Treated With Plasma Exchange

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Background: Either encephalopathy or left ventricular (LV) failure complicated with Kawasaki disease (KD) is rare but occasionally fatal. We experienced a critical case simultaneously complicated with both of them and successfully rescued by plasma exchange (PE).

Case report: A 4-year-old girl was hospitalized with a high fever lasting 7 days, conjunctival injection, reddened and swollen lips, cervical lymphadenopathy and erythema of the palms and soles. Laboratory tests revealed that her white blood cells count 35,400/µl, C-reactive protein was 35 mg/dl, N-terminal pro-brain natriuretic peptide was 15,317 pg/ml, and interleukin-6 reported afterward was 354 pg/ml. Echocardiography showed that LV ejection fraction was 40%. She was diagnosed as KD and was treated with 2g/kg of intravenous immunoglobulin (IVIG) and oral aspirin on the 7th day of illness. On the following day, however, her blood pressure declined to 80/40mmHg and LV function was becoming gradually poorer despite of intravenous injection of dobutamine. As her consciousness was unclear and electroencephalogram (EEG) indicated slow waves, she was additionally treated with D-mannitol. Infliximab is not indicated because of heart failure. Therefore, repetitive PE was started immediately after deep sedation with mechanical respiratory assist. Her fever, EEG and LV function began improving by PE consecutive 3 days, however, those findings recurrently worsened at every interval of PE. IVIG and steroid pulse therapy were added on the 12th day after PE. On the 13th day, she became defervescent and her consciousness became clear and EEG normalized. She returned to daily life without cardiac or neurologic abnormalities after discharge.

Conclusions: PE is a rapid and sufficiently effective strategy for a critical KD case when infliximab is not indicated or immediate
effectiveness of steroid including pulse therapy is not expected.


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Outcome Of Patients With Kawasaki Disease Treated With Intravenous Pulse Methylprednisolone As Primary Therapy: An 8 Year Single Center Experience

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Kawasaki disease (KD) is a medium vessel vasculitis with predilection to affect the coronary arteries. While intravenous immunoglobulin (IVIG) remains the standard primary treatment, the cost remains a big burden for parents of patients in developing countries. Steroids do have a role in IVIG-resistant KD but studies on its benefit in addition to IVIG as primary treatment are conflicting. In our institution, parents who cannot afford IVIG consented to intravenous pulse methylprednisolone (IV MP) as an alternative primary treatment.

Objective: To review the outcome of KD patients treated with IV MP as primary treatment.

Methods: Retrospective chart review of patients who fulfilled the diagnostic criteria for KD and treated with IV MP (30 mg/kg/dose, maximum of 1 gm/dose, given once daily for 3 consecutive days) plus high dose Aspirin from January 2006 to December 2013.

Results: A total of 36 patients were included in the study with a mean age of 4.2 years (range 0.4-12.6). The F:M ratio was 1:1. Majority (75% - 27/36) of the patients received the treatment before the tenth day of illness. There was clinical improvement in all patients with lysis of fever and resolution of all signs and symptoms immediately after the first dose of IV MP. For all patients, baseline echocardiography was done by a single pediatric cardiologist and was repeated after 2 months, 6 months, then yearly. At baseline, 36 patients had pericardial effusion, 13 with perivascular brightness, 15 with coronary ectasia and 8 with valvular abnormalities (MR, AR, TR). Follow up evaluation after 2 months showed no echocardiographic abnormalities in all patients, up until the yearly echo. None of the patients developed coronary aneurysm. There was no reported immediate nor long term side effects from the steroid therapy.

Conclusion: Intravenous methylprednisolone is effective in controlling the clinical manifestations of KD and in preventing cardiac complications. It is safe and well-tolerated by patients. It can be an alternative first line treatment for KD patients whose parents cannot afford the high cost of IVIG.


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Sivelestat Sodium Hydrate Treatment for Patients with Kawasaki Disease refractory to initial intravenous immunoglobulin therapy

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Background: There are still no definite treatments for refractory Kawasaki disease (KD). In this pilot study, we evaluated the safety and efficacy of a new protocol consisting of sivelestat sodium hydrate (SSH) combined with additional intravenous immune globulin (IVIG) for KD patients who were resistant to initial IVIG therapy.

Methods: We prospectively collected clinical data of KD patients who were resistant to initial IVIG (2g/kg for one day) and received SSH (0.2mg/kg/hour for consecutive 5 days) combined with additional IVIG (2g/kg for one day) as a second-line therapy at Chiba University hospital between December 2006 and March 2014. We defined patients who remained febrile (37.5°C or more of an axillary temperature) after 36 to 48 hours after start of initial IVIG therapy or who had recrudescent fever associated with other symptoms of Kawasaki disease as being resistant to initial
IVIG.
Results: Thirty five KD patients were enrolled in this study. No serious adverse effect was noted. The median total duration of fever was 8 days (range 6 to 17 days) and the incidence of coronary artery lesion (CAL) was 5.7% (2 of 35 patients). Among a total of 35 patients, 24 (69%) of them responded promptly to be afebrile 36 to 48 hours after the start of the additional IVIG with SSH. One of these 24 patients developed CAL. The other 11 (31%) failed to become afebrile 36 to 48 hours after the start of the additional IVIG with SSH therapy. Of these 11 patients, one developed CAL. Before initial IVIG, there was no difference in demographic and laboratory data except the age, body weight and % Neutrophils. However, after initial IVIG therapy, there appeared significant difference in % Neutrophils and C-reactive protein levels and both of which were higher in additional IVIG with SSH therapy non-responders than in responders.

Conclusions: Additional IVIG combined with SSH for the additional treatment of KD patients who were refractory to initial IVIG therapy was safe and the incidence of CAL is acceptable considering the severity of patients in this study.


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Long term Prognosis After Methylprednisolon pulse Combination Therapy For Refractory Kawasaki Disease

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Background: We previously investigated the molecular mechanism and the clinical utility of intravenous methylprednisolone-pulse (IVMP) plus intravenous immunoglobulin (IVIG) combination therapy (IVMP+IVIG) for patients with Kawasaki disease (KD) in the acute phase (Pediatr Res 2009, Pediatrics 2012). However, the long-term prognosis after IVMP+IVIG still remains unclear.

Objective: To examine the long-term prognosis after IVIG+IVMP.

Methods: Forty-six patients (Age: 5-70 months, male: 27) who were enrolled in this study were treated with IVMP+IVIG during the period from 2007 to 2014 at Kitasato University Hospital who were all predicted to show resistance to initial IVIG according to their Egami score (J Pediatr 2006). The IVMP therapy (30mg/kg, 1dose) was administered for 2 hours before starting the IVIG therapy. Heparin (10U/kg/h, continuous infusion) was used concomitantly from 2 hours before the start of IVMP therapy and it was thereafter continued for 24 hours. The long-term prognosis of coronary artery lesions (CALs) and adverse events between the time of diagnosis and 5 years after IVMP+IVIG were determined. The "Z-score 2.5-5" and "Z-score >5" were defined as dilatation and an aneurysm, respectively, according to the AHA guidelines.

Results: Dilatation cases based on the Z-score 2.5-5, were identified in 15 of 46 patients (32.6%) at diagnosis, in 15 of 46 patients (32.6%) after 1 month, and in 3 of 36 patients (8.3%) after 1 year. All patients in whom coronary artery abnormalities were observed at 1 year later demonstrated regression. No patients showed a Z-score ≥5 in all phases. Thirty-six patients (78.2%) showed prompt defervescence owing to the combination therapy. The patients had adverse event at acute phase, 16 of 46 patients (34.7%) for hypothermia, 5 patients (10.8%) for hypertension, 2 patients (4.3%) for bradycardia, and 4 patients (8.6%) for recurrent fever. No patients experienced any serious adverse events (short stature, hyperlipidemia, abnormal glucose tolerance) after IVMP+IVIG during the long-term follow-up.

Conclusions: This study showed IVMP+IVIG combination therapy to therefore effectively prevent CALs in KD patients that are predicted to be resistant to initial IVIG according to their Egami score.


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Patient Condition Adaptive Path System of Kawasaki Disease

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Background: In Japan, 2 guidelines are published, the clinical guidelines for medical treatment of acute stage Kawasaki disease (KD) (2012) and guidelines for diagnosis and management of cardiovascular sequelae in KD (2013). Patient Condition Adaptive Path System (PCAPS) is a technique to structure clinical knowledge. It places "patient condition" as a core, to which multiple "target conditions" are linked. On the other hand, patients of KD were focused the severity of the disease and therapeutic strategy influences the improvement.

Purpose: The purpose is confirming the PCAPS KD contents, which complied two Japanese Guidelines and to evaluate adaption of the contents.

Methods: PCAPS content is composed of Clinical Process Chart (CPC) and Unit Sheet (US). CPC is an overhead view of clinical path consisting of a chain of units. CPC was made according the guidelines, and coronary evaluation, CHF, cardiac catheterization and ACS unit can activate on time. CPC stratify the patient’s severity. US are composed of specific healthcare tasks in a unit.

Results: We confirm PCAPS KD contents on the base of 2 guidelines. We can evaluate diagnostic process and severity of KD by route analysis using CPC (figure). We can visualize relationship between treatments and severity by US. US are effective to support the decision on treatment and examinations. From the analysis, there are no lack of the unit and route, and confirm the advice to decision making.

Conclusions: PCAPS can easily analyze the severity and clinical process from CPC route analysis because PCAPS is electrical path which can automatically store the data of each hospital. From US data, there are possibilities to find new severity score.


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Steroid Treatment in the Acute Phase of Kawasaki Disease in Mexican Children. Are they Useful?

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Background. Intravenous immunoglobulin (IVIG) and aspirin is the standard initial therapy in the treatment of Kawasaki disease (KD), which is proven to decrease the incidence of coronary artery aneurysms from 25% to less than 5%. There is increasing evidence for steroid therapy as adjunctive primary therapy with IVIG especially in those patients who are at increased risk of coronary artery aneurysms and in patients with risk of IVIG resistance. However, clinical trials evaluating the use of corticosteroids plus IVIG have produced confusing results.

Objective. To evaluate the clinical efficacy and safety of steroids plus intravenous immunoglobulin (IVIG) combination therapy (IVIG+S) for the initial treatment of patients with KD to prevent coronary artery aneurysms (CAA) compared with the standard treatment with intravenous immunoglobulin plus aspirin (IVIG+A) in a Children’s Hospital in Mexico City.

Material and Methods. An observational, comparative, retrospective and case-control study of all patients treated with IVIG for KD in our Institution from August 1995 to May 2014. The clinical presentation, laboratory results and coronary artery abnormalities in the IVIG+S and the IVIG+A groups were analyzed and compared.

Results. We studied 295 patients with KD treated with IVIG, 136 (46.1%) received IVIG+A treatment and 159 (53.9%) received IVIG+S treatment. We didn’t found adverse reactions in the patients treated with steroids. The IVIG+S group were older 43.25 ± 43.04 than the non-steroid group 32.07 ± 24.51 (p < 0.008). Steroids were commonly use in incomplete cases (p < 0.059) and in patients with cardiac complications at diagnosis: pericardial effusion (p < 0.056) and pericarditis (p < 0.013). The steroid group has slightly more days of fever after the IVIG
Poster Abstract Presentations (continued)

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A Case Of Slowly Progressing Giant Coronary Aneurysm In A Patient With Intractable Kawasaki Disease

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BACKGROUND: Some patients with intravenous immunoglobulin (IVIG)-resistant Kawasaki disease (KD) do not respond to intravenous methylprednisolone (IVMP). Infliximab (IFX; anti-TNF-α antibody) is an alternative medication for intractable KD. Its effectiveness in preventing coronary aneurysms from progressing is being reported. We herein report a case of intractable KD that slowly progressed to giant aneurysm despite a second IFX infusion.

METHODS: A 2-year-old boy visited our hospital with a 2-day history of fever. On day 3 after fever onset, a swollen cervical lymph node, redness of the BCG (bacilli Calmette Guérin) inoculation site, and indurated erythema of the palms with soles were observed. On day 5, conjunctival injection, strawberry tongue, red lips and truncal rash were present. The patient was diagnosed with KD and treated with IVIG and acetylsalicylic acid (ASA).

RESULTS: The fever persisted for 24 h after IVIG treatment. A second dose of IVIG was infused. However, the fever continued. Then IVMP was infused. On day 9, the fever resolved. On day 10, two-dimensional echocardiography (2DE) showed mild dilations (Φ 3.0 mm) of both coronary arteries (CAs). On day 18, the fever recurred. Follow-up 2DE showed dilated CAs (left main coronary artery [LM], Φ 4.0 mm; right coronary artery [RCA], Φ 4.0 mm). Therefore, IFX was intravenously infused. On day 19, the fever had resolved and the patient went home. On day 22, the fever recurred. Thus, a second infusion of IFX was done. On day 24, the fever resolved. Follow-up 2DE showed that the diameters of the CAs were 4.0 mm (LM), 7.0 mm (left anterior descending coronary artery [LAD]), 3.0 mm (RCA). On day 28, a mild fever was still present. On day 47, follow-up 2DE indicated that the diameters of the CAs were 3.0 mm (LM), 8.0 mm (LAD), 2.5 mm (RCA). On day 159, follow-up 2DE showed slightly increased regression of CAs. The patient has been undergoing regular 2DE and taking ASA since he left the hospital.

CONCLUSIONS: This was a very rare case of KD that was resistant to standard treatment comprising high-dose steroids and TNF-α blockade. We have reported this case to inform clinicians who may encounter such patients with KD in the future. A high index of suspicion and keen observations are strongly recommended for cases of intractable KD.

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Usefulness Of Kawasaki Disease Risk-scoring Systems For Initial Intravenous Immunoglobulin Resistance In Korean Patients with Kawasaki Disease

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Intravenous immunoglobulin (IVIG) infusion in the acute stage is the standard therapy in patients with Kawasaki disease (KD). Although some risk-scoring system made in Japan are widely used, there are few reports that describe the usefulness of risk-scoring systems to predict initial IVIG resistance. This study aimed to
investigate which risk-scoring system of KD is the most useful. And this study evaluated the usefulness of N-terminal pro-brain natriuretic peptide (NT-proBNP) as an additional criteria of risk-scoring system. In this study, 228 patients with a diagnosis of KD who received IVIG treatment were viewed retrospectively. Of these 228 patients, 27 were nonresponders who received additional rescue therapy. The Kobayashi score (responders n=201, non-responders n=27) showed statistically significant difference between IVIG-sensitive and IVIG-resistant patients, yielding a sensitivity of 83 % and specificity of 67 %. The Egami score (responders n=201, non-responders n=27) also showed statistically significant difference between IVIG-sensitive and IVIG-resistant patients, yielding a sensitivity of 38 % and specificity of 92 %. The Sano score (responders n=108, non-responders n=15) also showed statistically significant difference between IVIG-sensitive and IVIG-resistant patients, yielding a sensitivity of 52 % and specificity of 90 %. The new risk-scoring system (Kobayashi risk-scoring + NT-proBNP > 1093 pg/mL, responders n=201, non-responders n=27, high risk ≥ 5 points) also showed statistically significant difference between IVIG-sensitive and IVIG-resistant patients, yielding a sensitivity of 83 % and specificity of 71 %. This findings show the new risk-scoring system is helpful in determining patients at risk for non-responders to initial IVIG therapy. This study suggest that in patients with high risk defined as ≥ 5 points, risk calculation by new scoring system are likely to fail to the initial IVIG therapy and may require further rescue therapy in Korean Kawasaki disease patients.

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**J. Cho:** None.  
**K. Yoon:** None.  
**S. Cha:** None.

**128 Efficacy Of Plasma Exchange For Refractory Kawasaki Disease: The Earlier, The Better**

Kunio Hashimoto, Hideki Motomura, Hiroyuki facilities in Japan and been covered by health insurance since 2012.  

**Methods:** We reviewed medical records of five KD patients, aged 3 to 44 months, who were treated with PE in Nagasaki University Hospital from December 2012 to August 2015.  

**Results:** All patient were treated with two courses of intravenous immunoglobulin (IVIG). After IVIG that had offered little or no improvement, two of the five patients used infliximab and another used cyclosporine A before PE. PE was performed for the consecutive 3 or 5 days until defervescence and clinical improvement were obtained. Acute inflammatory changes were successfully ameliorated upon PE therapy in all five patients, although two patients who had already developed CALs before PE on days 20 and 21, respectively, residual CALs were confirmed one year after the treatment. No CALs had developed in the remaining three patients who started PE therapy within nine days after onset (days 8, 8 and 9, respectively). PE therapy was carefully performed in the intensive care unit, and no severe adverse events occurred.  

**Discussion:** PE therapy is able to ameliorate acute inflammation in most cases of severe KD refractory to standard IVIG therapy; however, it is critical to start PE therapy earlier than day-10 in order to prevent CALs. Thus, pediatricians have to make prompt decision on referral of their KD patient who did not respond IVIG to the institutions where PE is applicable in Japan.

**K. Hashimoto:** None.  
**H. Motomura:** None.  
**H. Moriuchi:** None.

**129 Adaptation of Infliximab Therapy for Gamma Globulin Treatment Resistance Kawasaki Disease**

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**Background:** Infliximab (IFX) which is an anti-TNFα monoclonal antibody is effective in the treatment of gamma globulin treatment (IVIG) resistant Kawasaki disease (KD). On the other hand, plasma exchange therapy (PE) became insurance adaptation as treatment for IVIG-resistant KD in Japan. It is necessary to clarify the position of IFX as an additional treatment for IVIG-resistant KD.**

**Purpose:** We examined
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retrospectively the efficacy of IFX for IVIG-resistant KD and discussed its adaptation.

Method; We studied 30 cases (boys 18 cases, 12 cases of girls) who underwent IFX treatment in our hospital because they were IVIG-resistant KD. Between the invalid group and the effective group of IFX treatment, we compared the age, gender, the time of administration, the sick days, CRP value and the presence or absence of coronary artery lesions (CAL) before the treatment in patients.

Result; Clinical symptoms and laboratory data has improved in 22 cases of the 30 cases, but 8 cases underwent plasma exchange because IFX was invalid. Compared to the disabled group and effective group of IFX, the proportion with CAL was significantly higher in the disabled group (87.5% invalid group vs effective group, p <0.05). There was no significant other factor between the two group. Discussion; We have to suppressed the inflammation in order to inhibit CAL. To do so, the enforcement period and selection of additional treatment are important. Because treatable facility is limited, PE is not able to carry out in all cases. In this study, the possibility that can predict efficacy of IFX by the presence or absence of CAL in the IVIG-resistant KD has been shown. we should clarify the adaptation of IFX by continuing further study to find the relevant factors.


130 Clinical Efficacy Of Modified RAISE Protocol In Acute Kawasaki Disease

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Backgrounds and Objectives: RAISE protocol demonstrated that IVIG plus prednisolone (PSL) therapy reduced the incidence of coronary artery abnormalities (CAAs) in children with high risk of refractory Kawasaki disease (KD). However, this protocol has longer hospital stay because PSL is tapered over the next 15 days when CRP was under 5mg/L. We proposed modified RAISE protocol which PSL is tapered over 9 days. The aim of this study was to evaluate clinical utility of modified RAISE protocol.

Methods: This is a retrospective study to evaluate clinical data from KD between May, 2012 and August, 2014. Composite outcomes included incidence of relapse and coronary arterial abnormalities. Using Kobayashi score, children were divided into high and low risk group.

Results: We enrolled 36 KD patients with high risk group in total 147 patients with KD. Median of age was 33 months (range 2-83 months), 13 males. Median days of illness were 4.0 (range 2-7) and Kobayashi score was 6.0 (range 5-9).

Overall, 31 children (86.1%) were responders, whereas 5 children were non-responders (resistance; 1 (2.8%) relapse; 4 (11.1%)). Among 5 non-responders, 4 patients received methylprednisolone pulse therapy (mPSL) and the remaining one patient administrated two times mPSL and infliximab. During follow-up (1-29 months), 3 children (8.3%) had CAAs (dilatation: 3 patients). Modified RAISE protocol was not inferior to conventional RAISE protocol (CAAs 3.3%, p=0.68, responder 84.3%, p=1.0, resistance 5.0%, p=0.92, relapse 10.7%, p=0.66).

Conclusions: Clinical safety and efficacy of modified RAISE protocol (3days ×3) were similar to conventional RAISE protocol (5days ×3).


131 Retrospective Study Of The Timing Of Additional Therapy For Severe Kawasaki Disease Before And After The Induction Of RAISE Study Protocol

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Background: The RAISE study showed that combination therapy with intravenous immunoglobulin (IVlg) and prednisolone (PSL) improved coronary artery outcomes in patients with severe Kawasaki disease (KD). We encountered KD cases in which fever and findings such as WBC were masked by the steroid administration in combination therapy. We hypothesized that combination therapy might delay second- and third-line therapy for
severe KD.
Purpose: The goal of the study was to investigate whether combination therapy with IVIg and PSL might delay second- and third-line therapy for severe KD patients.
Methods: We retrospectively investigated clinical data from acute KD patients admitted to our hospital from January 2011 to September 2014. We examined the following: 1) prediction score for refractory KD 2) first-line therapy for KD (IVIg group, n=10; IVIg/PSL group, n=11); 3) additional rescue therapy such as additional IVIg, steroid pulse therapy, plasma exchange, and so on 4) period from KD onset to end of main therapy for KD; 5) day of increased albumin from previous examination; and 6) day of CRP reaching <1.0 mg/l.
Results: Seventy-four acute KD patients were admitted to our hospital during the study period. Only 1 KD patient had coronary artery lesions (CAL) at 1 month after onset. Detailed data were as follows: 1) Twenty-one patients were at high risk for refractory KD. 2) number of patients with additional IVIg (IVIg, 6/10; IVIg/PSL, 6/11); 3) number of patients with steroid pulse therapy (IVIg, 4/10; IVIg/PSL, 4/11); 4) period from KD onset to end of main therapy (IVIg, 8.3 days; IVIg/PSL, 8.7 days); 5) day of increased albumin (IVIg, 12.0 days; IVIg/PSL, 11.8 days); 6) day of CRP reaching <1.0 mg/l (IVIg, 13.7 days; IVIg/PSL, 11.4 days). No differences between IVIg and IVIg/PSL groups were seen for any factor.
Discussion and conclusion: In this study, overall frequency of CAL was 1.3%, lower than that reported from nationwide surveillance in Japan. This study found no differences between groups in regard to frequency or timing of additional therapy and response. We concluded that combination therapy with IVIg and PSL did not delay the timing of additional therapy for acute KD. The cohort for this retrospective study was small, and further investigation is thus needed.


132 Methylprednisolone Pulse Therapy for Kawasaki Disease with Symptomatic Myocarditis

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Purpose: Kawasaki disease (KD) is an acute febrile illness of infants and young children that is characterized by a systemic vasculitis, especially involving the coronary arteries. Although, sometimes, subclinical myocarditis is combined in KD, symptomatic myocarditis is extremely uncommon. We report a 7 year old boy who developed hypotension and decreased left ventricular systolic function (EF 40%) in the acute phase of KD.
Case: A 7 year old boy (height 115 cm, body weight 20 kg) was admitted because of 2 days of persistent fever and left cervical lymphadenopathy (white blood cell count 17,870 /mm³, C reactive protein 23.6 mg/dL). Conjunctiva injection and lip redness developed on the 4th day of illness, and hypotension and tachycardia (SBP 59/DBP 29 mmHg, HR 153/bpm) were combined. The echocardiography revealed a decreased ejection fraction (EF) (40%) without chamber dilatation and normal coronary artery size (LM 1.9mm, z score=-1.3, RCA 2.3mm, z score=0.4). The level of N terminal pro BNP was 28,000 pg/mL. With a diagnosis of KD with myocarditis, he was initially treated with inotropics and intravenous immunoglobulin (2 g/kg). Without clinical improvement in spite of initial treatment, A change of coronary arterial size (LM 2.9mm, z score=1.2, RCA 3.1mm, z score=2.3) was developed and decreased LV systolic function (EF 45%) and fever were persisted. Then, he was given 3 daily pulses of intravenous methylprednisolone followed by tapering doses of oral prednisolone. He showed prompt clinical recovery after pulse therapy of intravenous methylprednisolone (SBP 95/DBP 49 mmHg, HR 98/bpm). Although EF was improved (59%), coronary arterial dilatation was progressed (LM 3.4mm, z score=2.4 RCA 5.5mm, z score=7.9). Conclusions: The present case serves to highlight the fact that methylprednisolone should be considered as the priority in children with KD who have symptomatic myocarditis during the acute stage.


133 Assessment of Therapeutic Effect of Medium-Dose Intravenous Immunoglobulin
as An Initial Treatment for Kawasaki Disease in Korean Children

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Objectives: A high-dose (2g/kg) intravenous immunoglobulin (IVIG) has been generally incorporated into the acute treatment protocols for Kawasaki disease (KD), with ongoing debates on this issue. The aim of this study was to assess the effectiveness of medium-dose (1g/kg) IVIG as an initial treatment of KD in Korean children.

Methods: A retrospective study was done in a total of 255 children with KD, in whom 91 patients (group 1, mean age; 2.8 ± 2.5 years) had 2g/kg of IVIG and 164 patients (group 2, mean age; 2.7 ± 1.7 years) had 1g/kg of IVIG as an initial treatment of KD, along with 30-50 mg/kg of aspirin. Echocardiography (Echo) was done during admission, around 2 weeks, 2 months, and 1 year after the onset of fever according to our protocol. Patients who completed one-year Echo study were included in this study. Patients’ demographic, laboratory, and Echo findings were recorded, and compared between groups. Coronary artery lesions (CAL) were defined as a coronary artery diameter > 2 SD of normal mean for age or coronary artery stenosis. The primary end point was the incidence of CAL at 1 year after treatment. The secondary end points were the incidence of CAL at 2 weeks and 2 months study, and clinical outcomes. Comparisons between groups were done using an unpaired t-test or Fisher’s exact test.

Results
There was no significant difference in age, gender, and laboratory findings before treatment between the two groups. Group 1 had higher incidence of CAL at 2 weeks (32/91, 35.2 % vs. 33/164, 20.2 %, p = 0.011), but similar incidence of CAL at 2 months (18/91, 19.8% vs. 24/164, 14.6%, p > 0.05) and 1 year (6/91, 6.6% vs. 10/164, 6.1%, p > 0.05) compared with group 2. Group 1 had a higher proportion of patients needed additional dose of IVIG (23/91, 25.3% vs. 15/164, 9.1%, p = 0.001), but received significantly lower total dose of IVIG (1.3 ± 0.7 g/kg vs. 2.1 ± 0.5 g/kg, p < 0.001) compared with group 2. There was no difference in duration of fever after IVIG and duration of hospital stay between the two groups.

Conclusion: This study demonstrated that medium-dose IVIG is as effective as high-dose IVIG for the treatment of KD in terms of CAL prevention, defervescence, and duration of hospital stay. Further prospective and randomized study is needed to verify this.

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Early Immunoglobulin Therapy and Outcomes of Kawasaki Disease

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Background and Objectives: Kawasaki disease is the leading cause of acquired heart disease among children in most industrialized countries. However, only few descriptive studies discussed the pros and cons of early immunoglobulin therapy. The aim of this study is to see the effect of early immunoglobulin therapy on Kawasaki disease outcomes.

Methods: This study enrolled patients who received immunoglobulin therapy for the first time. Basic data was analyzed for descriptive epidemiology. Clinical risk factors of acute coronary aneurysm, chronic coronary aneurysm and recurrence rate were analyzed.

Results: Totally 5235 patients of first attack of Kawasaki disease were enrolled. Among them, 1156 children were classified as early immunoglobulin therapy. The odds ratio for acute aneurysm and needing long-term anti-coagulant therapy were 0.94 (95% CI, 0.77~1.16) and 1.01 (95% CI, 0.77~1.32) respectively. The recurrence rate was higher for early immunoglobulin therapy group. The adjusted odds ratio was 1.86 (95% CI, 1.07~3.23).

Conclusions: Early immunoglobulin therapy might not benefit the coronary outcomes for children of Kawasaki disease. On the contrary, it might be associated
Effectiveness Of Live Vaccines Following Intravenous Immune Globulin Therapy During The Convalescent Phase Of Kawasaki Disease Using The Schedule Recommended In Japan

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Background
There are differences between Japan and the United States regarding recommended timing of live virus vaccinations after treatment of Kawasaki disease patients with intravenous immune globulin (IVIG): 6 months in Japan and 11 months in the U.S. The prevalence of antibodies to these vaccines using either vaccination schedule remains undetermined.

Objective
The present study aimed to evaluate the effectiveness of the live virus vaccination schedule for Kawasaki disease recommended in Japan.

Methods
This was a prospective observational study. Kawasaki disease patients aged 6 months and older without past history of or vaccination against measles, rubella, varicella-zoster (VZ), or mumps were enrolled. The children were vaccinated against measles, rubella, VZ, and mumps 6 months after IVIG. Serologic tests for IgG-class specific antibodies to each vaccine virus were performed prior to IVIG; 2 days, 3 months, and 6 months after IVIG, and 3 months after vaccination. The primary outcome was seroprevalence of positive antibodies, which was defined as serum concentration more than 4 IU/mL.

Results
A total of 24 children (mean month age 16.8 ± 2.7 at vaccinations, 70.8% male) were enrolled. The rate of measles, rubella, VZ, and mumps seropositivity was 12.5% (3/24), 0% (0/24), 12.5% (3/24), and 0% (0/24), respectively, just before vaccination. The rate increased to 91.7% (22/24), 87.5% (21/24), 20.8% (5/24), and 8.3% (2/24), respectively, 3 months after vaccination. There were no serious adverse events.

Conclusions
Use of the Japanese vaccination schedule led to extremely low seroprevalence of VZ and mumps antibodies but acceptable seroprevalence of measles and rubella antibodies. This study is ongoing and more cases (up to 30, the target sample size) are needed before the appropriateness of the timing of vaccination in Japan can be discussed.

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A Case of Complex Congenital Heart Disease with Postoperative Complications of Impaired Consciousness and Several Arrhythmias due to Encephalitis in the Acute Stage of Kawasaki Disease

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Background: In addition to muscular and medium arteries, Kawasaki disease causes inflammation in nerves and the myocardium. However, arrhythmia severe enough to be problematic is rare. Patient: At age 1 day, the patient was in a state of shock and was diagnosed with Taussig-Bing anomaly and aortic arch coarctation. At age 4 days, he underwent
aortic arch reconstruction and pulmonary arterial banding. At age 2 months, he underwent arterial switch operation and ventricular septal defect closure. No significant arrhythmias were observed. At age 5 years 6 months, he had a fever, and 5 days later, he developed rash, conjunctival hyperemia, and redness of the lips and fingertips. Kawasaki disease was diagnosed on day 7 after symptom onset. The patient presented with disorientation, so electroencephalography and magnetic resonance imaging were performed and revealed overall slow-wave activity and cerebral edema, respectively, indicating complicated encephalitis. Sinoatrial block and sinus arrest were also observed. The patient received ultrahigh-dose γ-globulin therapy and steroid pulse therapy for encephalitis. The fever resolved at a total γ-globulin dose of 4 g/kg. The other main Kawasaki disease symptoms also disappeared. By day 18, his consciousness completely recovered but the sinus arrest remained. On day 20, an atrial flutter developed from tachycardia that was treated with electric shocks. Sinus arrest at a maximum of 5.7 s was observed at that time, and bradyarrhythmia-tachycardia syndrome was suspected. On the same day, the sinus arrest improved gradually and largely disappeared 3 days later. The atrial flutter also disappeared. Discussion: Severe arrhythmia that requires treatment is rare in Kawasaki disease. Our patient underwent surgery for a complex cardiac anomaly. Thus, the requisites for arrhythmia were present when the Kawasaki disease caused myocardial inflammation, which is thought to cause severe symptoms.

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137 Efficacy Of Raise Protocol For Children With Incomplete Kawasaki Disease

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Background Although RAISE study demonstrated that intravenous immunoglobulins (IVIG) plus prednisolone (PSL) therapy for refractory Kawasaki disease (KD) reduced coronary artery aneurysm, the study population included a few incomplete KD. The aim of study was to evaluate the efficacy of RAISE protocol for incomplete KD.

Methods Children with incomplete KD which have 4 or less major symptoms of KD were enrolled. Using Kobayashi score, children were divided into low and high risk for IVIG resistance. Children with low risk group received IVIG monotherapy, whereas IVIG plus PSL therapy administrated for high risk group. Retrospectively, we assessed initial treatment response and coronary artery abnormalities (CAAs).

Results Overall, 63 incomplete KD (age; median and range 17 months (1-115 months), sex ratio; boys:girls 37:26) were enrolled. Median day of illness at diagnosis was 5 day of illness (2-10 days). Low risk group included 52 cases (83%) and the remaining 11 cases were high risk group. In low risk group, 87% of children (45 cases) were initial treatment responders. All 7 non-responders were responded to additional methylprednisolone steroid pulse therapy. All 11 children with high risk group were responders to the initial treatment. Five cases have equal to greater than 2.5 of Z-Score, which were all low risk group. All CAAs regressed to normal coronary diameter within 1 month.

Conclusions RAISE protocol was useful for the treatment of incomplete KD without any CAAs.


138 Early Therapeutic Intervention With IVIG Is Effective In Infants Less Than 3months With Kawasaki Disease

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[Background] Kawasaki disease (KD) in infants less than 3 months (<3M) is reported rare, but incomplete type or coronary artery lesion are more frequent than in older ages. [Purpose] To elucidate the correlation between treatment effect and age in KD. [Methods] A total of 367 children with KD were admitted in our hospital from 2007 to 2014. A Comparison was made among 3 age groups (<3M, 3 months to less than 5 years (3M-5Y) and 5 years or older (≧5Y)) from the view points of disease type (complete or incomplete depend on major symptoms are 5 or less out of 6), effect of initial intravenous immunoglobulin (IVIG) and coronary artery lesion (dilation or aneurysm formation). [Results] Incomplete type of KD was seen in 82% of <3M (14/17), whereas 6.6% (20/300) in 3M-5Y and 4.0% (2/50) in ≧5Y. Initial IVIG was unsuccessful in 24% (4 cases) in <3M, 22% (66 cases) in 3M-5Y and 38% (19 cases) in ≧5Y. Coronary artery lesion was observed in 5.8% (1 case) in <3M, 0.6% (2 cases) in 3M-5Y and 2% (1 cases) in ≧5Y. [Discussion] Since the time from the initial symptom of KD to the first visit to our department was shorter in <3m infants (1.53 days) than the older age groups (4.18 days in 3M-5Y and 4.44 days in ≧5Y), majority of <3M infants with KD showed less than 5 major symptoms; polymorphous exanthema in 88%, lip and oral cavity findins in 76%, bilateral bulbar conjunctival congestion in 59%, extremities changes in 23%, cervical lymphadenoapathy in 18%. We make a diagnosis of KD in <3M infants when labolatory data suggests vasculitis and/or echocardiography reveals abnormal findings, together with major clinical symptoms even less than 5. Based on these diagnostic process , we started initial IVIG by 4 days and achieved satisfactory results.


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Transcriptional Regulation By Infliximab Therapy In Kawasaki Disease Patients With Immunoglobulin Resistance

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Background: Infliximab (IFX) is a known monoclonal antibody against TNF-α that is used to treat Kawasaki disease (KD) patients with intravenous immunoglobulin (IVIG) resistance. The transcriptional modulation of inflammation following IFX therapy has not been reported in KD patients. Methods: We investigated the transcript abundance profiles in whole blood obtained from eight IVIG-resistant KD subjects treated with IFX therapy using microarray platforms and compared them to those in initially IVIG-responsive subjects. A pathway analysis was performed using WikiPathways to search for the biological pathways of the transcript profiles. Four transcripts changed by IFX therapy were subsequently validated using RT-PCR. Results: The pathway analysis showed the reduced abundance of transcripts in the nucleotide-binding oligomerization domain, matrix metalloproteinase, and inflammatory cytokines pathways and the increased abundance of transcripts in the T cell receptor, apoptosis, TGF-β, and IL-2 pathways. Additionally, the levels of four transcripts (peptidase inhibitor-3, matrix metalloproteinase-8, chemokine receptor-2, pentraxin-3) related to KD vasculitis and IVIG resistance decreased after IFX therapy. Conclusions: The administration of IFX was associated with both the signaling pathways of KD inflammation and several transcripts related to IVIG resistance factors. These findings provide strong theoretical support for the use of IFX in KD patients with IVIG resistance.


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A study on 15 patients with Kawasaki disease who underwent coronary bypass surgery at our hospital

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**Background:** Kawasaki Disease (KD)-related coronary artery aneurysm results in stenotic lesions due to thrombus formation and intimal thickening. In its acute phase, KD may follow an acute course due to thrombotic occlusion leading to myocardial infarction. On the other hand, in the convalescent phase, it does not follow a rapid course due to the development of collateral circulation and often occurs with chest pain. In this study, we retrospectively analyzed the following variables in patients who underwent bypass surgery: clinical course until initiation of surgical treatment, indication of surgical treatment.

**Subjects and Methods:** The subjects were 15 patients who underwent coronary artery bypass graft (CABG) surgery at our hospital (male:female ratio, 8:7; age, 24-58 years; mean age, 38.3 years). In these subjects, we examined the age at onset, period until initiation of surgical treatment, presence or absence of symptoms, radiographic findings, indications for surgical treatment, and operative methods.

**Results:** The age at onset of KD was between 6 months and 12 years. For 3 patients, KD was not diagnosed in childhood and the diagnosis was based on calcification and chest radiography findings. The period from onset to surgical treatment ranged 7-42 years (mean, 25.6 years). Most of the subjects underwent surgical treatment during adulthood. Radiography showed bilateral lesions in 14 patients, complete occlusion of the right coronary artery in 5 patients, and calcification in 4 patients. Collateral circulation developed in all subjects who underwent surgical treatment during adulthood. Although exertional chest pain was observed in 9 patients, no patient required emergency CABG. Surgical treatment involving the bilateral inferior mesenteric arteries was performed in 14 patients. In 2 patients, a bulky mass was resected from the right coronary artery.

**Conclusion:** The mean age at surgery was approximately 40 years. There were many subjects in whom the time elapsed since disease onset was long, which was presumably attributed to the development of collateral circulation. Therefore, it is necessary to examine such patients using diagnostic imaging or stress myocardial scintigraphy even if they are asymptomatic.

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**A Case of Kawasaki Disease with Re-dilatation of a Coronary Artery Aneurysm after Regression**

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[Background] In patients with Kawasaki disease (KD), re-dilatation of coronary artery lesions (CAL) after regression is very rare. Here we report a case of KD with CAL re-dilatation after regression.

[Case report] A 15-year-old boy was diagnosed with KD at 1 year of age and was treated with intravenous immunoglobulin (IVIG, 400 mg/kg × 5 days). On day 14, echocardiography revealed CAL on the right coronary artery (RCA) and left coronary artery (LCA). Coronary arteriographic findings were as follows: segment 1, 3 mm in diameter; segment 6, 5 mm in diameter. He was prescribed aspirin, ticlopidine, and warfarin for 3 years. When he was 3 years old, coronary angiography showed complete CAL regression. His medications were discontinued and he underwent routine follow-up by echocardiography on which the CAL were not seen. At 14 years of age, coronary CT revealed re-dilatation of the LCA. Coronary angiography showed the same findings: 7 mm in diameter at the bifurcation between the LAD and the left circumflex artery, while the other regions were intact. He restarted aspirin and warfarin. The mechanism of CAL re-dilatation remains unclear; however, it is very important to follow patients carefully and routinely using echocardiography and/or coronary computed tomography, especially in cases with a history of CAL.

**K. Oka:** None. **T. Minami:** None. **T. Anzai:** None. **S. Furui:** None. **A. Yokomizo:** None. **T. Ishii:** None. **T. Sato:** None. **K. Kataoka:** None. **T. Yamagata:** None.

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**Plasma Exchange Therapy in a Patient with Refractory Kawasaki Disease Initially Treated**

with Intravenous Immunoglobulin and Prednisolone

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Prednisolone combined with intravenous immunoglobulin (IVIG) is the standard option for the initial treatment of Kawasaki disease (KD) in Japan, as described in the 2012 Japanese guidelines for KD. However, there is still debate regarding treatment in patients with refractory KD initially treated with IVIG plus prednisolone, especially in those with comorbid coronary artery aneurysm (CAA). Here, we present the case of a 3 year-old-girl initially treated with IVIG plus prednisolone, whose clinical and laboratory parameters improved after plasma exchange therapy (PE). She was admitted to a local hospital on day 4 of illness and diagnosed as having severe KD (Kobayashi score, 7). Therefore, prednisolone plus IVIG was administered as initial treatment. The initial course was ineffective. She was treated with methylprednisolone pulse therapy, and a second and third round of additional IVIG, but low-grade fever persisted. After these treatments the patient’s general condition had improved and major KD symptoms improved by day 13 of illness, despite a high serum C-reactive protein level (19.9 mg/dl) and hypoalbuminemia (1.8 g/dl). Expanding medium-sized aneurysm was detected on the same day, so she was immediately referred to our hospital for further treatment. The CAA continued to expand, so PE was performed for 3 consecutive days and prednisolone was gradually reduced from day 15 of illness. After that, she became afebrile and CAA progression stopped. Laboratory findings such as serum C-reactive protein and albumin levels were dramatically improved after PE. This case suggests that PE might be effective for refractory KD initially treated with IVIG plus glucocorticoids and may stop the CAA development. Doctors must remain aware that patients treated with glucocorticoids may have masked clinical conditions, and take care not to underestimate the signs of refractory KD.


Clinical Consideration of Kawasaki Disease Development in Younger and Older Children

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[Background]Kawasaki disease (KD) is an acute febrile illness of childhood. Most KD patients are children aged from 6 months to 4 years, although a small number of cases occur in children less than 6 months or over 5 years of age. KD symptoms are not easily observed in younger and older children, and so it is necessary to understand how the features of KD change with age.[Objective]This study aimed to evaluate the clinical features of KD in children less than 6 months and greater than 5 years of age in our hospital. [Methods]Patients diagnosed between October 2006 and September 2013 were divided into 2 groups: group A included 19 infants less than 6 months old and group B included 222 children who were more than 6 months old (1). On the other hand, patients were divided into another 2 groups: group C which included 219 children less than 5 years old and group D which included 29 children who were more than 5 years old (2). The features and symptoms of KD were compared between the groups; in particular, white blood cell counts, neutrophil ratios, platelet counts, total bilirubin, aspartate transaminase, alanine transaminase, sodium, C-reactive protein, fibrinogen, D-dimer, and intravenous immunoglobulin unresponsive scores were compared. [Results](1) Few infants less than 6 months old had changes in their extremities or cervical lymph node swelling; most of the infants less than 6 months old had incomplete KD. The neutrophil ratio before treatment tended to be significantly lower in infants less than 6 months old. (2) Most of the children over 5 years old had erythema, but few had significant cervical lymph node swelling. The neutrophil ratio before treatment tended to be significantly higher in infants over 5 years old. [Discussion]The symptoms of KD are not easily observed in young infants with a continuing high fever and children diagnosed with pyogenic cervical lymphadenitis, and these patients sometimes have to wait a long time to be diagnosed with KD. It is important to carefully observe the clinical progress of young infants with a continuing high fever and children diagnosed with pyogenic cervical lymphadenitis.
K. Sakurai: None.

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Lung Parenchymal Consolidation during typical Kawasaki Disease

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Introduction;
Kawasaki disease (KD) is a systemic vasculitis of childhood throughout the body. We report a patient who complicated by severe pneumonia of lung parenchymal consolidation (LPC) during typical KD clinical course.

Case reports;
A 7-yr-old male who had a past history of KD at 3-yr-old, visited a general practitioner with fever, sore throat and neck pain. Three days later, after being treated with CTRX/TBPMPI, he was transferred to our hospital because of bilateral lymph nodes swelling and a generalized erythema and rash.
On admission he was still febrile and had bilateral conjunctival injections, cervical and axillary lymphadenopathy and markedly reddened pharynx, without edema. We diagnosed him as KD and treated him with aspirin and IVIG at a dose of 2.0g/kg, but the condition worsened; he developed dyspnea and dry cough. Crackles were noted on rt-lung auscultation, along with rt-basal dullness to percussion of the thorax.
Chest radiography and a subsequent computed tomography scan revealed disseminated patchy infiltrates and ground-glass alterations with massive pleural effusions on rt-lung, and enlarged axillary and mediastinal lymph nodes.
Some kinds of microbiology (including Mycoplasma) and virology (Epstein-Barr virus, cytomegalovirus, parvovirus B19), from all sampled sites (pleural effusion, blood, pharyngeal swab and cerebrospinal fluid), were negative for pathogenic specimens.

So we treated him as intractable KD with second-IVIG and m-PSL, which led to the quick resolution of fever and progressive amelioration of pneumonia. Echocardiography showed normal ventricular size and function without coronary artery lesion (CAL). Thereafter, he was finally afebrile. At the first follow-up visit, 1 month after discharge, he had fully recovered.
Clinically, echocardiographically and radiographically, no residues were noted.

Conclusion;
Several manifestations of broncho-pulmonary involvement in KD have been described. But there are very few case of LPC. We should consider the possibility that LPC were secondary to pulmonary arteritis.

S. Sato: None.

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Long Term Follow-up Of Children With Kawasaki Disease (KD) Treated With Infliximab (IFX) - Our Experience At Chandigarh, North India

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Background:
Tuberculosis (TB) is endemic in India. Flare-up of TB is a concern in children treated with IFX.

Objective:
To report long-term follow-up of children with KD treated with IFX.

Patients and methods:
Study design: Review of records of 17 children with KD who had received IFX. Median age was 1.5 years (range 2 months to 6 years)
Study setting: Pediatric Rheumatology Clinic, Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research, Chandigarh, North India.


Patient group: Patients with diagnosis of KD and given IFX were included and analyzed. 15 of these patients had received intravenous immunoglobulin (2g/kg) as first line therapy. Dose of IFX was 5-7 mg/kg given intravenously. Screening tests for TB (chest X-ray, tuberculin test) were not carried out prior to IFX infusion.
Duration of follow-up:6 -12 months in 6 patients;13-30 months in 5 patients;45-65 months in 5 patients and 80 months in 1 patient (mean follow-up 30.6 ± 24.4 months).

Results: None of the patients had any significant adverse reactions during infusion of IFX. On follow-up none of these patients has developed TB or any other significant infection. Twelve (12)/17 patients showed coronary artery abnormalities (CAAs) (table). Post IFX, 66% (8 of 12) patients with KD showed improvement in CAAs on follow-up.

Conclusion: In our experience use of IFX was not associated with flare-up of any significant bacterial infection (including TB) during follow-
up. 8/12 patients with CAAs showed resolution.


146 Third Intravenous Immunoglobulin Is An Effective Option For Kawasaki disease Patients Resistant To Cyclosporin A

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Background: About 10-20% of patients with Kawasaki Disease (KD) who fail to respond to IVIG, show a high prevalence of CAL. The new guideline (2012) has proposed several options for second- and third-line therapy for patients resistant to IVIG. However, there are still no definite treatment options for refractory KD. We have reported that cyclosporin A (CsA) is a well tolerated, safe and promising option for patients resistant to IVIG. However, certain subgroups of such patients may also be resistant to CsA. In this study, we examined if a third course IVIG might be effective for patients resistant to CsA.

Patients and Methods: Between April 2008 and May 2014, 42 Japanese patients who met the diagnostic criteria for KD and received CsA treatment were enrolled as study subjects. All patients were resistant to both initial (2 g/kg for 24 hours) and additional IVIG, and were then administered CsA orally (Neoral®, oral solution, Novartis Pharma Co. Ltd., Tokyo, Japan). The initial dose of CsA was 4mg/kg/day, and it was divided into two equal daily doses every 12 hours. The dose of CsA was adjusted to between 4 and 8 mg/kg/day to maintain a trough level of 60-200 ng/ml by reference to clinical and laboratory data such as body temperature and C-reactive protein level. After the start of CsA treatment, if patients remained febrile for more than 5 days, or if fever returned after an afebrile period within 5 days, CsA treatment was judged to be ineffective, and the patients were then given a third course of IVIG. We analyzed some laboratory data between CsA effective group and CsA resistant group.

Results: CsA treatment was judged to be ineffective in 14 of 42 (33%) patients. Eleven of those 14 patients received a third IVIG, and then, 8 (72.7%) patients of them became afebrile within 24hours. The other three patients became afebrile after a fourth IVIG. The serum levels of AST and soluble interleukin-2 receptor before the start of CsA treatment were significantly lower in CsA effective group than in CsA resistant group.

Conclusion: A third course of IVIG is an effective option for KD patients who are resistant to CsA.


147 Coronary artery aneurysms on day 4 after onset of Kawasaki Disease: A Case report

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[Background] Coronary artery aneurysm (CAA) in patients with Kawasaki disease (KD) almost always occurs after day 8, and the most early detection report of CAA was in an autopsy case on day 6 after onset. The possibility of CAA formation prior to day 6 has not been
documented.

Case report: A 10-month-old Japanese boy presented with a 4-day fever, conjunctival injection, erythema of the lips, erythema of the palms and soles, erythematous rush, and induration at a Bacillus Calmette-Guerin inoculation site. On day 4, echocardiography revealed coronary artery dilatation (right coronary artery [RCA], 4.6 mm; left main trunk [LMT], 4.6 mm; left anterior descending [LAD] artery, 3.4 mm). Laboratory data were as follows: white blood cell count, 19,400/µL; C-reactive protein, 15.2 mg/dL; albumin, 3.2 g/dL; high-density lipoprotein cholesterol, 20 mg/dL, and erythrocyte sedimentation rate, 48 mm/h.

He was diagnosed with KD and treated with oral aspirin 30 mg/kg/day and intravenous immunoglobulin (IVIG) 2 g/kg. His fever subsided the next day. On day 17, periungual peeling of the fingers and toes was noted. His fever recurred and he treated with additional IVIG 1 g/kg, after which his fever subsided again. On day 20, the aneurysms had not increased in size (RCA, 3.3 mm; LMT, 3.6 mm; LAD, 2.4 mm). On day 44, although echocardiography showed a mild coronary artery dilatation, a coronary angiogram showed no apparent abnormality. He had no obvious fever or symptoms of KD prior to this course of KD. This case may help clarify the pathophysiology of CAA in patients with KD.


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The Optimal Duration Of Asa Treatment After Acute Phase Of Kawasaki Disease Based On Inflammatory Markers

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Purpose: Outcomes of Kawasaki disease (KD) are determined by the development of cardiovascular complications. Low dose aspirin (ASA) treatment is used as antithrombotic effect after acute phase of KD for 6-8 weeks. There are no standardized inflammatory markers used as guidance for completing low dose ASA treatment. The optimal duration of low dose ASA treatment is not determined. The aim of this study is to decide the duration of low dose ASA treatment based on inflammatory markers.

Methods: We enrolled 80 KD children admitted to the Chungnam National University Hospital, South Korea between Sep 2012 and May 2014. We reviewed the medical records for clinical characteristics, duration of fever, cardiovascular complications and laboratory data on admission. Inflammatory markers were measured every 7-14 days at OPD after immunoglobulin (IVIG) and high dose ASA treatment in acute phase. Low dose ASA was stopped when the level of inflammatory markers were down to the normal without any cardiovascular complications. Echocardiograms were performed at admission, discharge and prior to completion of ASA treatment when the inflammatory marker turned to normal. Results: 80 KD patients, (Complete, n=44; Incomplete, n=36). The incidence of cardiovascular complications was similar both two groups. No significant differences in the laboratory studies either complete or incomplete KD. The levels of inflammatory marker were normalize after the acute phase as 13.0±13.6 days for platelets, 13.8±8.3 days for CRP, 14.4±9.6 days for d-dimer, and 24.1±10.5 days for ESR. The duration of raised CRP levels showed significantly shorter in incomplete group compared to complete groups (p=0.02). No new coronary lesions were developed among patients who didn't have the coronary lesions at subacute phase. Conclusion: The majority of the inflammatory marker levels were normalized within 2-3 weeks after acute phase of KD. There were no new cardiovascular complications when the duration of low dose ASA treatment was guided by level of the inflammatory markers. So, the optimal duration of low dose ASA treatment can be reduced to 3-4 weeks without development of coronary lesions.

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How Effective Is Steroid Combination Therapy For High-risk Cases Of Kawasaki Disease?

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Background: There are three scoring systems for the prediction of non-response to IVIG in
Japan. Steroid combination therapy for initial treatment is recommended for high risk cases in the new guideline from the scientific committee the Japanese society of pediatric cardiology and cardiac surgery in 2012. Objective: to evaluate efficacy of steroid combination therapy for high risk cases which have high scores in more than two prediction scoring systems. Subjects and Methods: From January 2009 to 2014, a total of 54 hospitalized patients with high scores in more than two prediction scoring systems were enrolled. The patients were separated into two groups. Group S (n=21): who were administered steroid+IVIG, Group N (n=33): who were administered only IVIG. Clinical data, clinical course, and circumstances of additional therapies were compared. Results: In the patients who had high scores in two prediction scoring systems, there were fewer patients who received additional therapies in group S compared to that in group N (13% 1/8 vs. 38% 8/21). However, for patients who had high scores in all prediction scoring systems, those who received additional therapies had not decreased in group S compared to that in group N (50% 6/12 vs. 46% 6/13). Conclusions: Steroid combination therapy is beneficial for the patient who has high scores in two or less prediction scoring systems. On the other hand, in the most severe cases those who have high scores in all prediction scoring systems, Steroid combination therapy is less efficacious and other additional therapy should be considered in the early stage to improve prognosis.

Y. Yoshikane: None. J. Hashimoto: None. S. Hirose: None.

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A Case Of Kawasaki Disease Complicated By Autoimmune Hemolytic Anemia In A Boy

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Introduction
Kawasaki disease is a systematic disease, usually affecting infants and toddlers. It can be characterized by rare complications or by unusual associations. One of these is autoimmune hemolytic anemia that has been observed seldom up to now. In this report, we present a case with this rare association.

Case
A previous healthy 7-year-old boy was transferred form a primary clinic due to fever and neck mass. Neck CT showed acute pharyngitis with focal abscess formation and multiple enlarged lymph nodes at both retropharyngeal space. He was treated intravenous antibiotics for 3 days. On the 4th hospital days, the patient sustained high fever and presented diffuse maculopapular rash, conjunctival injection without exude, erythema and edema of the hands and feet. Laboratory finding showed Hb 11.6 g/dL; hematocrit (Hct) 33.9 %; WBC count 15,350 µL; platelets count 308,000 µL; AST 123 IU/L; ALT 237 IU/L; CRP 103.14 mg/L; creatinine kinase (CK) 28 IU/L; CK-MB 0.6 ng/mL; pro-BNP 783.2 pg/mL. Mild dilatation of right coronary artery (4.14mm) was noted in echocardiogram. The patient was diagnosed Kawasaki disease and treated intravenous immunoglobulin (IVIG) (2g/kg) and aspirin.

Retreatment with IVIG was administered for persistence of fever 48 hours after the first infusion. Thereafter, his symptoms gradually improved. On the 12th hospital day, his follow-up laboratory finding showed decreased Hb 7.1 g/dL and Hct 20.8 %; reticulocyte 10.71 %; peripheral blood smear: normocytic normochromic anemia with anisopoikilocytosis, immune hemolytic anemia; Direct polyclonal antiglobulin test positive. There was no hemodynamic instability. Prednisolone 2mg/kg/day P.O. was given for hemolytic anemia and hemolysis resolved following treatment. On follow-up, hemoglobin and hematocrit increased gradually. He made a good clinical recovery without cardiovascular complication.

Conclusion
A 7-year-old boy presented with the fever, skin rash, conjunctival injection and lymphadenopathy. He was diagnosed Kawasaki disease. Autoimmune hemolytic anemia occur on the way of improving state after treatment. The authors report a case of autoimmune hemolytic anemia during Kawasaki disease.


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Optical Coherence Tomography post-processing towards an automated quantification of coronary artery wall alteration subsequent to Kawasaki Disease
ABSTRACTS
Poster Abstract Presentations (continued)

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INTRODUCTION: Statistical mathematical processing of medical imaging promotes operator-independent interpretation. We sought to identify discriminative image features for a histological disambiguation of KD related coronary (CA) lesions. The ultimate goal is to develop a fully automated algorithm for the quantification of the degradation/healing state of the CA wall structure post KD.

METHODS: We analyzed OCT CA recordings from two KD patients with (KD+AN+) and two patients with no history of CA aneurysm (KD+AN-), vs a non KD patient (KD-).

RESULTS: In KD-, regardless of the radial region of interest (ROI) position in the image, the OCT mean signal intensity presents centrifugally two peaks corresponding to the intima and media, constantly separated (17.1±2.0 pixels) (fig. 1A). In KD+AN- the peaks may disappear (Fig. 1-B left medial hyperplasia) and the distance between remaining crests vary between ROIs (22.7±6.9 Pixels). In KD+AN+ these peaks disappear (Figure 1-C) and the signal intensity changes drastically between ROIs due to wall restructuration. Figure1-C shows a hatched signal that maybe that of a laminar structure. In this case the variation of gradient intensity may be a discriminative feature.

CONCLUSION: Mathematical modeling of CA wall layers is feasible. While the consistency of the distance between media and intima peaks may discriminate KD- from KD+ and while the gradient intensity may detect restructuration in KD+AN+, ongoing investigation to discriminate CA lesions include signal homogeneity, energy and contrast. Texture analysis with anatomical correlates (e.g., calcium, fibrosis and clots) may allow automated diagnoses.

M. Abdelali: None. F. Cheriet: None. A. Dionne: None. N. Dahdah: None.

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Tri-Dimensional Fusion Image of Multidetector 64-Slice-Computed Tomography and Single-Photon Emission Computed Tomography enables us to Evaluate Complicated Hemodynamics in Patients with Coronary Artery Lesions after Kawasaki Disease

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Introduction: An important complication of Kawasaki disease (KD) is myocardial ischemia and acute myocardial infarction which occurs by thrombosis in coronary aneurysms and severe stenosis. The most characteristic features of coronary artery lesions (CALs) are dilation or aneurysm in acute stage and stenosis after convalescence stage. As these lesions exist singly or multiply in one coronary branch or
multiple branches, coronary hemodynamics can be complicated. Ordinal methods have less potential for detection of these diseased states. Recently, Fusion imaging from coronary CT angiography (CTA) /SPECT has been thought good method for evaluation of location and severity of myocardial damages in adults. Therefore, we evaluate CALs, ischemia, and infarction after KD by Fusion imaging.

Patients and Method: Seventeen patients (16 males and 1 female, age 10 to 34 y) were subject. Eight patients had coronary artery bypass grafting (CABG). These tests were performed 8 to 30 years after onset of KD. CTA are performed by 64-slice-CT (LightSpeed VCT: GE Healthcare), and SPECT (Infinia: GE) by Tc-tetrofosmin was performed at rest and at stress after infusing adenosine. CTA and SPECT images were fused by the software (CardIQ Fusion: GE).

Results and findings: In all cases, we had enough good images to detect the location of CALs and the area of ischemia.
1) Fusion images showed that no patient had significant stenotic findings at the anastomosis of bypass-graft at least several years after CABG.
2) Coronary native small branches arose from giant aneurysm were occluded by thrombosis and sub-aneurysmal lesions were infracted which were not detected by ordinal method.
3) Minimum sized myocardial ischemic lesions along to the normal visual epicardial coronary artery were detected and were suspected the existence of abnormal micro-coronary circulation caused by fibrous plaque or micro-thrombosis.
4) Collateral arteries at the stenotic and/or occluded lesions with or without ischemia were clearly detected by Fusion method.

Conclusion: Fusion images can visualize morphologically and functionally complicated CALs, myocardial ischemia and myocardial infarction after KD. Also, we can realize that peripheral coronary vessels are damaged with myocardial ischemia.


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Automated Angiographic Assessment Of Coronary Artery Vasomotion In Kawasaki Disease Patients

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Background
Mechanical properties of coronary arteries (CA) hold clues to vascular health and viability. Traditionally assessed with intracoronary imaging, we present an angiography-based system to assess CA vasomotion using automatic vessel segmentation and spatio-temporal tracking. Elastic moduli computed from dynamic CA calibers are compared between non-KD patients (CTL), KD patients with no CA aneurysms (KDAN-), and those with aneurysms (KDAN+).

Methods
Proximal CA angiograms are automatically segmented and tracked over a cardiac cycle. CA centerline is extracted and the mean caliber is computed from diameters along its length. The resulting caliber variation reflects the CA vasomotion (Figure 1a). We then calculated the Vasomotion Standard Deviation (VSD) and CA recoil with the mean constriction velocity (MCV). Finally, Elastic Pressure moduli were computed using trans-myocardium pressure gradients.

Results
We analyzed 51 left CA segments from 23 patients (5 CTL, 5 KDAN-, 13 KDAN+). Data are mean ± SD normalized pixels (npx). VSD was significantly reduced \( (p<0.01) \) in KDAN+ (0.25±0.05) and KDAN- (0.27±0.04) vs CTL (0.38±0.07 npx). Coronary recoil was significantly reduced \( (p<0.05) \) in KDAN+ vs CTL, with MCV 3.50±0.67 vs 4.59±1.94 npx/sec. Pressure-dependent stiffness characteristics were equally atypical (Figure 1b).

Conclusion
The proposed angiography-based stiffness assessment system shows abnormal CA vascular physiology in our cohort of KD patients. These results concur with previous invasive studies. The potential usability of this system for vascular health assessment could be applied to previously recorded CA angiograms for risk
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CMR Feature Tracking in Kawasaki Disease convalescence

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Objective: To determine whether left ventricular (LV) myocardial deformation indices can detect subclinical myocardial abnormalities in Kawasaki Disease (KD) convalescence. We hypothesized that subclinical myocardial abnormalities due to inflammation represent an early manifestation of the disease that persist in convalescence.

Background: Myocardial inflammation has been described as a global finding in the acute phase of Kawasaki Disease. Despite normal LV systolic function by routine functional measurements, reduced longitudinal strain (S) and strain rate (SR) have been detected by echocardiography in the acute phase, which may potentially predict late onset heart failure.

Method and results: Peak systolic LV myocardial longitudinal, radial and circumferential S and SR were examined in 29 KD convalescent patients (15 males; mean (SD) age 11 (6.6) years, range 3-27 years; median interval from KD onset 5.8 (5.4) years) and 10 healthy volunteers (5 males; mean age 14 (3.8) years, range 6-19 years) with the use of cardiac magnetic resonance feature tracking (CMR-FT). Routine indices of LV systolic function were normal in both groups.

Comparisons were made between normal controls and (i) the entire KD group, (ii) KD group subdivided by coronary artery involvement. Compared to controls, KD patients had lower longitudinal S. Average longitudinal and circumferential S at all levels was lower in KD patients compared normal controls. In subgroup analysis, both KD patients with and without any history of CAD had similar longitudinal and circumferential S at all levels and lower when compared against controls. There was a non-significant trend for lower circumferential and longitudinal strain in KD patients with persisting CAD when compared against those with regressed CAD.

Conclusion: In this CMR-FT study in KD convalescent patients with preserved conventional functional indices, we observed a trend for lower circumferential and longitudinal strain in KD patients compared to normal controls, irrespective of their coronary artery status.


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Long-term Aortic Root Dilation in Kawasaki Disease with Coronary Aneurysm


Introduction: Aortic root dilation is a known finding in the acute/subacute phase of Kawasaki disease (KD). These changes may be inflammatory and related to the degree of coronary artery (CA) dilation, and may lag when compared to CA changes. Long-term changes in the aorta have not been previously reported.

Methods: A retrospective review of patients with KD from our institution was conducted, identifying individuals with American Heart Association (AHA) Risk Level 3, 4 or 5 over a 20 year period (1994-2014). Aortic annular and root dimensions were measured at the most recent echocardiogram and converted to z-score measurements. When possible, ascending aorta
dimensions were measured, and all studies were evaluated for the presence of aortic regurgitation. Time from KD diagnosis to the last echocardiogram was determined. Patients with disease processes predisposing to aortic dilation were excluded, as were those with duration of echocardiographic follow-up <1 year.

Results:
Fifty-three patients were identified, with a median age at diagnosis of 29 months (SD 42, 1.2-162 months). Twenty-seven (51%) were AHA Risk Level 3, 20 (38%) Risk Level 4 and 6 (11%) Risk Level 5. The mean time from diagnosis to latest echocardiogram was 7.3 years (1.4-17.3 years). Aortic annular and root dimensions were obtained in all patients (mean aortic annular z-score -0.06, mean aortic root z-score 0.67). Four patients (8%) had a dilated (z-score >2) aortic root, one also had a dilated annulus. Ten patients (19%) had borderline root dilation (z-score >1.5). Ascending aorta dimension measurements were possible in 72% (38/53) of the cohort, of which only 1 (3%) had a z-score >2 and 3 (8%) had a z-score >1.5. Importantly, no patients demonstrated aortic regurgitation.

Conclusion:
In patients with history of KD and significant coronary artery involvement, borderline/mild dilation of the aortic root is not uncommon at intermediate to long-term follow-up, suggesting the possibility of a higher degree of aortic involvement in the acute and subacute phase of the disease process. The ascending aorta appears to be less affected and there was no evidence of functional derangements of the aortic valve. Accurate measurement of the aortic root dimension at all stages of KD is warranted.

M. Carr: None. C.R.P. Schuette: None. E. Pahl: None.

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Serial Evaluations of Coronary Artery Abnormalities in Kawasaki Disease Patients Should Include Assessment for the Development of Luminal Myofibroblastic Proliferation and Chronic Thromboses: a Preliminary Echocardiographic Study


Introduction: We recently reported that luminal myofibroblastic proliferation (LMP) is an active process of smooth muscle-cell derived myofibroblasts and their matrix products that can cause progressive coronary artery (CA) stenoses in KD patients. Serial echocardiography to assess for high risk CA changes, with periodic cardiac functional assessments in selected patients, is the current standard of care for monitoring patients with CA abnormalities. Monitoring for LMP/chronic thromboses is not routinely performed.

Hypothesis: We hypothesized that echocardiographic images from KD children with severe CA abnormalities could suggest the presence of LMP and/or chronic thromboses, indicating the potential for progression to CA stenoses.

Methods: We reviewed echocardiographic studies from a convenience sample of 28 KD patients with multiple aneurysms/giant aneurysms, to determine whether LMP and/or thrombosis could be identified on serial imaging.

Results: In 12 of the 28 patients, images were highly suggestive of LMP and/or thromboses. This could only be assessed in the proximal segments of the left main, circumflex, left anterior descending and right CAs. Detection was enhanced by optimizing the depth and sector width for the coronary artery segment of interest and use of magnification on the review station. Variations in echocardiographic techniques such as low frequency probes, harmonics, persistence, excessive compress or low gain settings made the assessment difficult. 4 patients in this cohort required CA bypass and 1 died from myocardial infarction due to progressive LMP. Distal vessel occlusion could not be visualized by echocardiography.

Conclusions: Images highly suggestive of LMP/chronic thromboses were evident in at least a third of patients with severe CA disease, including one patient who died of progressive LMP stenosis documented at autopsy. Echocardiography could not distinguish between LMP and chronic thrombosis as the cause of CA stenoses. Our study highlights the need for improved serial imaging for ongoing LMP/thromboses in AHA risk group IV. Patients with these complications may require more frequent cardiac functional assessments than are routinely recommended, to avoid adverse outcomes.
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Functional and Structural Intermediate Vascular Phenotypes Relating to Long-Term Cardiovascular Risk in Kawasaki Disease

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Background: It is uncertain whether Kawasaki disease (KD) increases overall long term cardiovascular risk, especially in those without demonstrable coronary artery lesions. Data from non-invasive vascular assessment, extrapolated from studies of subclinical atherosclerosis, are conflicting.

Methods: Patients at least 2 years post-KD and healthy controls had fasting plasma glucose, lipid profile, high sensitivity C-reactive protein, carotid-femoral pulse wave velocity (PWV), carotid intima-media thickness (cIMT), abdominal aorta intima-media thickness (aIMT), retinal vascular calibre, carotid and aortic elastography performed.

Results: 37 controls and 45 patients with KD (21 with regressed or persistent coronary artery changes) were studied at mean ± sd of 10.5 ± 5.7 years following KD. Compared to controls, KD patients did not have increased traditional cardiovascular risk factors; blood pressure, body mass index, waist-to-hip ratio, glucose, cholesterol, high density lipoprotein cholesterol, low density lipoprotein cholesterol, triglyceride and smoking history.

Of the cohort, 26 patients (age 15.38 ± 6.19 years) and 27 controls (age 18.7 ± 7.11 years) have had cIMT, aIMT and carotid elastography analysed. The maximum aIMT in KD patients was 0.65 ± 0.15 mm, compared to 0.63 ± 0.13 mm in controls, with the most marked difference in those with coronary artery changes at 0.68 ± 0.14 mm. After adjusting for age, sex, systolic blood pressure, aortic diastolic diameter and high sensitivity C-reactive protein, the average maximum aIMT in all KD patients was 0.071 mm larger (95% CI -0.005, 0.147) than controls. Aortic elastography and Doppler pulse wave analysis are underway. Otherwise, there are no detectible differences in PWV, cIMT, carotid elastography, or retinal vascular calibre between KD patients and controls.

Conclusion: Compared to carotid artery characteristics, changes in the abdominal aorta may be more discriminative markers of long-term cardiovascular risk in KD. Focus on large arteries in longitudinal KD vascular studies are warranted. Recruitment and analysis are ongoing and further results will be presented.


158
Central arterial elasticity in patients post Kawasaki Disease - a Cardiac Magnetic Resonance Imaging (CMR) study

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Background: Measures of central arterial elasticity such as aortic pulse wave velocity (APWV) have been shown to correlate with development of atherosclerosis. Endothelial dysfunction after Kawasaki disease has been shown to persist despite resolution of anatomically demonstrable coronary anomalies and this may be reflected in abnormal central arterial elasticity. Measurement of APWV by CMR is most robust but has seldom been reported in KD patients.

Aim: In a novel pilot study, we measured the APWV using CMR in patients with no coronary complications post KD. We compared this to age and gender matched published controls and APWV values measured on ultrasound.

Methods: 10 KD patients (with no coronary involvement) in our hospital database, at least 12 years post KD diagnosis, with no known personal cardiovascular risk factors or family history of premature cardiovascular disease, were recruited. Each subject underwent both MRI and
ultrasound investigations to determine the APWV. The results were compared using standard (z) scores calculated from published norms.

Results:
3 of the 10 KD subjects had significant z scores using CMR measurements of APWV ranging from +2.07 to +3.35. However, no significant difference was found on overall non parametric comparisons of measurements.
The US measurements of APWV all did not yield significant z scores. Z scores obtained from US and CMR measurements for the same subject showed no concordance.
Conclusion:
Central arterial stiffness tends to be higher in KD patients many years following the acute illness when assessed by CMR methods. CMR may be a more sensitive method than ultrasound for assessing central arterial stiffness post KD. The clinical implication of these findings require longitudinal follow up.


159 New Insight of Coronary Wall Structural Changes from an Optical Coherence Tomography (OCT) study Following Kawasaki Disease.

Nagib DAHDH, Audrey DIONNE, Div of Pediatric Cardiology, CHU Ste-Justine, Montreal, QC, Canada; Ragui IBRAHIM, Div of Cardiology, Pierre-Boucher Hosp, Longueuil, QC, Canada; Catherine GEBHARD, Div of Cardiology, Montreal Heart Inst, Montreal, QC, Canada; Anne FOURNIER, Div of Pediatric Cardiology, CHU Ste-Justine, Montreal, QC, Canada

Background Coronary artery aneurysms (CAA) are a serious complication of Kawasaki disease (KD). Coronary imaging usually describes aneurysms, stenosis and dilatation. Optical coherence tomography (OCT) is a technique useful for intracoronary imaging and coronary wall structure characterization.
Method KD patients scheduled for routine coronary angiography underwent OCT imaging between June 2013 and August 2014. Subjects’ clinical courses with echocardiography and angiography were reviewed to contrast with OCT findings.
Results OCT was performed on 18 patients 9.0 ± 5.1 years after KD at 12.4 ± 5.5 yo (range 3.5-21 yo). Of those, 14 (77.7%) had a history of CAA (7 giant CAA, 7 regressed CAA at time of OCT). Prophylactic intracoronary nitroglycerin was given (88.4 ± 45.5 μg/m2). Total X-ray exposure was 10.9 mGy/kg. One patient had a transitory uneventful vasospasm at the site of a former CAA, otherwise no major complications occurred (such as dissection, thrombosis, ischemia, arrhythmia). OCT findings were intimal hyperplasia in 15/18 (83.3%) on aneurysmal and regressed aneurysm segments. Intimal hyperplasia measured 390.8 ± 166.0 μm for the affected segments, compared to 61.7 ± 17.0 μm for the unaffected segments (p<0.001).
Destroyed media, fibrosis, calcifications, macrophage infiltration, neovascularization and white thrombus were also seen (Table 1). In two cases with previously implanted stent, the neo-intima was identified, measuring 80-160 μm.
Conclusion In our experience, OCT proved safe and insightful in the setting of KD. The observed coronary structural changes correspond to histological findings described in the literature late after KD.

<table>
<thead>
<tr>
<th>Table 1 : OCT Findings</th>
<th>nb/total (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intimal hyperplasia</td>
<td>15/18 (83.3%)</td>
</tr>
<tr>
<td>Destroyed media</td>
<td>13/18 (72.2%)</td>
</tr>
<tr>
<td>Fibrosis</td>
<td>13/18 (72.2%)</td>
</tr>
<tr>
<td>Calcifications</td>
<td>5/18 (27.8%)</td>
</tr>
<tr>
<td>Macrophage infiltration</td>
<td>8/18 (44.4%)</td>
</tr>
<tr>
<td>Neovascularization</td>
<td>6/18 (33.3%)</td>
</tr>
<tr>
<td>White thrombus</td>
<td>3/18 (16.7%)</td>
</tr>
</tbody>
</table>


160 Angiography Based Comparison of Echocardiography Z-value Equations for the Case Definition of Coronary Artery Dilatation Following Kawasaki Disease

Nagib Dahdah, Frederick Trinh Tan, Chantale Lapierre, Joaquim Miro, Anne Fournier, CHU Ste-Justine, Montreal, QC, Canada

Introduction: Echo-based coronary artery (CA) Z-value is the current standard for the case
Poster Abstract Presentations (continued)

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Investigating the Added Value Of Repeated ECHO Imaging In Patients With Kawasaki Disease and Always-Normal Coronary Arteries

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Background: Echocardiography (echo) is recommended in patients (pts) with KD at baseline, 2 wks, and 6 wks after fever onset to detect coronary artery (CA) abnormalities. However, echo imaging is expensive and in infants and toddlers often requires sedation, which is burdensome and carries some risk.

Objective: To assess the benefit of additional echo imaging in uncomplicated KD pts with normal CAs at baseline and 2 wks.

Methods: In this retrospective two-center study, eligibility criteria were: 1) admission and treatment at center for acute KD; 2) no significant congenital heart disease; 3) available echo measurements of both the right (R) CA and left anterior descending (LAD) at ≤ Day 10 (baseline), 2 (±1) wks and 6 (±3) wks; and 4) normal CAs = RCA and LAD z scores [zMax] ≤ 2.0 and no aneurysms.

Results: Of 2,600 pts treated for KD from 1976 - 2014, 457 had normal CAs at baseline and 2 wks and met other inclusion criteria. Of these, 57% were male; median age was 3.3 yrs [IQR 1.8 to 5.4 yrs]; 77% had complete KD; and 14% received IVIG retreatment. At 6 wks, 450 (98.5%) had normal CAs. Of the remaining 7 pts, zMax was 2.0-2.4 in 5 (1.1%); their z scores subsequently normalized at 1 yr. The zMax was 2.5-2.9 in 1 (0.2%) pt who remained on low dose aspirin until 6 mos, when ECHO normalized. The zMax was ≥3.0 in 1 pt (0.2%, 95% CI [0.0%, 1.2%]) with a dilated LAD, which was normal 3 wks later. Sensitivity analysis using zMax of <2.5 was similar (98.0% with nl CAs at 6 wks).

Conclusion: New CA abnormalities are rarely detected at 6 wks in KD pts with normal CAs at baseline and 2 wks. The 6 wk echo may be unnecessary for uncomplicated KD pts with normal CAs at baseline and 2 wks.

Figure - CA zMax shown as mean (+), median,
A Case of Fatal Kawasaki - Correlation Between Optical Coherence Tomography and Pathology

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Background Coronary artery aneurysms (CAA) develop in up to 30% of untreated patients with Kawasaki disease (KD). This may lead to ischemic heart disease and sudden cardiac death, which is extremely rare nowadays.

Method A 3 mo infant presented with severe KD 27 days after onset of fever. He died few days later of multi vessel obstruction and aneurysms. OCT was performed post mortem and correlated with pathology findings.

Results The patient presented with shock, inferolateral ischemia on ECG and high Troponin-i (from 6.45 to 59 µg/L 2 days later). Echocardiography showed severe myocardial dysfunction with diffuse coronary dilation and right CAA. Arterial Doppler demonstrated thrombosis of aneurysmal axillary, subclavian and iliac arteries, which corroborated with clinically ischemic limbs. Withdrawal of support was implemented due to multiorgan failure. OCT images from the proximal RCA, LAD, carotid and pulmonary arteries were obtained post mortem. The circumflex coronary could not be accessed by the OCT catheter, which was occluded on pathology exam. The carotid (figure TOP) and pulmonary arteries were normal on OCT and histology. RCA and LAD (figure BOTTOM) showed aneurysmal dilatation, with marked intimal hyperplasia and preserved media on OCT. Pathology confirmed these findings, with destruction of internal elastic lamina, luminal myofibroblastic proliferation, neovascularization, and attenuation of the media in some sections.

Conclusion This is the first report of pathologic correlation in a severe KD case with OCT imaging at the sub-acute stage, which adequately identified structural wall changes.
Cardiology, Pierre-Boucher Hosp, Longueuil, QC, Canada; Catherine GEBHARD, Div of Cardiology, Montreal Heart Inst, Montreal, QC, Canada; Nagib DAHDAH, Div of Pediatric Cardiology, CHU Ste-Justine, Montreal, QC, Canada

Background Coronary artery aneurysms (CAA) are a serious complication of Kawasaki disease (KD). Regression of CAA occurs in 50% of the cases on follow up. Actual imaging techniques often described these segments as normal, whereas studies have shown significant endothelial and smooth muscle dysfunction.

Method KD patients scheduled for angiographic follow-up between June 2013 and August 2014 underwent OCT imaging. We compared coronary intimal changes in coronary artery segments with no history of CAA to segments with regressed CAA, and segments with persistent CAA. The intima was measured in sections adjacent to the CAA for the segments with persistent CAA, at the former CAA and adjacent sections for those who regressed, and at various corresponding sections for segments with no history of CAA.

Results OCT was performed on 18 patients at 12.4 ± 5.5 years. Overall 14/18 (77.7%) had a history of CAA. Of those, 7/14 (50.0%) had regressed CAA at time of OCT. Data was analyzed according to echocardiographic and angiographic progress of CAA segments. Accordingly, all 18/18 persistent CAA segments and 11/11 regressed CAA segments had significant intimal hyperplasia, compared to 1/13 with no history of segmental CAA (P<0.001). The intensity of intimal hyperplasia is displayed in Table 1.

Conclusion Despite normal angiographic features, regressed CAA segments displayed significant intimal hyperplasia, similarly to those with persistent CAA. These features may present a risk of adverse coronary events.

Table 1

<table>
<thead>
<tr>
<th>Type</th>
<th>Persistent CAA segments</th>
<th>Regressed CAA segments</th>
<th>Segments no history of CAA</th>
<th>K1</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>RCA Intima (μm)</td>
<td>488.3 ± 186.7</td>
<td>256.2 ± 94.2</td>
<td>55.0 ± 17.3</td>
<td></td>
<td></td>
</tr>
<tr>
<td>LAD Intima (μm)</td>
<td>452.0 ± 164.1</td>
<td>202.5 ± 155.6</td>
<td>122.2 ± 121.2</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CX Intima (μm)</td>
<td>366.7 ± 258.9</td>
<td>373.1 ± 130.6</td>
<td>54.0 ± 8.9</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*, p<0.05 Persistent vs Regressed CAA segments; †, p<0.05 Regressed vs segm with no history of CAA.


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Thrombotic Risk Assessment in Kawasaki Disease Patients with Coronary Artery Aneurysms using Transluminal Attenuation Gradient Analysis

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Background: Coronary artery aneurysms (CAA) put patients (pts) at risk for thrombosis and myocardial infarction. Clinical guidelines recommend systemic anticoagulation for giant CAA, diameter ≥ 8mm. Pt-specific modeling and computer simulations in KD pts suggest that hemodynamic data can predict regions with increased risk of thrombus formation and may be superior to simple assessment of the geometry of the aneurysm. Specifically, regions with high Particle Residence Time gradients (PRTg) have correlated with regions of thrombus formation.

Methods: Transluminal Attenuation Gradient (TAG) is determined from the change in radiological attenuation on CT angiography (CTA) images in Hounsfield units per vessel length. TAG analysis has been used for characterizing coronary artery stenoses; however this approach has not been used for CAA. We analyzed the correlation between TAG and PRTg in KD pts with CAA and evaluated TAG for prediction of thrombotic risk.

Results: Pt-specific anatomic models for flow simulations were constructed from CTA image data from 6 KD pts with CAA and one normal control. TAG was calculated for all aneurysmal vessels and one control vessel. TAG values for the CAA were markedly lower than for the non-aneurysmal vessel (mean -23.76 vs. -2.21). In addition, TAG values were compared to PRTg and other hemodynamic data obtained for each pt.

Conclusion: TAG analysis is a new technique that can be applied to pt data obtained non-invasively through CTA. Thrombotic risk stratification for CAA and decisions about whether to start systemic anticoagulation may be improved by incorporating TAG and should...
be evaluated in future prospective studies.

164 Coronary Artery Dilatation in Kawasaki Disease is Associated with Anatomical Coronary Dominance: An Angiography-Based Study

Baher M Hanna, Chantale Lapierre, Frédérick Trinh Tan, Larent Desjardins, Anne Fournier, Nagib Dahdah, CHU Ste-Justine, Univ of Montreal, Montreal, QC, Canada

Introduction: Coronary artery (CA) dilatation in Kawasaki disease (KD) is best determined by elevated Z-scores. Z-score equations, do not take into account anatomical CA dominance. We hypothesize that, except for CA aneurysms, CA dominance influences dilatation status in KD (Z-score > 2.5). Material and Methods: We retrospectively analyzed CA status in KD patients followed at our institution for persistent CA dilatation. All patients who had a diagnostic catheterization between 2002 and 2012 were considered. Serial echocardiographic dimensions of LCA, RCA, and LAD upon diagnosis, 1 week, 2 weeks, 4 weeks, 2 months, 3-6 months, and 9-12 months later were normalized to BSA using published CA Z-score equations. Data were contrasted with CA angiography description of CA dominance: right or left dominance was adopted when the respective CA supplies both diaphragmatic LV free wall and posterior inter ventricular septum (IVS); Co-dominance was when posterior IVS was supplied by RCA and diaphragmatic LV free wall by LCA. Results: Of 69 potential patients, 16 were excluded (9 never presented a CA dilatation and 7 had CA aneurysms). The interval between acute onset and selective CA angiography of the remaining 53 patients was 69.5±52.8months at 9.2±5.2years old. Of the latter, 20(37.7%) had LCA-dominance, 31(58.5%) RCA-dominance, and 2(3.8%) Co-dominance. Upon KD onset, the LCA-dominant subset had 14/20(70%) ipsilateral dilatation vs. 6/20(30%) contralateral dilatation. Similarly, RCA-dominant dilatation was ipsilateral in 21/31(68%) vs. 10/31(32%) contralateral dilatation (p=0.89). On late follow-up, persistent CA dilatation was similar between LCA-dominance 6/14(43%) and RCA-dominance 10/21(47%) (p=0.94). The interval between onset and normalizing CA Z-score was 1.16±1.65 vs. 2.45±3.6years in ipsilateral vs. contralateral subsets (p=0.19). From the inflammatory perspective, serum albumin was significantly lower in patients with contralateral CA dilatation (p=0.02). Nevertheless, other inflammatory markers did not show a significant difference. Conclusion: Transitory CA dilatation following KD is closely related to anatomical dominance. This may be a reflection of vasodilation during immune carditis rather than coronary vasculitis.


165 Reappraisal of Coronary Abnormalities Using Systemic Focused Coronary Echocardiographic Imaging in Kawasaki Disease

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BACKGROUND: Coronary artery abnormalities (CAA) is an important complication in children with Kawasaki disease (KD). The incidence of CAA used to be around 5-10% after acute phase of KD. So far, there had been scanty information about the systemic approach to examine the status of coronary in children with KD. We thus developed a systemic focused coronary echocardiographic imaging (SFCEI) in Kawasaki disease.

METHODS: Between July 2013 and June 2014, a total of 35
patients with acute phase Kawasaki disease was enrolled in this study. Echocardiography of 100 normal pediatric patients was used for control. In this study, we employed the Siemens ACUSON SC2000 echocardiography system with 8V3 transducer (3-8MHz) for examination. All the patients was examined at diagnosis, 1 week, 2 weeks and repeating at 6-8 weeks after the onset of illness. Assessment of right coronary (proximal and distal portions), left main (middle portion), left anterior descending (proximal and distal portions) and circumflex arteries(proximal portion) was performed in each patients. Coronary abnormality is considered at the presence of any one of the following: 1) dilatation or aneurysm formation 2) lack of tapering 3) irregularity 4) intimal thickening(brightness) RESULTS: Various coronary artery abnormalities were present in Kawasaki disease, include dilatation in 11(31%) patients, aneurysm formation in 2(6%) patients, lack of tapering in 13(37%) patients, irregularity in 12(34%) , and intimal thickening(brightness) in 23(65%) patients. Overall, coronary artery anomalies was present in 32(91%) of our patients in acute phase of disease. CONCLUSION: Our result showed that the incidence of coronary artery abnormalities in Kawasaki disease is higher than previously reported. Echocardiography can provide an accurate and timely diagnosis regarding the presence of cardiac and coronary artery lesions in Kawasaki diseases. With our SFCEI method, more detailed and comprehensive features of coronary artery abnormalities other than coronary aneurysm and dilatation can be provided.

K. Hsieh: None. C. Lin: None. H. Wu: None. Y. Hong: None.

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CT Calcium Scoring Detects Coronary Artery Pathology In Patients With A Remote History Of Kawasaki Disease

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Background: As a result of the acute vasculitis associated with Kawasaki disease (KD), subsets of patients with a remote history of KD have coronary artery aneurysms and may develop coronary artery stenoses with associated risks of late morbidity. Hence, there is a need for effective non-invasive testing to detect coronary artery pathology and risk stratify patients with a remote history of KD. In a pilot study we previously showed that computed tomography (CT) coronary artery calcium (CAC) scoring with relatively low radiation doses detects late CAC in patients with aneurysms and a remote history of KD.

Methods: We performed CT calcium volume scoring in 166 subjects (median age 19.5 years) with a remote history of KD (median interval from onset of KD to CT 15.1 years). Coronary arteries were classified as normal (n = 100), transiently dilated (n = 23), persistently dilated (n = 10), resolved aneurysm (n = 9), or aneurysm (n = 24) based on the initial echocardiograms. We defined coronary artery pathology as the presence of a coronary artery aneurysm or stenosis.

Results: All subjects with coronary arteries classified as normal, persistently dilated, or resolved aneurysm had zero CAC. All but one of the subjects with transiently dilated coronary arteries had zero CAC (the one subject with a CAC score of 666 mm$^3$ had a history of severe left main coronary artery stenosis requiring bypass surgery). Of the 24 subjects with coronary aneurysms, all but 5 had CAC (median volume score 542 mm$^3$; range 17 mm$^3$ to 8,218 mm$^3$). Four of the 5 subjects with aneurysms and no CAC were imaged within 6 years of their episode of acute KD. For subjects imaged 9 or more years after their acute KD (n=144), the presence of CAC on CT had a sensitivity of 95% and a specificity of 100% for detecting coronary artery pathology.

Conclusions: For patients with a remote history of KD, CT calcium scoring is a sensitive and specific test for detecting coronary artery pathology. Patients with coronary artery aneurysms secondary to KD develop late CAC, which may be severe. The pathophysiology and clinical significance of this calcification are currently unknown.
ABSTRACTS

Poster Abstract Presentations (continued)


168 Evaluation Of Coronary Arterial Sequelae Due To Kawasaki Disease Using Optical Coherence Tomography

Nobuyuki Kakimoto, Hiroyuki Suzuki, Dept of Pediatrics, Wakayama Medical Univ, Wakayama, Japan; Takashi Kubo, Dept of Cardiovascular Med, Wakayama Medical Univ, Wakayama, Japan; Tomohiro Suenaga, Takashi Takeuchi, Dept of Pediatrics, Wakayama Medical Univ, Wakayama, Japan; Shoichi Shibuta, Dept of Pediatrics, Kinan Hosp, Tanabe, Japan; Yasushi Ino, Takashi Akasaka, Dept of Cardiovascular Med, Wakayama Medical Univ, Wakayama, Japan; Norishige Yoshikawa, Dept of Pediatrics, Wakayama Medical Univ, Wakayama, Japan

Objectives:
Optical coherence tomography (OCT) is an intracoronary arterial imaging modality employing near-infrared light to create images. OCT makes it possible to distinguish the three layers of the coronary arterial wall. However, few previous studies have used OCT to evaluate coronary arterial lesions (CAL) in Kawasaki disease (KD). Here we report the use of OCT to evaluate CALs in KD.

Patients and Methods:
Fifteen patients aged between 11 and 29 years were admitted to undergo coronary angiography (CAG) for follow-up of KD. The male : female ratio was 11:4. Their ages at disease onset and when OCT was performed were 1m - 10y11m (median; 1y2m), and 11y1m - 29y3m (median; 16y2m), respectively. The interval between disease onset and OCT examination was 5y1m - 24y4m (median; 13y2m). Repeated CAG was performed on the basis of the criteria stipulated in the guidelines for cardiovascular sequelae in KD (JCS 2008). At the time of the latest CAG, we performed not only regular CAG but also IVUS and OCT (C7 OCT imaging system, St Jude Medical, St. Paul, MN, USA) for coronary arteries between December 2012 and August 2014.

Results:
We demonstrated fresh thrombus, stenosis, fibrotic intimal thickening with lamellar calcification and partial disappearance of the tunica media in CAL. Fibrotic intimal thickening and disruption of the tunica media are demonstrated in all patients. In addition, OCT demonstrated intimal thickening and disruption of the tunica media in completely regressed lesions and even in regions where CAG had shown normal coronary arterial walls in the acute phase.

Conclusions:
Our data suggest that fibrotic intimal thickening and disruption of the tunica media may be basic changes of coronary arterial sequelae in KD. The use of OCT for evaluation of KD vasculitis may clarify the mechanisms responsible for coronary arterial sequelae and be useful for prognostication of CAL.


169 Impact of Resistance to Intravenous Immune Globulin on Changes of Left Ventricular Myocardial Deformation Over Time in Children with Kawasaki Disease

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Introduction: This study aimed to assess the impact of resistance to intravenous immune globulin (IVIG) on left ventricular (LV) myocardial deformation in children with Kawasaki disease (KD) during the acute and convalescent phases of illness. Few studies have elucidated the impact of resistance to IVIG on the progressive changes of myocardial mechanics over time in patients with KD.

Methods: We studied 26 patients with KD and 8 normal control subjects. Of the 26 patients, 16 were IVIG non-responders. Echocardiograms were obtained during the acute and convalescent phases of KD. Standard echocardiographic data and peak systolic global LV longitudinal strain [strain(ε)] were obtained using vector velocity imaging.

Results: During the acute phase of KD, peak systolic global LV longitudinal ε decreased significantly in both IVIG non-responders (-21.18 % ± 3.97) and responders (-20.94 % ± 3.15) compared to controls (-24.99 % ± 2.23). Although in the acute phase, LV ejection fraction (EF) was significantly higher in the IVIG non-responders (55.38 % ± 5.14) compared to the
Poster Abstract Presentations (continued)

responders (50.2% ± 6.53), peak systolic global LV longitudinal ε was not significantly higher in the IVIG non-responders compared to the responders. During the convalescent phase, peak systolic global LV longitudinal ε tended to increase in non-responders (-21.62% ± 3.98) and responders (-21.83% ± 2.61) compared to the acute phase, but remained significantly decreased in both groups compared to controls. The increment of peak systolic global LV longitudinal ε from acute to convalescent phase tended to be smaller in the IVIG non-responders compared to the responders. The proportion of patients with coronary dilatations in both IVIG non-responders (4 of 16) and IVIG responders (2 of 10) did not differ significantly.

Conclusions: The increment of peak systolic global LV longitudinal ε over time tended to be smaller in the IVIG non-responders compared to the IVIG responders. Resistance to IVIG may delay normalization of myocardial mechanics in IVIG non-responders. Further studies with larger number of patients, as well as long-term follow-up of myocardial deformation in KD are necessary.

S. Kang: None. D. Yon: None.

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Re-evaluation of Carotid Intima-Media Thickness by Z-score in Children and Adolescents After Kawasaki Disease

Nobutaka Noto, Masataka Kato, Yuriko Abe, Hiroshi Kamiyama, Kensuke Karasawa, Mamoru Ayusawa, Shori Takahashi, Nihon Univ, Tokyo, Japan

Objectives: The carotid intima-media thickness (CIMT) is a reliable screening method for vascular alterations even in a pediatric cohort; however, reference values of CIMT established recently by LMS methods for childhood and adolescence are limited when comparing patients after Kawasaki disease (KD) and controls. We tested the hypothesis that there are significant differences between the values of CIMT expressed as absolute values and z-scores in children and adolescents after KD and controls.

Methods: We reviewed 12 published articles regarding CIMT on patients after KD and controls. Absolute values (Ab) of the mean±1 SD of CIMT in patients after KD and controls were transformed to z-scores (Zs) using age-specific reference values established by Jourdan et al. (J: 247 Caucasian subjects aged 10-20 years) and our own data (O: 175 Asian subjects aged 6-20 years), and the results were compared between the two references. In this study, the mean age of the study population derived from each article was designated the representative age for transformation.

Results: In either reference (J) or (O), there was no significant sex difference in CIMT at any given age. The mean CIMT of (Ab) and (Zs) transformed by (J) or (O) were significantly different between patients after KD and controls, at 41.6% (Ab), 66.6% (Zs) by (J), and 83.3% (Zs) by (O) among 12 articles, respectively. Therefore, patients after KD had significantly higher (Zs) by (O) than those of controls (0.66±0.71 vs. 0.03±0.68, p=0.006, respectively). Compared with reference values, the controls of (O) were within the normal range. However, there were no significant differences in (Zs) by (J) between the two groups (1.72±0.77 vs. 1.23±0.83, p=0.116, respectively). When we assessed 9 articles dealing with Asian subjects, the difference of (Zs) between the two groups remained significant only by (O) (p=0.015). In contrast, when we assessed 3 articles dealing with mainly Caucasian subjects, there was no significant difference in (Zs) between the two groups with both (J) and (O).

Conclusions: These results indicate that age and race-specific reference values for CIMT are mandatory for performing an accurate assessment of the vascular status in healthy children and adolescents and particularly in those after KD.


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A Mitral Regurgitation May be an Early Diagnostic Clue to Kawasaki Disease in Young Infants with Atypical Presentations

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Background: Very young infants with Kawasaki disease (KD) often present with atypical features that render diagnosis difficult and the incidence of coronary complications high. Picking up clues at early phase of KD can be critical. Herein we present 3 cases of KD in very young infants who showed mitral regurgitation (MR) around the 7th day from the onset of fever. They received IVIG around 7th fever day. However, the advice for short-term follow up echocardiography (ECHO) was neglected as clinical course thereafter were so unusual. Giant coronary aneurysms developed in all the patients later.

Case 1: A 31-day-old infant got admission care for sepsis. ECHO at the 7th day from the onset of fever showed trivial MR and the patient received IVIG. Follow up ECHO was recommended, but was not conducted as clinical course was ambiguous for KD thereafter. Being treated with steroids due to skin rash and eosinophilia that masked patient’s fever, the infant reappeared to hospital with cardiogenic shock 10 days later. ECHO revealed giant aneurysms in the right coronary artery (RCA) and CT angiography for pulsating axillary masses revealed axillary aneurysms.

Case 2: A 67-day-old infant was admitted with fever and persistent thrombocytopenia. ECHO done at the 5th day from the onset of fever due to red lips showed non-specific findings. Follow up ECHO at the 7th fever day showed newly developed MR. IVIG and steroids was added on for persistent fever, but severe leukocytosis ensued and clinical course was also ambiguous for KD. Defervescence was achieved with infliximab. The infant showed coronary aneurysms.

Case 3: A 80-day-old infant was admitted with fever and seizure, and treated for sepsis. On the 6th day from the onset of fever, MR was shown on ECHO and the patient received IVIG and steroids. However, fever and severe anemia, left shift of leukocytes, and severe thrombocytopenia persisted for two weeks. Giant coronary aneurysms, as large as the ascending aorta, developed in the RCA. Pulsatile masses identified in the axilla were found to be large aneurysms on CT angiography.

Conclusion: A newly developed MR, even trivial, around the 7th day from the onset of fever may be a clue to the diagnosis of KD and short term follow up ECHO is recommended for ongoing febrile infants younger than 3 months.


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Tissue Doppler Imaging as a Predictor of Immunoglobulin Resistance in Kawasaki Disease

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Background: Kawasaki disease (KD) causes myocarditis and left ventricular dysfunction during the acute phase of the illness. Despite treatment with intravenous immunoglobulin (IVIG), a significant number of patients are IVIG resistant (fail to defervesce or experience recrudescent fever). We evaluated KD patients in the acute phase using Tissue Doppler Imaging (TDI) to assess if myocardial dysfunction may predict IVIG resistance.

Methods: All patients with acute KD presenting to Children's Hospital Colorado from February, 2007 to March, 2014 were included in this study. All patients underwent echocardiograms with TDI (pulsed wave sample Doppler were placed at the tricuspid, septal, and mitral annuli) upon diagnosis with KD. Patients were divided into two groups: IVIG Responder group and IVIG Resistant group. Group differences were assessed using Wilcoxon-Mann-Whitney and Chi-square testing. Receiver Operating Characteristic (ROC) Curve analysis was utilized to determine threshold values of TDI measurements associated with IVIG resistance. Results: Fifty-one age matched (+/- 6 months) IVIG Responder patients were compared to 51 IVIG Resistant group [33.49 (17.30 - 62.89) months vs 44.57 (20.13 - 77.07) months, p <0.44]. There were 34 males in Responder group versus 33 males in Resistant group (p< 0.83). There were significant differences in the tricuspid, septal, and mitral early diastolic velocities (E') (p< 0.05, p< 0.001 and p<0.01) respectively. ROC analysis demonstrated that tricuspid E' < 0.15 cm/s, septal E' < 0.12 cm/s, and mitral E' < 0.16 cm/s were good predictors.
of IVIG unresponsiveness (AUC = 0.66, 0.66, and 0.70 respectively). There were no differences between the systolic velocities (S’) or late diastolic velocities (A’).

Conclusions: IVIG resistant KD patients present with significantly greater diastolic dysfunction compared to responders in patients with KD. TDI may be a useful tool to differentiate KD patients who may be IVIG resistant.


173 Coronary artery aneurysm measurement and z-score variability in Kawasaki Disease

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Background: Coronary artery (CA) z-scores are commonly used for clinical decisions in Kawasaki disease (KD). We evaluated reliability in CA measurement, reproducibility of z-score calculation, and frequency with which different z-score formulas lead to divergent management strategies.

Methods: We randomly selected 21 KD patients (pts) with ≥1 CA z-score 1.5-3 and all KD pts with ≥ 1 CA z-score 7-14 (n=20). Two echocardiographers measured LMCA, LAD and RCA. Inter- and intraobserver reliability were calculated. T-tests were used to compare CA z-score using 3 commonly used formulas (Boston, DC and Montreal).

Results: Median age at KD echo was 1.2 y (0.2-11.5 y). Interobserver reliability was high for LAD (intraclass correlation [ICC] 0.970) and RCA (ICC 0.943) and lower for LMCA (ICC 0.725). Intraobserver reliability was also high for LAD and RCA (ICC 0.991 and 0.999) and lower for LMCA (ICC 0.946). Z-scores for the 3 formulas were similar at smaller CA size, i.e., z < 3, but varied markedly at larger CA dimensions (Figure). Z-scores for the same CA dimension calculated by each of the 3 formulas resulted in disparate classification of normal vs. mild dilation in 7/21 (22%) pts, and different guidance for anticoagulation based on CA z ≥10 in 10/20 (50%) pts.

Conclusion: Although CA measurements have high inter- and intraobserver agreement, CA z-scores vary dramatically based on the z-score formula, particularly at larger CA dimensions. Discrepancies in CA z-score between calculators impacts not only the distinction between normal and mild dilatation, but most importantly, the recommendation of anticoagulation for pts with larger CA dimensions.


174 Relationship between Kawasaki Disease Related-Angiopathy and Pressure Wave Reflection in the Arterial System

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Background: Recently we reported that the carotid arteries of Kawasaki disease (KD) appear to develop mild sclerotic changes shortly after onset using the speckle tracking echocardiography. However, it remains to be elucidated what factors hemodynamically may induce these sclerotic changes.

Objectives: The aim of this study was to investigate the relationship between KD related-angiopathy and arterial pressure wave reflection using the two-dimensional speckle tracking echocardiography and radial augmentation index (AIX).

Subjects & Methods: We studied a cohort of children with history of KD. The subjects were 87 KD patients (age, 9.7±2.9 years) and 93 healthy controls (11.3±3.2 years). As for our methodology, the two regions of interest (ROI)
ABSTRACTS

Poster Abstract Presentations (continued)

for speckle tracking were manually positioned at near and far carotid arterial walls using a Philips iE33. Continuously, we examined the following strain values: (A) peak strain in expansion phase, (B) peak strain before aortic valve closure, and (C) strain value at aortic valve closure (Figure 1). Also, we examined two ratios, B/A and C/A, for emphasizing recoil function. Concurrently, the radial Alx were obtained.

Results: KD patients had significantly the lower A values, the higher B/A, and the higher radial Alx, compared with controls. Furthermore, there was good correlation between B/A and radial Alx in KD.

Conclusions: It is well known that a higher Alx results from earlier arrival of reflected pressure waves and an early return of reflected waves is closely correlated with peripheral stiffness. Therefore, these results indicate that peripheral angiopathy may induce sclerotic changes of carotid arteries in KD patients.

Figure 1:
Simultaneous Recordings of Carotid Artery Pressure and Strain (A)

Y. Shimizu: None. T. Nakamura: None. G. Ko: None. C. Akita: None. Y. Saikawa: None.

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Dual source 128-slice computed tomography coronary angiography: A low radiation paradigm in evaluation of Kawasaki disease at Chandigarh, North India

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Objective: To evaluate the feasibility of low dose computed tomography coronary angiography (CTCA) on a dual source scanner in children on follow up for Kawasaki disease (KD).

Methods: A prospective study comprising 20 consecutive children with KD was conducted from November 2013 to August 2014 on 128-dual source second generation Siemens Definition Flash with either prospective or retrospective electrocardiographic (ECG) gating. A radiologist blinded to the clinical profile and echocardiography (ECHO)/ stress thallium data evaluated each scan. Peak Kilovolts (KVp), milliampere (mA) and radiation dose (dose length product-mGycm and effective dose milliSieverts-mSv) were recorded. Another radiologist correlated CTCA data with clinical/other imaging data.

Results: Demographic/clinical data and scan parameters are given in Table. Mean effective dose was 1.25 mSv (range 0.22 to 2.74), with prospective ECG gating in 8 patients, it was even lower (0.22 to 0.91 mSv). Six of the 20 patients showed abnormalities including ectasia (n=3), aneurysm (n=2) and stenosis (n=3). More than one abnormality was seen in 2 patients. Four children with normal ECHO had abnormalities detected on CTCA. Stress thallium scintiscan had been performed in 16 patients with mild/moderate reversible perfusion defects detected in 14. Six of 14 patients with moderate perfusion abnormalities had an abnormal CTCA.

Conclusion: In our experience, dual source CTCA is a feasible low radiation dose modality in evaluation in patients with KD.

Future impact: Dual source CTCA has potential to be standard of care for evaluation of coronary artery abnormalities in KD.

Y. Shimizu: None. T. Nakamura: None. G. Ko: None. C. Akita: None. Y. Saikawa: None.

176 Persistent Peripheral Arteritis Long After Kawasaki Disease - Another Documentation Of Ongoing Vascular Inflammation -

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A 22-year-old male patient, who was suffered from Kawasaki disease (KD) at 1 year and 1 month of age and left with bilateral axillary arterial aneurysms (AAA) and regressed coronary aneurysm, visited us because of left hand edema and itchiness. He has been taking aspirin for thromboprophylaxis of AAA and well without any vascular event for these 20 years and does not have any sign of inflammatory disease. Digital subtraction angiography of bilateral arms revealed complete occlusion of left AAA with multiple collateral arteries supplying blood flow to the distal arm and persistent giant right AAA with 12 mm in diameter with only mild stenosis proximal to this AAA. To determine if the active inflammatory process is going on the axillary artery wall, the patient underwent positron emission tomography (PET) using fluorodeoxyglucose (FDG) with co-registration of multi-detector x-ray computed tomography, PET indeed showed significant FDG uptake inside and part of the outer wall of the left AAA and only minimum FDG uptake at the right AAA. For left arm ischemia, he underwent resection of the left AAA and successful axilla-brachial artery bypass surgery using a reversed autologous saphenous vein graft that relieved his symptoms. Histological examination of the resected wall of AAA showed significant intimal thickening and the immunohistochemistry study labeling CD68, as the marker of macrophages, showed relatively dense staining of the intimal thickening of left AAA wall compatible with FDG uptake. This is the first documentation of persistent inflammation of peripheral arterial wall long after KD using FDG-PET that must have resulted in peripheral arterial remodeling.


177 Follow-up Study of Thrombus in Coronary Aneurysms due to Kawasaki Disease.

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The features of MR coronary angiography (MRCA) are able to detect arterial walls and thrombus in aneurysms clearly by using the sequences of black blood methods. Up to now 262 patients have been followed up by MRCA(the average 3.5 times ±2.3 times), The duration of the follow up is 4.7years±3.3years, During the periods, the coronary arterial lesions have changed as follows; decreased size of aneurysms in 116 patients out of the 262 (44.3%), enlargement of aneurysm in 2 (0.8%), newly appeared or progressed degree of localized stenosis in 26 (9.9%), appearance of occlusion in 5 (1.9%), recanalized vessels in 20 (7.6%). These changes are related to thrombus formation, thrombolysis and thickening of arterial walls. The thrombus often change their locations in the aneurysm, sizes, even disappear and some of them develop to recanalized vessels. Thin membranes in aneurismal lumen and tiny polyps on the intima were often detected (Fig).These constructions and thrombus in aneurysms are observed to be still changeable even more than 2 decades after the onset of Kawasaki disease. Therefore, MRCA is the most convenient for following up CAL frequently and noninvasively.
Measurements of coronary aneurysms due to Kawasaki Disease by Dual-Source Computed Tomography (DSCT)

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[Background]Diameters of coronary artery aneurysms (CAAs) due to KD in the acute phase can strongly predict long-term prognosis of coronary artery lesions. Recently, Computed Tomography Angiography (CTA) has been used in the diagnosis of coronary artery lesion (CAL).

[Purpose]The purpose of this study was to determine whether measurements of coronary artery diameters by CTA using DSCT can be used instead of coronary angiograms (CAG) during cardiac catheterization.

[Methods]Twenty-five pts (22 males and 3 females) with CAL due to KD were evaluated. Their ages ranged from 5 months to 38 years (median 11 years). CTA was performed between July 2007 and July 2013, and CAG was done within one year. A prospective Electrocardiogram (ECG) -triggered CTA was performed on a DSCT (SOMATOM® Definition (from July 2007 to October 2009) or SOMATOM® Definition Flash (from October 2009 to July 2013); Siemens Healthcare, Germany). ECG-gated scans were performed in 19 cases and Flash Spiral scans in 6 cases. Two pediatric cardiologists measured the diameters of CAAs twice in each maximum intensity projection (MIP), curved multi planer reconstruction (MPR) and CAG. We measured 161 segments in total (segment1-3, 5-7, 11, 13). Diagnostic accuracy was expressed as $\kappa$ coefficient. A Bland-Altman analysis was also used to assess the inter-observer, intra-observer and inter-material agreement.

[Results]The visualization capability of coronary arteries was excellent. One segment was not visualized by CTA. Detection rate in CTA, comparing with CAG, was 99.7%, and the diagnostic quality of CTA was excellent ($\kappa=0.93$). Excellent inter-observer agreement for diameters of CAAs was obtained for MIP, MPR and CAG and for the intra-observer agreement. The inter-modality agreement was also excellent (MPR-CAG : $y=0.9x+0.40$, $r=0.97$, $p<0.01$ MIP-CAG : $y=1.0x+0.1$, $r=0.94$, $p<0.01$). We also studied the diameters in normal segments. We also obtained good correlation between inter-observer, intra-observer and inter-modality (MPR-CAG : $y=1.0x$, $r=0.89$, $p<0.01$ MIP-CAG : $y=1.0x+0.1$, $r=0.88$, $p<0.01$).

[Conclusion]We found a significant good correlation in the measurements of coronary artery between CTA and CAG. Measurement of the diameters of coronary artery by CTA is reliable and useful.

Evaluation Of Coronary Artery Lesion In 9 Infantile Kawasaki Disease Patients Using 320row Area Detector Ct

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Introduction: Recent advances of CT technology have made it possible to obtain clear coronary artery lesion (CAL) image. However, high dose radiation exposure is inevitable. Also it becomes difficult to obtain adequate images when patient’s heart rate is high. Recently 320row area detector CT (ADCT) has been introduced. Using this device, clear coronary artery images are obtainable with low dose radiation exposure.
Also it provides adequate image for high heart rate patients. However, there is few report which describe its utility for infantile patients.

Aim: To evaluate the feasibility of 320row area detector CT for evaluation of CAL for infantile KD patients.

Subjects and methods: Nine infants who have CAL due to KD have been evaluated. Mean age at examination was 30.5+/−22.0 (mean+/−SD) months, weight was 13.6+/−6.5 kg and mean time elapse from diagnosis of KD was 18.7+/−16.0 months. Patients were evaluated using ADCT and findings obtained were compared with either coronary angiography (CAG) or echocardiography. Radiation exposure dose were also explored.

Results: All patients have accomplished examination and adequate images were obtained. Mean heart rate at examination was 105+/−27 bpm. Examinations were conducted to two patients with breath holding and others with spontaneous breathing. Compared with CAG and echocardiography, similar results were obtained. Mean effective radiation dose was 6.14+/−2.22 mSv.

Conclusion: Infantile KD patient’s CALs were able to be evaluated by ADCT with relatively low dose radiation exposure, without breath holding. ADCT have contributed to reduce the need for repeated invasive CAG.


180 Coronary Artery Aneurysms Identified At School Cardiac Screening

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Because most significant complication of Kawasaki disease (KD) is coronary aneurysms, echocardiography is an indispensable part of clinical practice and quality control of echocardiography is mandatory. On the other hand, Japanese government has enforced a law of regular school cardiac screening (SCS) at 1st, 7th, and 10th grader in 1995 and all patients with a history of KD were screened for coronary artery lesion. In this study we report 2 patients with coronary aneurysms picked up by SCS.

Case1: A 6-year-old boy was diagnosed with KD at 3 year old and received immunoglobulin (2g/kg/day). His condition improved within 8 days of illness and echocardiographic finding of coronary artery was “normal” in acute phase and at 1and 3 months after the onset of KD. Since then he did not visit clinic for follow-up. At 1st grader SCS, he was diagnosed as having giant coronary artery aneurysms by echocardiography. Indeed coronary angiography revealed sequential coronary aneurysms of 10.8 mm and 12.3 mm in diameter at segment 6 and 5 with a 99% stenosis in between them. Because of signs of coronary ischemia on myocardial perfusion scan, he underwent percutaneous coronary interventions and coronary artery bypass graft surgery later.

Case2: A 9-year-old boy was diagnosed with juvenile idiopathic arthritis and his fever continued 10 days. He underwent echocardiography at 9 days of illness but coronary artery lesions were not found. At 7th grader SCS, he was diagnosed as having coronary artery aneurysms by echocardiography. Coronary angiography revealed coronary artery aneurysms of 6.1mm and 6.1 mm in diameter at segment 1 and segment 6. Since then he has been placed on oral aspirin.

These 2 cases highlight the issue concerning timing and quality of echocardiography and importance of SCS in detecting patients with coronary undiagnosed aneurysms.


181 Kawasaki Disease in Children Six Months and Below - Clinical Experience from Chandigarh, North India

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Kawasaki disease (KD) is a medium vessel vasculitis of childhood. Clinical presentation in infancy is often characterized by paucity of symptoms. We report our experience of managing 15 children with KD aged 6 months and below at the Advanced Pediatrics Centre, Post Graduate Institute of Medical Education
ABSTRACTS

Poster Abstract Presentations (continued)

and Research, Chandigarh, India. To the best of
our knowledge there are no data on this aspect
of KD from any developing country.

OBJECTIVE
To describe the clinical and laboratory profile of
children with KD aged 6 months and below in
our cohort

METHODS
Records of Pediatric Rheumatology Clinic from
1994 - 2014 were analyzed. Fifteen of the 415
children with KD, diagnosed on the basis of
American Heart Association criteria, were aged
6 months and below. Fourteen children were
given intravenous immunoglobulin and 3 also
received infliximab.

RESULTS
Incomplete KD was present in 13 children
(87%). Mucosal changes were present in 11
(73%); extremity changes in 10 (66%); rash in 9
(60%); conjunctival injection in 8 (53%) and
lymphadenopathy in 3 (20%) children. Irritability
at presentation was noted in 13 (87%); 4 (26%)
had respiratory symptoms and 2 (13%) children
had BCG scar reactivation. Eleven patients were
diagnosed beyond day 10 of illness. Of 12
patients, in whom C-reactive protein was
estimated, 11 had raised levels.

Thrombocytopenia was seen in 3 patients - one
of these developed scrotal gangrene. Coronary
artery abnormalities were present in 5 (33%) patients. Two children died from disease related complications - one of these had giant coronary artery aneurysm.

CONCLUSIONS
Incomplete forms of KD are commonly seen in
children below 6 months of age. This may result
in delayed diagnosis.

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<td>Fever &gt; 5 days</td>
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<td>Delay in diagnosis (&gt; 10 days)</td>
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<th>LABORATORY PARAMETERS</th>
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Proposal of Strategy for Threatened Rupture of Super-giant Coronary Aneurysm; Rare and Fatal Complication with Kawasaki disease

Mamoru Ayusawa, Hiroshi Kamiyama, Ami Chou, Masataka Kato, Hirofumi Watanabe, Akiko Komori, Yuriko Abe, Yuki I Kawamura, Shori Takahashi, Nihon Univ, Tokyo, Japan

Background: Prognosis of Kawasaki disease and its main complications, coronary artery aneurysm (CAA) and myocardial ischemia were remarkably improved by intravenous immunoglobulin (IVIG) and other additional anti-inflammatory and anti-coagulation therapy. In contrast, rupture of coronary artery aneurysm is a rare, and still definitely fatal complication. Though approximately 10 cases were reported with sporadic occurrence in every three to four years in Japan, there is no patient whose life was saved. Case report: We experienced a 5-year-old boy who had already developed left CAA of 9 mm in diameter on the 7th day from onset of fever. Despite of repeated IVIG, left CAA was rapidly expanding day by day and
finally the diameter became 18mm on the 12th day. Early in the next morning, sudden cardiac arrest was noted, but resuscitation was not effective. Autopsy revealed cardiac tamponade caused by rupture of very fragile wall of huge left CAA. Discussions: After this experience, we have tried to carry patients into the intensive care unit with deep sedation, if patient’s CAA is expanding more than 10mm within 2 weeks in acute stage of Kawasaki disease. Furthermore, we also recommend use of antihypertensive drugs such as calcium channel blocker and/or beta-blockers. We also have advised to colleagues in other hospitals to try in the same way when they asked for the management of similar cases. At least three patients with huge aneurysm were survived with this method in recent reports. If patient has strong inflammation sustaining with expanding huge aneurysm, plasma exchange and all possible anti-inflammatory agents including steroid or infliximab under the percutaneous cardiopulmonary support and surgeons’ stand-by until inflammation will disappear. Following repair or plasty of coronary aneurysm and coronary artery bypass surgery may be considered, but possibility and results are unknown. Conclusions: Because of its rarity, it is difficult to detect exact indication of deep sedation or intensive care, however, earlier and more cautious management will be safer for ‘super-giant’ aneurysm. Concerning to the sustaining inflammation with huge aneurysm, we would like to hear advices for this strategy from cardiac surgeons and pediatric intensivists.


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Mortality in children with Kawasaki disease: 20 years of experience from a tertiary care centre in North India.

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Background
Kawasaki disease (KD) is a common vasculitic disorder of childhood. Reported mortality in KD in the West is 0.08 %. We report clinical profile of 4 children who succumbed to KD during 1994-2014 at Advanced Pediatrics Centre, Post Graduate Institute of Medical Education and Research Centre, Chandigarh, India. To the best of our knowledge, this is the first report on mortality in KD from any developing nation.

Objectives
To study the clinical and laboratory profile of 4 children with KD who died at our centre.

Methods
During the period 1994-2014, a total of 415 children were diagnosed to have KD based on American Heart Association criteria. M:F ratio was 1.9:1 and 96 children were aged 2 years or less. Children with KD received 2 g/kg of intravenous immunoglobulin (IVIg) and 50-80 mg/kg/day of aspirin initially and 3-5 mg/kg/day later. 2-D echocardiography was done once during the acute phase and then 6-8 weeks later on follow up. 4 amongst these died and their details were analysed by study of clinical records.

Results
We report 4 deaths (2 boys, 2 girls) in this cohort of 415 children with KD. All 4 were below 2 years of age and had had significant delays in diagnosis and referral (Table). Symptomatic myocarditis was noted in 2 children, while 2 of them had thrombocytopenia.

Conclusion
We report a mortality of about 1% in children with KD. Delays in diagnosis and referral contributed significantly to this mortality.

An Atypical Presentation of Incomplete Kawasaki Disease

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Background:
Kawasaki disease (KD) is a systemic panvasculitis that can cause coronary artery aneurysms (CAA) in up to 25% if left untreated. Rarely, aneurysms of other medium-sized arteries have also been reported to occur. The incidence of systemic artery aneurysms (SAA) with typical KD can be as high as 2.2%. Incomplete KD with SAA is not well described. We report a case of diffuse SAA in a 12-year-old boy with incomplete KD and giant CAA.

Case Presentation:
The patient presented with fever, malaise, abdominal pain, rash and cervical lymphadenopathy. Suspicion for the presence of a pericardial effusion on an abdominal CT scan prompted echocardiographic assessment. By echo, multiple giant CAA in all three coronary arteries was noted. Incidentally, on an aortogram after performing pericardiocentesis, it was noted that he had diffuse ectasia and aneurysms of every arterial branch off the aorta. Selective angiograms confirmed the presence of aneurysms in all medium-sized arteries throughout the body including pulmonary arteries. The patient was treated with IVIG, methylprednisolone and high dose aspirin. Incomplete KD was suspected. However, because of the systemic vasculitis, cyclophosphamide therapy was administered. Patient responded well to therapy with improvement in clinical symptoms. Anticoagulation with heparin was transitioned over to maintenance warfarin therapy. Patient remains asymptomatic 2 years later with large, but stable CAA.

Conclusions:
Incomplete KD can manifest with giant CAA and SAA. Immunosuppressant therapy may be necessary for systemic involvement. Anticoagulation is needed to prevent thromboembolic manifestations.

Is Lymph-Node-First Kawasaki Disease a High-risk Group for Coronary Aneurysm?

JENG-SHENG CHANG Sr., Yu-Chih Huang, Children's Hosp of China Medical Univ, Taichung, Taiwan

Cervical lymphadenopathy (CLA) is the least common main feature in patients with Kawasaki disease (KD), comprising only 42%-65% of all diagnoses. Nonetheless, several studies have shown that KD patients who first present with remarkable CLA and fever (NF-KD) are older in age and exhibit stronger inflammation than that of typical KD (tKD) patients. Therefore, whether NF-KD patients are also a high-risk group for intravenous immunoglobulin resistance (rIVIG) and coronary arterial aneurysm (CAA), and whether tKD with CLA (tKD-CLA) is associated with higher inflammatory indices than tKD without CLA warrants investigation. Previous retrospective (R) and prospective (P) studies have shown varied results (Table). In this study, we reviewed 10 years of medical records from a tertiary referral hospital and identified 42 NF-KD patients. These NF-KD patients were then...
ABSTRACTS
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compared with 113 tKD-CLA and 105 tKD patients from the same database over the same period. Significant trends of increasing values were noted in age, neutrophils, CRP, ESR, GOT, and doses of IVIG among these 3 groups of patients ($p$ = 0.03 to < 0.0001). NF-KD patients presented with larger cervical LN (3.7 ± 7.0 cm) complicated by higher CAA (12/42 vs. 25/218, $p$ = 0.008) and by moderate to extremely high CAA (6/42 vs. 4/218, $p$ = 0.002), and suffered more CHF or shock at the acute stage (6/42 vs. 6/218, $p$ < 0.001) than all of the tKD patients. The size of LN did not correlate with CAA occurrence, but the presence of bilateral CLA showed a higher risk for CAA than unilateral CLA did (6/10 vs. 6/32, $p$ = 0.02).

Author(Hospital No.) Method NF-KD tKD-CLA tKD LN(cm) CAA rIVIG
Nomura Y (1) R 16 106 65 > 1.5 + +
Kanegaye JT (1) P 53 . 287 3.0 ± 1.0 - -
Kubota M (1) R 29 62 107 > 1.5 - -
Sung RYT (14) R 170 526 > 1.5 - -
Chang JS (1) R 42 113 105 3.7 ± 7.0 + +

This study showed that NF-KD patients, particularly those with larger lymph nodes, are a high risk group for CAA complications. The tKD-CLA patients also exhibited a tendency for higher inflammation. Previous pathological studies of swollen CLA have reported tissue edema in the sinus and paracortical areas of LN, as well as vessel thrombi in severe cases. Further study of swollen CLA is warranted to determine the pathological correlation between CLA severity and CAA complications in KD patients.

J. Chang: None. Y. Huang: None.

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Endothelial Cell Function in Young Adults with History of Kawasaki Disease

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Background: The endothelium is a single layer of epithelial cells that lines the blood vessels and is a major component in maintaining vascular homeostasis. Impaired endothelial cell (EC) function can contribute to cardiovascular disease states, but whether there is an association between endothelial dysfunction and the presence of coronary artery aneurysms after Kawasaki disease (KD) is unknown.

Methods: We enrolled 110 teens and young adults, ages 16 to 30 years, with a history of KD (61% male), as well as 30 healthy controls (HC, 53% male). EC function (reactive hyperemic response after a 5 minutes brachial artery occlusion) was measured using the EndoPAT 2000. Reactive hyperemia index (RHI) and PAT ratios were determined. KD subjects were categorized based on their worst coronary artery status (normal, transiently dilated/resolved aneurysm, aneurysm).

Results: The mean age of KD subjects and HC at the time of EndoPAT was 25 ± 9 and 26 ± 7 years, respectively ($p$=0.42). Mean time since onset of KD was 23 ± 19 years. Subjects with a history of transiently dilated/resolved aneurysms had a higher mean lnRHI compared to other KD subjects (0.91 vs 0.74, $p$=0.01) and HC (0.72, $p$=0.02). When PAT ratio was evaluated as a function of time after occlusion release, those with transiently dilated/resolved aneurysms had a trend toward a more favorable profile while other groups appeared similar (Figure).

Conclusion: Most young adults with a history of KD have normal EC function. Individuals with a history of transiently dilated coronary arteries had a paradoxical trend toward better EC function, which may indicate healthier vasculature. The significance of this finding merits further study.

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Carotid Artery Strain in Young Adults with a History of Kawasaki Disease

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**Background:** Measuring carotid strain is a noninvasive way to assess the mechanical properties of the arterial wall. Whether there is an association between carotid strain and coronary artery status after Kawasaki disease (KD) is unknown.

**Methods:** We enrolled 82 young adults, ages 15 to 30 yrs, with a history of KD (58% male), as well as 16 healthy controls (HC) of similar age (56% male). Carotid wall strain was measured from cine loops of common carotid artery B-mode ultrasound data using an offline optical flow analysis algorithm. Strain was normalized for age (Z-score) using a regression equation derived from a separate series of healthy young adults. Subjects were categorized based on their worst coronary artery status (normal, transiently dilated, aneurysm).

**Results:** The mean age of KD subjects and HC at the time of carotid measurements was $25 \pm 8$ and $28 \pm 8$ years, respectively ($p=0.30$). Mean time since onset of KD was $20 \pm 8$ yrs. KD subjects with transiently dilated coronary arteries had significantly higher carotid strain compared to those with normal coronaries ($p=0.002$) and to HC ($p=0.01$) (**Figure**); those with CAA had a nonsignificant trend toward lower carotid strain compared to other groups. KD subjects with normal coronaries had carotid strain similar to HC.

**Conclusion:** Young adults with a history of KD with normal coronary arteries also have normal carotid artery strain. Individuals with a history of transiently dilated coronary arteries had a paradoxical trend toward higher carotid strain. Thus, KD patients whose dilated coronary arteries return to normal may have healthier vasculature compared to other KD patients. The significance of this finding merits further study.


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Natural History of Coronary Artery Aneurysms in Kawasaki Disease in US population and Risk Factors for Persistent Aneurysms

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**Background:** The late natural history of coronary artery aneurysms (CAA) after IVIG treatment in the US is not well described.

**Methods:** We evaluated all KD patients (pts) at 2 centers from 1984-2014. Entry criteria were: 1) IVIG treatment; 2) CAA, defined as LAD or RCA z-score $\geq 3$ or Japanese Ministry of Health criteria; and 3) $\geq 1$ follow-up (fu) echo. Kaplan Meier curves evaluated time to CAA regression ($z < 2.5$) and Cox regression examined factors associated with persistent CAA and major adverse cardiac events (MACE= death, MI,
Continuous Vascular Remodeling Related To Development Of Arteriosclerosis Or Atherosclerosis In Kawasaki Disease ~

Kenji Hamaoka, Maiko Fuji, Yuki Kuchitsu, Ayako Yoshioka, Akiko Okamoto, Chintsu Suzuki, Tomoyo Yahata, Akihiro Nakamura, Kazuyuki Ikeda, Kyoto Prefectural Univ of Med, Kyoto, Japan

Background: Atherosclerotic coronary heart disease has recently emerged as a clinical issue among young individuals with a history of Kawasaki disease (KD), which is a systemic vasculitis unique to children. However, whether or not and how KD promotes atherosclerosis remains unclear. We hypothesized that, analogous to the pathogenesis of arteriosclerosis or atherosclerosis, endothelial injury and the resultant intimal thickening are induced in coronary arteries after attenuation of vasculitis.

Methods: We used a rabbit model of KD developed by Onouchi et al. and performed histopathological analysis of the coronary arteries at acute (1, 3, 5, and 7 days) and chronic (3 months) phases of the disease.

Results: In these rabbit models, a pan-arteritis with significant intimal cellular hypertrophy was histologically detected in the acute phase, and arterial intimal thickening was observed during the chronic phase. Immunohistochemical analysis of the coronary arteries revealed that the thickened intimal lesions observed during the chronic phase comprised abundant α-smooth muscle actin (α-SMA)-positive cells, most of which concomitantly expressed vascular cell adhesion molecule-1 and nuclear factor-κB. Although macrophages positive for RAM11 were barely detected, macrophage colony stimulating factor was strongly expressed in migrating smooth muscle cells in the intimal layer. In addition, the accumulation of proteoglycan as extracellular matrix was distinctly visible in the thickened intima, indicating progressive accumulation of lipids and proliferation of smooth muscle cells within the lesion.

Conclusions: These findings suggest that, in KD-associated vasculitis, the migration of α-SMA-positive cells into the thickened intima might induce continuous vascular inflammation and remodeling, which might progress to coronary arteriosclerosis or atherosclerosis.

K. Hamaoka: None. M. Fuji: None. Y. Kuchitsu: None. A. Yoshioka: None. A.
Atherosclerosis risk and Carotid Intima-Media Thickness after Kawasaki Disease in Mexican Children

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Background. Kawasaki disease (KD) is an acute febrile illness characterized by systemic vasculitis of unknown etiology. Recent studies have shown that even after resolution of the disease, endothelial dysfunction persists and may progress to premature atherosclerosis. Carotid intima-media thickness (cIMT) is a well-established indicator for atherosclerosis in both pediatric and adult patients.

Objective. To assess whether patients after Kawasaki disease (KD) have increased risk factors and abnormalities suggestive of premature atherosclerosis by measuring the cIMT compared with healthy control subjects.

Material and Methods. One hundred and three patients with KD aged 102.12 ± 41.82 months (61.94 ± 33.23 after the acute episode) and 83 age-matched healthy control subjects were examined for family, medical and dietary history, serum markers of atherosclerotic risk and inflammation and carotid intimal-medial thickness (CIMT) with vascular ultrasound scanning.

Results. Patients and control subjects were similar in age, gender, family and dietary history, body mass index and blood pressure. We found no difference in the levels of triglycerides and glucose. And the levels of total cholesterol (162 ± 39.2 vs 150 ± 37.4), low-density lipoprotein cholesterol (102.57 ± 32.3 vs 89.6 ± 33.5), and high-density lipoprotein cholesterol (47.38 ± 17.65 vs 39.5 ± 17.54) were slightly higher with no statistical significance. The cIMT was slightly higher in the KD group (0.48 ± 0.1 vs 0.45 ± 0.15) We did found higher levels in the lipid profile and in the cIMT in patients with KD with coronary lesions compared with children with KD without coronary lesions the warrant further study.

Conclusions. There is no clear evidence of increased atherosclerosis in Mexican children with KD, but there is evidence of an altered lipid profile and in the cIMT in patients with KD with coronary lesions compared with children with KD without coronary lesions the warrant further study.

Long Term Coronary Angiography of Giant Coronary Aneurysms after Kawasaki Disease in Mexican Children

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Kawasaki Disease (KD) is an acute febrile illness characterized by systemic vasculitis of unknown etiology. Coronary artery aneurysms (CAA), is one of the most important aspects of this disease. Some patients with KD develop giant coronary aneurysms (z-score > 10) and coronary stenosis, leading to ischemic heart disease.

Objective. To determine the outcome of giant coronary artery lesions caused by KD and the value of coronary angiography in the evaluation and follow-up of coronary artery lesions in Mexican children.

Materials and Methods. From our Institutional database, 34 patients (23 men and 11 women) who developed giant aneurysms from 1995 to December 2013 were identified. Information on patient demographics, catheter and surgical interventions, and most recent status was collected from medical records.

Results. The average age at onset of KD was 13.5 months, and the median observational period was 70 mo. (5 to 163 mo.). During this period 11 patients showed CAA regression, 21 patients persist with CAA and 2 patients died at follow-up. In 9 patients with persistent giant CAA or coronary stenosis we performed cardiac catheterization to evaluate the coronary anatomy and findings of myocardial ischemia. Coronary bypass was performed to alleviate coronary ischemia in 1 patient, this patient developed dilated cardiomyopathy one year after the surgery and died. The overall survival rate in our series is 97%.

Conclusions. Despite being a small series, the long-term survival of patients with KD complicated by giant coronary aneurysms in our center is relatively good. However further
research should focus on the indications for and effectiveness of percutaneous and surgical coronary interventions.

L.M. Garrido-garcia: None. J.L. Colin: None. A. Bobadilla-aguirre: None.

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Hemophagocytic lymphohistiocytosis following kawasaki disease:Differential Diagnosis in IVIG Refractory Kawasaki Disease

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Introduction: Hemophagocytic lymphohistiocytosis (HLH) is a systemic inflammatory disorder characterized by uncontrolled histiocytic proliferation, hemophagocytosis and up-regulation of inflammatory cytokines. Thus, both HLH and Kawasaki disease (KD) are characterized by prolonged fever, and are diagnosed by a clinical and laboratory scoring system, concurrent manifestation of HLH and KD has been described in the literature. We describe two cases of children who diagnosed as KD initially, but after intravenous gamma globulin (IVIG) failed to produce clinical response, were found to have HLH.

Case report: A 3-year-old boy who had previous KD history 5 months ago was admitted for 9day fever and skin rash. His symptoms were fulfilled KD criteria, and echocardiography showed dilated right coronary artery of 4.2mm. He was treated with 2 cycles of IVIG until fever subsided. However, 2 days later, he got fever again and cytopenia (Hb<9.0), hypertriglyceridemia, high level of ferritin was shown and had splenomegaly on physical examination. In the suspicion of HLH, bone marrow biopsy was done and revealed hemophagocytosis, consistent with HLH. A second case of 11-month-old boy admitted for 8-day fever with Kawasaki feature. Although, he showed incomplete feature (fever, skin rash, conjunctival injection, cervical lymphadenopathy), echocardiography showed dilated left main coronary artery (3.5mm) and treated with IVIG. However, 2 days after IVIG administration, he was still pyrexial. The laboratory findings fulfilled 5 diagnostic criteria of HLH; bicytopenia (anemia, thrombocytopenia), hypofibrinogenemia, hyperferritinememia, hemophagocytosis in bone marrow, raised level of soluble IL-2 receptor. In both cases, the patients treated according to the HLH protocol 2004, and after that clinical symptoms and laboratory findings were improved. Several causes of febrile illness, EBV, CMV, rubella, parvo-viral infection, for example, were excluded.

Comment: There is considerable overlap between the clinical syndromes of KD and HLH and early recognition and treatment of these two disease entity is imperative to avoid fatal outcomes in severe cases. Thus, these should both be considered and excluded in any child with unremitting fever and rash.


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Neurological Prognosis Of Infliximab Therapy Against Immunoglobulin Refractory Kawasaki Disease

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Background: Infliximab (IFX) which is an anti-TNFα monoclonal antibody is effective in the treatment of gamma globulin treatment (IVIG) resistance Kawasaki disease (KD). It has been reported that TNFα adjusts the gene expression of myelin protein components and cause demyelination. Furthermore, at IFX treatment, the possibility of onset of the demyelinating disease in rheumatic diseases, and the exacerbation of the underlying disease in demyelinating disease have been suggested. Objective : To evaluate the neurological prognosis in pediatric cases who underwent treatment with IFX against IVIG resistant KD, were examined for the presence or absence of demyelination and delayed myelination. Methods : It is targeted for the 10 cases of IVIG refractory KD patients who received IFX 5mg/kg administration. Informed consent was obtained from the parents of all participants. We evaluated the candidate child’s mental
Poster Abstract Presentations (continued)

development by the intelligence test (WISC-IV) and investigated the presence of demyelination and delayed myelination by brain MRI. Results: All cases were above 6 years old, and more than a year had passed since they received medication of IFX. In all cases, abnormalities of neurological findings and psychomotor developmental delay after treatment were not observed. There was no obvious abnormality in eight cases (boys of 5 cases, girls of 3 cases, 6-11 years of age at the investigation) who underwent the WISC-IV; Full Scale IQ 97.4 ± 12.5, Verbal Comprehension Index 92.8 ± 11.9, Perceptual Reasoning Index 103.9 ± 17.9, Working Memory Index 97.1 ± 15.5, Processing Speed Index 100.9 ± 9.7. In addition, in nine cases (boys of 4 cases, girls of 5 cases, 6-16 years of age at the investigation) who underwent brain MRI, there was no evidence of demyelination and delayed myelination. Conclusion: In this study, there were not existed the findings of demyelination, delayed myelination, and mental retardation in IFX administration cases. However, it is necessary to repeat examination how the IFX medication to children make adverse effects on central nervous system.


195 Kawasaki Disease in a four-year-old girl with History of Acute Myeloid Leukemia; Report of a Case and Literature Review

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Background: Kawasaki disease (KD) and acute myeloid leukemia (AML) both occur predominantly in young children. However, considering that the incidence rate of cancer during 0-14 years of age in Japan is 10.1 per a hundred thousand and that of KD during 0-4 years of age is 260 per a hundred thousand, there is little possibility of the same individual developing 2 diseases. Both inside and outside Japan we found at least 19 case reports of KD some relevant to cancer. Herein, we report a case of KD in a four-year-old Japanese girl with history of AML. Case report: A four-year-old Japanese girl was diagnosed with KD at 3 days of illness. She had the medical history of AML-M7 at her age of 1. She had no chimeric genes and was classed as intermediate risk. She had been treated following JPLSG AML05 protocol including etopoide, cytarabine (Ara-C), mitoxantrone, idarubicin, methotrexate (MTX), hydrocortisone (HDC) and triple intrathecal therapy (Ara-C, MTX and HDC). More than 2 years had passed without recurrence since her last chemotherapy. When we diagnosed her as KD, laboratory findings showed WBC 15.5×10^3/µl with 85% neutrophils, hematocrit 33.7%, platelet count 19.1×10^5/µl, CRP 10.5mg/dl, serum albumin 3.8g/dl and BNP 12.2pg/ml. She responded well to IVIG (2g/kg) plus prednisolone (2mg/kg/day) and ASA (30mg/kg/day). Although BNP transiently had increased to 151.8pg/ml at 5 days after onset, neither coronary arterial abnormalities nor myocardial complications were detected at 1 year of illness. Conclusions We experienced the rare case of KD in a four-year-old Japanese girl with history of AML. She responded well to IVIG and any cardiovascular complications were not detected at 1 year of illness. Referring to only this case, it is unclear whether the history of AML could influence developing and progress of KD or not. The possibility of the same individual developing KD during 0-4 years of age and cancer during 0-14 years of age would be 2.6 per 10 million in Japan. However, among three hundred thousand cumulative patients of KD in Japan, 14 cases have been reported that they had developed cancer during 0-14 years of age. To discuss the relation to character of cancer, chemotherapy and severity or compilations of KD, more case should be evaluated.


196 The Characteristics of Patients with Kawasaki disease Presented with Fever and Cervical Lymphadenopathy at Admission
ABSTRACTS

Poster Abstract Presentations (continued)

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Purpose: Of the principal diagnostic criteria of Kawasaki disease (KD), cervical lymphadenopathy is the least common. However, it may be misdiagnosed as bacterial cervical lymphadenitis. We evaluated the characteristics of patients with KD presenting with only fever and cervical lymphadenopathy at admission.

Methods: This study enrolled patients diagnosed KD from January 2013 to May 2014. All of patients were divided to three groups: group 1 had only fever and cervical lymphadenopathy at admission; group 2 had typical manifestations with cervical lymphadenopathy; group 3 had typical manifestations without cervical lymphadenopathy.

Results: Ninety eight patients (group 1 in 13, group 2 in 31, group 3 in 54) were examined. The median age of group 1 was significantly older than group 2 and 3 (P=0.001). The duration of fever before admission at our hospital was more prolonged in group 1 than in group 2 and 3 (P=0.001). In comparison between groups, the laboratory results at the admission day were not significantly different. However, group 1 showed significantly elevated white blood cell counts, elevated neutrophil counts, and decreased lymphocyte counts after first intravenous immunoglobulin administration (P=0.001, P=0.001, and P=0.003). The frequency of additional intravenous immunoglobulin treatment did not have significant difference. Group 1 had significantly increased duration of hospitalization, and frequency of second line treatment such as systemic steroid or infliximab than group 2 and 3 (P=0.000, P=0.024, and P=0.007). The development of a coronary artery dilatation (z score >2.5) was higher in group 1 than in group 3 (P=0.008).

Conclusions: KD with cervical lymphadenopathy as main presentation indicates a severe form of KD associated with increased risks of second line treatment such as systemic steroid or infliximab and coronary artery dilatation. KD should be suspected in the older children with antibiotics non-responsive, prolonged fever and cervical lymphadenopathy. For differentiation between responder and non-responder for first line treatment, white blood cell counts and their subset after first intravenous immunoglobulin administration may be beneficial.

**Y. kim:** None. **C. Shin:** None. **M. Hyun:** None. **D. Lee:** None.

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**Coronary Aneurysm and Ectasia In Adults**

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Background: We investigate the status of coronary aneurysm or ectasia in adults.

Methods: We retrospectively reviewed all coronary angiograms and coronary computed tomography angiograms (CT) performed at Hanyang University Hospital between January 2011 and August 2014.

Results: Coronary angiography was performed in 4383 patients. Coronary CT was performed in 4099 patients. Coronary aneurysm or ectasia was detected in 28 patients (0.63%) on coronary angiography and in 21 patients (0.51%) on coronary CT angiography. Mean age of patient with coronary aneurysm or ectasia on angiography or coronary CT is 60.5(SD 14.7) or 58.0(SD 11.2). Mean age of patient with coronary aneurysm or ectasia on angiography or coronary CT is 60.5(SD 14.7) or 58.0(SD 11.2). Mean age of patient without coronary aneurysm or ectasia on angiography or coronary CT is 60.5(SD 14.7) or 58.0(SD 11.2). For 28 patients with coronary aneurysm or ectasia on coronary angiography, male and female ratio was 16:12. Age was for 57.6(SD 11.9) for male and 64.5(SD 17.6) for female. For 21 patients with coronary aneurysm or ectasia on CT angiography, male and female ratio was 14:7. Age was for 53.9(SD 8.3) for male and 66.1(SD 13.4) for female. The age gap between male and female was increased for patients with coronary aneurysm or ectasia on both studies. These suggest adult with coronary aneurysm or ectasia might have Kawasaki disease in young age.

Conclusions: The mean age of male patients with coronary aneurysm or ectasia was lower than that of female patients without coronary aneurysm or ectasia. This indicates adult with coronary aneurysm or ectasia might have Kawasaki disease in young age.

**N. Kim:** None. **J. Hwang:** None.
ABSTRACTS

Poster Abstract Presentations (continued)

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Vasospastic Angina In A School Child Long After Kawasaki Disease

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Though it has been already reported that the endothelial function was impaired in patients with a history of Kawasaki disease (KD) and coronary artery aneurysms, vasospastic angina has been rarely reported, especially in school child.

A 13-year-old school child referred to us because of repeated chest pain on exercise and reverse redistribution in myocardial perfusion scan. His past history included KD at 2 years of age that was complicated by resistance to initial immunoglobulin treatment and he was left with coronary aneurysms; left main trunk (LMT) of 6.1mm, left anterior descending artery (LAD) of 6.0mm, and right coronary artery (RCA) of 6.0mm. He received oral warfarin treatment in addition to aspirin for 2 years and since then aspirin alone. Coronary angiogram at 7 years old showed LMT aneurysm of 6.1mm starting from orifice extending to bifurcation and regression of RCA aneurysm. He joined baseball club since 8 years old and has been doing well without any symptoms. In this summer, he started complain chest pain after 10 minutes of running 2-3 times a week that lasts for about 30 minutes. Though exercise stress test using treadmill did not show any abnormal electrocardiographic finding, stress myocardial perfusion scan using Thallous chloride-201Tl showed an area of reverse redistribution in the LAD territory. Baseline coronary angiogram at this time showed basically the same finding as that in the last study, intact RCA without stenosis and LMT aneurysm without any stenosis. However, provocative study using intra-coronary administration of 100 ug of acetylcholine, showed diffuse coronary artery spasm in all LCA branches and he indeed complained the same chest pain as that felt in exercise. In addition, intra-coronary administration of nitroglycerine completely reversed coronary spasm and chest pain.

Conclusion: Vasospastic angina with chest pain can occurred in the school child with coronary artery aneurysms without coronary stenosis long after KD.


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Afebrile Kawasaki Disease Beyond Diagnostic Guideline Evolving Coronary Artery Complication

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Kawasaki disease (KD) is diagnosed with clinical features. Presence of at least five days of fever is major criteria. Herein we report a 7 month -old boy diagnosed as afebrile kawasaki disease who initially presented with inflammation at the Bacille Calmette-Guerin (BCG) inoculation site (BCGitis) with multiple erythematous papular rash, followed by desquamation of finger tips at 11 day of illness. Laboratory test showed elevated ALT (110 U/L) and otherwise showed no specific finding. Clinical feature disappeared spontaneously except BCGitis. The patient did not fulfill the diagnostic criteria but progressive coronary arterial dilatation was noticed. Left coronary artery (LMCA) was dilated from Z-score 1.6 (3 day of illness) to 2.8 (11 day of illness). After treated with intravenous immunoglobulin (2g/kg), BCGitis disappeared and follow up echocardiogram showed normalized LMCA lesion (Z-score 1.0 at 17 day of illness). BCGitis was considered to be pathognomonic feature of this patient.

Diagnostic algorithm and guidelines are useful tool for the incomplete KD patients but clinicians should also be cautious for the patient with BCGitis even they are excluded by diagnostic guideline.

Key words : Afebrile Kawasaki disease, Guideline, BCGitis

S. Lee: None. N. Kim: None.

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Risk Factors Of Persistent Coronary Artery Dilatation In Taiwanese Children With Kawasaki Disease.

Ming-Yu Liu, Dept of Pediatrics, Natl Taiwan Univ Children's Hosp, Taipei, Taiwan; Hsin-Min Liu, Dept of Pediatrics, Natl Taiwan Univ Hosp...
Background:
Kawasaki disease (KD) is an acute, systemic vasculitis disease of childhood, which may lead to cardiovascular complications, particularly coronary artery (CA) dilatation or aneurysm formation, and could result in morbidity and mortality. The Z score of coronary artery decreased from initial value within first few 2-3 months after fever onset. We follow the echocardiographic measurements of KD patients over time, and attempt to find the associated factors of persistent dilated coronary artery.

Methods:
Initial presentations, clinical laboratory data, echocardiography measurements and treatment were obtained from the patients with acute Kawasaki disease over 4 years period in a single medical center hospital. The patients were divided into 3 groups according to the initial maximum Z score of any coronary artery which were normalized for body surface area. We followed the echocardiography regularly at initial acute phase, 2-4 week, 5-12week, and > 3 months after fever onset. The maximal Z score of any coronary artery branches > +2 at any time were defined as having abnormalities.

Results:
We included total 169 patients with acute KD during 2008-2012. A maximal Z score for any of the coronary artery branches greater than +2 at acute phase was noted in 31.4% (53 of 169) of patients. During the following-up period, all except one patients (1 of 138) of the patients with initial maximal Z score <+2.5, the coronary artery have no abnormality at the end of following up. In contrast, the patients with initial maximal Z score≥+2.5 were more likely to have persistent coronary abnormalities over time (5 of 31, P<0.001). We also found hypoalbuminemia (P=0.006) and unresponsiveness to initial intravenous immunoglobulin treatment (P<0.001) associated with deteriorated or persistent CA abnormality within one month of disease onset.

Conclusion:
Coronary artery dilatation with Z score≥+2.5 at acute phase of Kawasaki disease, hypoalbuminemia and IVIG unresponsiveness are significantly associated with persistent CA abnormality at one month after KD onset. That indicated how to avoid IVIG unresponsiveness at the initial treatment of KD is a critical issue.


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Emergence and Characterization of Premature Acute Coronary Syndrome in Young Adults with a Confirmed History of Kawasaki Disease in Japan: Clinical and Mechanistic Insight.

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Background: Sporadic cases of acute coronary syndrome (ACS) have been reported in adults with coronary sequelae presumably due to Kawasaki disease (KD). However, ACS in adults with a confirmed (whether followed-up or lost to follow-up) as well as unconfirmed history of KD is poorly characterized. Methods: To investigate ACS in such adults after KD during 2000-10, a nationwide survey was conducted in Japan. Results: A total of 67 patients (median age 35 yo, male 76%) were recruited. A diagnosis of KD was made in 32 during acute illness (Group A), in which 17 were lost to follow up. A KD
diagnosis was made retrospectively in the other 35 patients from coronary imaging at ACS (Group B). Overall, 67 patients were characterized by demonstrable thrombosis (74%) as well as the presence of giant aneurysms (GAN) (≥8mm) (38%), severe stenosis (>75%) (38%) and IVUS-derived calcification (92%) in culprit lesions. Group A represented younger age at ACS (26.5 yo vs. 40 yo in group B, p<.001), lower conventional coronary risks (87% vs 65%, p=.043), low percentage of severe stenosis (25% vs. 50%, p=.302) and high proportion of IVUS-derived calcification (86% vs. 100%, p=.335). In group A, patients who were followed up before ACS represented a higher proportion of GAN in culprit lesions (69% vs. 29% in KD patients lost to follow up, p=.030) as well as a shorter interval from acute KD (20 y vs. 27 y, p=.008) and higher percentage of medication before ACS (87% vs. 0%, p<.001). In the convalescence of acute KD in group A, the vessel size of prospective culprit lesion was 6.0-7.9mm in 36% and ≥8mm in 64%. Coronary angio, IVUS and MDCT of cases in 3 categories are presented. Conclusions: Premature ACS in young adults with a confirmed history of KD, significant coronary sequelae just after acute KD and low coronary risks is emerging in Japan. ACS in this population comprises two subtypes: ACS with GAN in culprit lesions in adults followed up for KD, as in childhood myocardial infarction in KD, and ACS in adults lost to follow up, characterized by the absence of GAN or severe stenosis and the presence of IVUS-derived calcification in culprit lesions, which was unmasked in this population. The present findings may give an insight into mechanisms in ACS, screening and medication, as well as recognition of KD in adulthood.


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Long-term Outcome Of Kawasaki Disease With Giant Coronary Aneurysms Which Waste Cardiac Follow-up; A Case Report

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We report 2 cases of Kawasaki disease (KD) which required surgical interventions long after initial diagnosis. Case 1: Twenty-one years-old male. He was diagnosed as KD at the age of 1. Despite he received intravenous gamma-globulin therapy, bilateral giant coronary aneurysms were formed. In addition, multiple aneurysms include abdominal, iliac and axillary arteries were formed simultaneously. Coronary angiography (CAG) was thought to be dangerous because of iliac artery aneurysm formation. He received medical follow-up with aspirin administration only. He referred to our department at the age of 13. Ischemic changes were confirmed on both treadmill exercise test and cardiac scintigraphy. CAG showed 75% right coronary artery (RCA) stenosis and 99% left main trunk stenosis. Coronary artery bypass grafting (CABG) was performed and his postoperative course has been uneventful. Case 2: Thirty-seven years-old male. He was diagnosed as KD at the age of 1. Left giant coronary aneurysms were formed and subsequently aneurysm was occluded. Aspirin was administrated, but he interrupted medication and follow-up for himself. He referred to our institution due to cardiopulmonary arrest during exercise. After successful resuscitation, CAG revealed total occlusion of RCA and 99% left coronary artery stenosis. Emergent CABG was performed and no postoperative sequel has occurred. Both cases didn’t receive sufficient assessment during the follow-up period. As a result, fatal cardiac event was occurred in case 2. Coronary aneurysm tends to change into combine aneurysmal and stenotic lesion. Long time follow up is necessary even if patients have no symptom. In addition, to decrease lost follow up patients,
we should explain the risk of sudden cardiac death repeatedly and emphasis necessity of long term follow-up and medication.


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Risk factors for development of coronary artery aneurysms in Kawasaki disease in Mexican Children

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Background: Kawasaki Disease (KD) is an acute febrile illness characterized by systemic vasculitis of unknown etiology. Cardiac sequelae, such as coronary artery aneurysms (CAA), are one of the most important aspects of this disease. Actually, it is the major cause of acquired heart disease in developed countries but its frequency in Mexico is still unknown. Objective: To establish the risk factors for development of coronary artery lesions in children with KD who were treated at the Instituto Nacional de Pediatría in Mexico City.

Material and Methods: An observational, comparative, retrospective case-control study of all patients diagnosed with KD in our Institution from August 1995 to May 2014. We reviewed the medical records and analyzed gender, age, weight, height, clinical manifestations, time from the onset of the symptoms to diagnosis, hemoglobin, leucocyte count, platelet count, ESR, C-RP, albumin, sodium, AST ASL, treatment used and the development of coronary artery aneurysms.

Results: We studied 384 cases of KD, 68% were male with a mean age at diagnosis of 39.02 ± 36.55 months. The mean duration of fever from the onset of the symptoms to diagnosis was 9.4 ± 5.79. An incomplete form of KD was diagnosed in 69 patients (19.4%). 150 patients developed CAA (39%). Multivariate analysis for CAA showed that younger age (p < 0.028) prolonged time to diagnosis (p < 0.001), central nervous system manifestations (p < 0.008) anemia (p < 0.001) leukocytosis (p < 0.005), thrombocytosis (p < 0.041) and elevated C-RP (p < 0.022) were the most important risk factors for development of CAA in our patients.

Conclusions: This is the largest series of KD in Mexico, with more cases diagnosed in recent years, so it appear that the disease is more common than initially thought. Also, the frequency of CAA is greater than the reported in the literature, but it appears that is related to a delayed diagnosis and treatment.


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Over 5 Years Follow-up of Kawasaki Disease with Atopic Bronchial Asthma

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Background: Recent epidemiological studies have suggested that some patients with Kawasaki disease (KD) have an atopic tendency. However, it is not clear what the long-term prognosis will be for KD-patient with allergic disease. We aim to investigate the long-term prognosis of KD-patient with allergic disease.

Subjects & Methods: We studied a cohort of KD-patient (n=58, follow-up age; 9.95±1.84 years), in whom we examined total serum IgE and specific IgE at KD-onset (onset age; 2.13±1.84 years). Using retrospective patient medical record analysis, we evaluated the prevalence of bronchial asthma at onset and follow-up of KD. In addition, we examined the hospitalization rate, medical history and family history in pediatric bronchial asthma after KD-onset.

Results: In our study, KD-patient had markedly higher total serum IgE and prevalence of bronchial asthma at onset of KD than the general children’s population, as reported by Japanese national government (Table 1). The prevalence of bronchial asthma at follow-up was similar to the general children’s population. 9 children had already had a diagnosis of a bronchial asthma at KD-onset. 8 children had subsequently developed bronchial asthma after KD-onset. In these 2 groups, however, 6 and 8 children, respectively, had remitted during follow-up. Nobody was hospitalized for
Poster Abstract Presentations (continued)

asthmatic exacerbation after KD-onset. Conclusions: These findings demonstrate that KD-patient with atopic bronchial asthma at onset have not developed severe allergic reaction. There results provide that the pathogenic mechanism of KD might weakly or transiently provoke an elevation of total IgE and the developing of allergies.

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<thead>
<tr>
<th>Studies</th>
<th>Age: average (range)</th>
<th>Prevalence</th>
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<tr>
<td>Our Study at KD-onset</td>
<td>2.1 (0-8) years</td>
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<tr>
<td>Our Study at follow-up</td>
<td>10.0 (6-17) years</td>
<td>5.2%</td>
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<tr>
<td>Asthma Infant Study*</td>
<td>(0-6) years</td>
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<td>Asthma Schoolchild study</td>
<td>(6-18) years</td>
<td>5.8%</td>
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Coronary Artery Thrombosis in an Infant with Kawasaki Disease without Giant Coronary Aneurysm and Iron Deficiency Anemia: a Case Report

Rungrote Natesirinilkul, Pimlak Charoenkwan, Rekwan Sittiwangkul, Suchaya Silvilairat, Yupada Prongpot, Faculty of Med, Chiang Mai Univ, Chiang Mai, Thailand

The major complication of Kawasaki disease is coronary aneurysm which can cause acute coronary disease in early adulthood. There are some reports of coronary artery thrombosis during the period of active Kawasaki disease in infants with giant coronary aneurysm. This report demonstrated a 5-month-old male infant who presented high-grade fever for 7 days. He was treated as urinary tract infection for 6 days before referral. At admission, he had fever, red lips and swelling of both feet, then was diagnosed Kawasaki disease. His EKG showed ST elevation at lead II, III and AVF. His initial echocardiogram revealed coronary dilatation with perivascular brightness; RCA 2.7 mm (Z-score 4.38), LMCA 2.88 mm (Z-score 2.83) and LAD 2.7 mm (Z-score 5.79). There was a clot 2.5 X 2.5 mm in LAD. However, his LV systolic function was normal (EF 76%). His blood test showed low hemoglobin as 8.9 g/dL and MCV as 61.9 fl, high white cell count 20,400/mm3 and platelet count as 606,000/mm3. His initial ESR and CRP elevated at 91 mm/hr and 52 mg/L, respectively. The cardiac enzymes were normal; CKMBmass 2.9 ng/mL (0-3) and troponin-T 0.004 ng/mL (< 0.4). He received IVIG 2.3 g/kg and aspirin 79 mg/kg/day and was closely monitored the vital signs and cardiac enzymes. His fever completely disappeared within 24 hours after treatment, then aspirin was decreased to 6 mg/kg/day. Also, he received intravenous heparin for 4 days, and then was switched to Enoxaparin. He was discharged uneventfully on day 22 of admission. Further blood test confirmed the diagnosis of iron deficiency anemia as follow: serum iron 30 ug/dL, transferrin-iron binding capacity 446 ug/dL and transferrin saturation 6.7% (< 16). He received iron supplement for 4 months. The clot in coronary artery gradually decreased in size and finally disappeared in seven months after diagnosis. So, the Enoxaparin was discontinued. He received low-dose aspirin for total course 15 months. His thrombophilia work up was unremarkable. Anemia which is one of the supplementary criteria for atypical Kawasaki disease should be properly evaluated for the cause. The study to find the association between iron deficiency anemia, which was reported as a risk for thromboembolic events, and severity of Kawasaki disease should be further investigated.

R. Natesirinilkul: 1. Employment; Significant; Dr.Rungrote Natesirinilkul is a Baxter’s Thrombosis/Hemostasis Program at the Hospital for Sick Children, who received 35,750 CAD/year. P. Charoenkwan: None. R. Sittiwangkul: None. S. Silvilairat: None. Y. Prongpot: None.

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Relationship between patients with Kawasaki disease and the role of Parents Association Kawasaki Disease (Parents Association)

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Katayama et al. indicated that the Parents Association for children with Kawasaki disease plays a significant role through four phases of
"the psychological development process over 10 years in mothers with children with Kawasaki disease." In the first phase, parents are bewildered, persistently worrying about their child’s poor physical condition with no clear cause. In the second phase, parents are confused by the diagnosis of Kawasaki disease and feel panicked not knowing what to do. In the third phase, they reexamine their attitudes as parents and alter their consciousness through an encounter with the Parents Association. In the fourth phase, parents begin to act proactively with the growth and development of children, facing the reality and future as the parents of children with Kawasaki disease. However, no detailed analysis has been reported regarding the significance of the Parents Association itself. Therefore, we analyzed the entire content of Parents Association newsletters from No. 1 through No. 192. Here we report the reevaluated significance of the Parents Association.

S. Okamoto: None.

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Follow-up Study in Kawasaki Disease By Treadmill Exercise Test And Echocardiography

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Kawasaki disease (KD) may result in coronary aneurysm formation and increased risk of cardiovascular complications such as ischemic heart disease. Therefore, the early detection, non-invasive monitoring and long-term follow-up of myocardial ischemia are essential. This study sought to determine the ischemic heart disease by treadmill exercise test and two-dimensional echocardiography. Three hundred and four patients with a history of KD from 1995 to 2005 were retrospectively analyzed. Among them fifty patients who agree with the study underwent exercise test and 2D-echocardiography. The patients were followed for 11.6 years (8 to 17) from disease onset. The coronary artery ectasia regressed in 21 patients. No stenotic lesion could be found in the coronary artery in follow-up echocardiography. And no significant ischemic changes were detected. There is no evidence of persisting coronary ectasia and dysfunction of cardiac perfusion in patients with previous KD in this study. However, these patients should be counselled to avoid potential risk factors for other complication such as atherosclerosis and long term follow up is needed into adult life.

S. Park: None. K. Park: None. J. Park: None.

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Kawasaki Disease In Infants. Experience in a Third Level Facility in Mexico City

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Background: Kawasaki disease (KD) is an acute febrile vasculitis of unknown origin. KD represents the most common cause of acquired heart disease in children in developed countries. Worldwide KD is uncommon in infants (younger than 3 months of age), and in Mexico there are few reports of KD in this group of age. Objective: To describe the clinical features, laboratory parameters, the incidence of coronary aneurysms, treatment employed and the outcome of infants with KD in a third level facility in Mexico City. Methods: A retrospective and descriptive study was performed on children younger than 3 months of age with KD from August 1995 to August 2014. We analyzed gender, age, clinical manifestations, hemoglobin levels, leucocyte count, platelet count, ESR, CRP, albumin, sodium, potassium, AST, ASL, time from the onset of the symptoms to diagnosis, treatment used, the development of CAA and outcome in the acute phase of the disease. Results: Eight infants were diagnosed with KD during the study period. The median age at diagnosis was 2.5 months (range 2-3 months). Five patients were male (62.5%). The median from the onset of the clinical manifestations to diagnosis of KD was 14 days (range 4 to 26 days). All patients received medical consultations (range 1 to 7) prior to diagnosis. An incomplete form of KD was present in 4 patients. Five patients (62.5%) received IVIG. Four patients (40%) received steroids and low dose aspirin. Five of our patients developed coronary aneurysms, all of them were categorized as giant aneurysms (Z-Score > 10); one of these patients died of cardiogenic shock in the acute phase of the disease. Conclusions. In Latin American countries are few reports of KD in infants. We present our experience in infants with KD. Near two thirds of
our patients developed coronary aneurisms; most of the patients with coronary aneurisms were associated with late diagnosis and therefore late onset treatment.

A.I. Ramirez-perea: None. L.M. Garrido-garcia: None.

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Kawasaki Disease in Patients Older Than 10-\text{years Old in a Children’s Hospital In Mexico City}

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Background: Kawasaki Disease (KD) is an acute febrile illness characterized by systemic vasculitis of unknown etiology. Cardiac sequelae, such as coronary artery aneurysms (CAA), are one of the most important aspects of this disease. Actually KD is most frequently presented in children younger than 5-\text{years old.}

Objective: To describe the clinical and laboratory features, cardiac sequelae and outcome in children older than 10-\text{years old with KD who were attended at the Instituto Nacional de Pediatria in Mexico City.}

Methods: An observational, descriptive, retrospective and transversal case study. We reviewed the medical records of patients older than 10-\text{years diagnosed with KD from August 1995 to May 2014, and analyzed gender, age, clinical manifestations, hemoglobin, leucocyte count, platelet count, ESR, CRP, albumin, sodium, potassium, AST, ASL, time from the onset of the symptoms to diagnosis, treatment used, the development of CAA and outcome in the acute phase of the disease.}

Results: We studied 18 cases of KD in patients older than 10-\text{years old, 72.2\% (13 of 18) were male with a mean age of 154 months (range 120 to 200). The time from the onset of the fever to diagnosis was 10.6 \pm 5.8 days, (range 3 to 21 days). Skin lesions were the most common manifestation of KD and cervical lymphadenopathy was the least common clinical feature. 2 patients presented with KD shock syndrome. Complete KD was diagnosed in only 50\% (9 of 18) of our cases. 16 patients received IVGG, 2 patients required a second GIGI dose and 10 patients also received steroids. 6 of 18 patients (30\%) developed CAA. There were no deaths in our group.}

Conclusions: KD in patients older than 10-\text{years old represent a clinical challenge because in the majority of the cases they presented with an atypical clinical picture which contribute to a delayed diagnosis. Also there is an increased risk of developing cardiac complications and CAA in this group of patients.}

I.E. Rios-olivares: None. L.M. Garrido-garcia: None.

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Acute Myocardial Infarction in the Acute Phase in Kawasaki Disease in Mexican Children.

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Background: Kawasaki disease (KD) is an acute febrile vasculitis of unknown origin. Despite treatment with intravenous immunoglobulin during the acute phase of the disease, up to 5\% of those affected will develop coronary aneurysms predisposing them to thrombotic complications that could result in myocardial infarction (AMI). In Mexico there are few reports of ischemic complications secondary to KD.

Objective: To describe the clinical features, the laboratory parameters, treatment used and the outcome of children who presented with myocardial infarction during the acute phase of KD in a third level facility in Mexico City.

Methods: From our Institutional Database of KD we search for children who presented AMI in the acute phase of the disease from August 1995 to August 2014. We analyzed gender, age, clinical manifestations, EKG and abnormal perfusion tests demonstrated the myocardial infarction in all cases. Two patients died in the acute phase of cardiogenic shock, one more patient died of dilated cardiomyopathy 12 months after coronary bypass surgery with an overall
mortality of 62.5% of this group.

Conclusions. AMI is a fatal complication of KD. In our small series it was associated with a delayed diagnosis of the disease and therefore the development of giant coronary aneurysms. Treatment of AMI in children after KD is a medical challenge with a poor prognosis in children.

W. Sarmiento-robles: None. L.M. Garrido-garcia: None.

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Characteristics of Kawasaki Disease in Chile: Temuco’s experience

Guillermo Soza, Carolina Cerda, Andreas Berkhoff, Claudia Lozano, Andrea Salgado, Hosp Dr. Hernán Henríquez Aravena, Temuco, Chile

Kawasaki Disease (KD) is a vasculitis mainly affecting children under two years old and harms arterial vessels (especially coronary) causing dilatation, aneurysms and eventual myocardial complications. Though etiology is unknown, a relationship with an infectious agent is suspected. Diagnosis is doing by clinical criteria and laboratory support. KD cases reported in Latin America go along absence of management protocols and it is not considered notifiable disease. In order to contribute to a greater understanding of this disease, a retrospective - descriptive analysis of 75 patients diagnosed with KD at the time of discharge was carried out from January 2005 to August 2014 at Hospital Dr. Hernán Henríquez Aravena, Temuco, Chile. Information was tabulated in Microsoft Office Excel 2007 and a statical analysis were performed using STATA 11.0 program. Average age 2 years 7 months (range 2 months to 17 years). Sex Male/Female 49%/51%. Prior consultations 85% (64/75). Initial diagnosis KD 51% (38/75). Fever 100% (75/75), 64%(48/75) about 39 ° C. Eye involvement 68% (51/75). Oropharyngeal erythema 87% (55/75). Strawberry tongue 40% (30/75). BCG erythema 19% (14/75). Rash 83% (62/75). Erythema/oedema of hands and feet 73% (55/75). Cervical adenopathy 41% (31/75). Irritability 55% (41/75). Leukocytosis 36% (27/75). Plaquetosis 69%(52/75) and periungual descamation 39% (29/75). Echocardiogram abnormal at startup 28% (21/75), (6/75)8% prior application of IVGG and 5%(4/75)remained with coronary involvement. A single dose of 2g/kg of Intravenous Gamma Globuline (IVGG) was administrated to 97%(73/75). Aspirin 50 mg/kg initial and 5 mg/kg during the following. A second dose of IVGG was required in 13% (10/75). Two patients were treated with anticoagulant for giant aneurysms and in one case, bilateral brachial aneurysms. Tipycal KD in 73% (55/75) and 27%(20/75) incomplete. Further clinical suspicion is needed, because a high percentage of patients had coronary involvement at diagnosis. Those who received early IVGG coronary involvement were lower. Prominent among coronary involvement factors are extreme age, atypical or incomplete forms and high RCP. Needed be considered KD as a notifiable disease, considering the economic and social implications.

G. Soza: None. C. Cerda: None. A. Berkhoff: None. C. Lozano: None. A. Salgado: None.

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Outcomes of KD by the KD type: Linking Inpatient and Outpatient Follow-up Data

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Background: The relationship between KD type and outcomes is not well described. We sought to describe the incidence of KD outcomes based on type of KD presentation.

Methods: Using an electronic medical record, we prospectively recorded clinical data for each KD encounter (initial treatment, 2 and 6 week follow up visits) for all pts treated with IVIG at our hospital and followed in our KD clinic from 11/2012-9/2014. Pts were grouped by KD type as determined on the day of treatment - Complete, Incomplete, or questionable KD (qKD), defined as incomplete KD and < 3 supplemental lab criteria. Late treatment was defined as IVIG given at > 10 days of fever. The correlation of KD type with outcomes of persistent fever requiring repeat IVIG, development of periungual peeling (PP), and coronary abnormalities (CAA) was assessed using chi-square.

Results: We studied 109 pts treated with IVIG; 95 were treated within 10 days of fever onset (14 late). Late treatment was most common in qKD (9/19=47%) compared to incomplete (4/22=18%) and Complete (1/68=1.5%), p<0.01. PP was least common in qKD (4/19=21%),
compared to Incomplete (12/22=54%) and Complete (49/68=72%), p<0.05. No pts with qKD developed CAA, compared to 5/67 (7%) of Complete and 3/18 (16%) of Incomplete pts treated within 10 days of fever, (p=0.16, NS). Late treatment more commonly had CAA (5/14=36%, v. 8/95=8%), relative risk = 4.2 (p=0.003). In pts with CAA, 10 /13 (77%) had CAA on the first echocardiogram. The remaining 3 pts (2 Complete, 1 Incomplete) had a pericardial effusion initially and developed CAA by the second echocardiogram. Need for repeat IVIG was not different between groups (Complete 16/68 = 24%, Incomplete 3/22=14%, qKD 2/19=11%, p=0.33). Of the 2 qKD pts who required a second dose of IVIG, one was subsequently diagnosed with juvenile idiopathic arthritis and the other with Bartonella henselae; neither developed PP or CAA.

Conclusions: The incidence of CAA was not statistically different between KD types, though no qKD pts developed CAA despite a higher incidence of late treatment with IVIG. In most pts who developed CAA, the initial echocardiogram showed either CAA or a pericardial effusion. PP was least common in qKD. In qKD, failure of initial IVIG should prompt re-evaluation of the diagnosis of KD.

K. Texter: None. J. Kovalchin: None. O. Ramilo: None. P. Jaggi: None.

215 Fatal Arrhythmia In The Adult Patient Of Kawasaki Disease

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We herein report the two adult patients hardly predictable sudden cardiac arrest caused by presumed Kawasaki disease (KD). Case 1: A 29- year-old man who had a history of KD at 10 months of his age complicated with bilateral giant coronary aneurysms, and was received a surgery of coronary artery bypass grafting (CABG) when he was 17 years old. He was transferred to emergency center because of sudden cardiac arrest during live concert and revived by automated external defibrillator (AED). Case 2: A 26-year-old man with a history of KD at 1year old of his age, complicated with bilateral giant coronary aneurysms, and was received a catheter intervention of rotational atherectomy (ROTA) to left anterior descending (LAD) artery at 16 years old of his age. He suddenly fell with ventricular fibrillation (VF) on playing futsal, and was hospitalized after revival by AED. Both of them had past history of myocardial infarction (MI) in their youths, however, did not have left ventricular dysfunction, symptomatic arrhythmia, and evidence of acute MI at admission. Therefore, it was difficult to strongly predict possibility of fatal arrhythmia in these cases. Finally, they received the second CABG’s for each after stabilizing and returned to their daily lives. It had been rarely reported a fatal arrhythmia in asymptomatic KD patients with normal left ventricular function with revival with recent spread of life support with public access of defibrillator. Our experiences may suggest one style with a paradigm shift in management of patients with coronary artery complications at the remote period of KD.


216 Natural History of Kawasaki Disease with Medium-sized Coronary Aneurysm: Long-term Follow-up in a Tertiary Medical Center

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Objectives

Patients with coronary artery aneurysms are at risk for thrombotic and stenotic complications later in their lives. The longitudinal changes of medium-sized coronary aneurysms caused by Kawasaki disease (KD) and their long-term outcome are still unclear in Taiwan.

Methods

We retrospectively reviewed medical records of KD patients with medium-sized coronary aneurysms (4-8mm). The longitudinal change of coronary diameters were re-evaluated by domestic coronary z score calculator. The coronary artery diameters were transformed to standard deviation units from the mean (Z-score) normalized for body surface area. We also look for the potential risk factors for the
Results
Between 1983 and 2012, 56 KD patients suffered from medium aneurysms. The male to female ratio was 41:15. The mean age of disease onset was 2.13 years old, and 39.3% (22 of 56) was diagnosed at below 1 year old. The mean follow up duration was 8.2 years. No death occurred in this group of patient, and only one patient with persistent coronary aneurysm and stenosis/calcification had clinical evidence of myocardial ischemia. However, coronary aneurysms persisted in 24 (42.8%) patients and were associated with stenosis in 8 patients (14.3%), and calcification in 4 patients (7.1%). The coronary aneurysm persistence-free survival rates at 6 months, and 1, 2, 5 years after KD onset were 81%, 69%, 52%, 43%, respectively. Chi-square analysis revealed KD patients with history of ever deterioration of coronary Z score were significantly associated with the persistence of coronary aneurysms (P = 0.0125). However, the initial aneurysm Z score (+4.43 vs +4.49), male gender or IVIG use were not risk factors to the persistence of coronary aneurysms.

Conclusion
The prognosis of Kawasaki disease patient who developed medium size coronary aneurysm was good. However, those with ever deterioration of coronary Z scores were high risk group to have persistent coronary aneurysms. Specific therapies to promote vascular health in these patients should be advocated.


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Difference of Coronary Artery Lesions or associated Pathogens between the Two Phenotypes of Kawasaki Disease

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Introduction: There are several reports that coronary artery lesions (CALs) are increased/or not increased in patients who predominantly showed arthritis in patients with Kawasaki disease (KD). Patients with eczematoid skin lesions which seem like atopic dermatitis have not been reported in association with CALs. We intended to evaluate the risk of development of CALs in patients with two different phenotypes.

Materials and methods: We retrospectively reviewed the medical records in 220 patients who diagnosed as KD and received IVIG treatment in Kyung Hee University Hospital at Gangdong from August 2006 to December 2013. In both patients groups (6 patients with arthritis and 52 patients with eczematoid skin lesion), we reviewed the state of coronary artery, clinical characteristics, associated viral or bacterial infections.

Results: In patients with eczematoid lesions (52/220, 23.6%), the ages of patients were significantly older, the duration of fever was longer, and the prevalence of CAL was significantly higher than that of controls (P=.000, P=.041, P=.033, respectively). In patients with arthritis (6/220, 3%), there were higher incidence of methylprednisolone or infliximab therapy (P=.000, P=.004, respectively), and higher incidence of viral infection like influenza A and B, rhinovirus, parainfluenza 2, metapneumovirus, and coronavirus OC43 (P=.018).

Conclusions: The incidence of CAL was higher in group of eczematoid skin lesion in KD patients than in group of patients with arthritis. Associated viral infections were higher in arthritis group, therefore, it is better to find associated pathogens aggressively that might be a certain trigger of the development of KD in this group of patients.

K. Yoon: None. S. Youn: None. M. Han: None. S. Cha: None.

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Weekly Exercise Increases Coronary Artery Diameter: A Case Report

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Background: Studies have reported that heparin and exercise may alleviate myocardial ischemia in patients with Kawasaki disease (KD). Moreover, exercise alone can alleviate ischemic heart disease, e.g., cardiac rehabilitation in adult coronary disease. Exercise induces secretion of some growth factors and improves endothelial function. We found that exercise may play a role in physiologically
increasing the diameter of the coronary artery (CA) in KD patients with history of coronary aneurysm.

**Clinical course:** We report the case of a 9-year-old boy who had been admitted to our hospital at 6 months of age. He had long-term fever, rash, peripheral edema, conjunctivitis, and strawberry tongue and was diagnosed with KD. We treated him with a high dose of gamma globulin and pulse therapy. Despite these treatments, he developed coronary aneurysms on both sides. In the left descending artery (LAD), the aneurysmal diameter was 8 mm. We initiated treatment with warfarin and aspirin and performed angiography twice in the acute phase and at one year after admission, followed by magnetic resonance coronary angiography every 6 months. At 6 years of age, the aneurysmal changes disappeared. We stopped warfarin and started regular exercise on a weekly basis (1 hour of running and 2 hours of baseball). After initiation of exercise, echocardiography showed that LAD diameter increased from 2.8 mm to 3.5 mm. At 9 years of age, we performed angiography and intravascular ultrasound (IVUS) to determine whether this increase in diameter was due to recurrent aneurysmal change or physiological change. The diameter of the LAD was 3.5 mm (±2 SD of normal). IVUS showed that there was a small amount of endothelial hypertrophy but no irregularity, calcification, or thrombus. Thus, we concluded that this dilatation was not an inflammatory change but a physiological change.

**Conclusion:** Regular exercise may play a role in improving CA lesions through arterial dilatation and improvement of endothelial function.


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**Long - Term Prognosis Of Patients With Kawasaki Disease Complicated By Significant Coronary Aneurysm (diameter ≥ 6 mm)**

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**Background**
Some patients with Kawasaki disease (KD) develop large coronary aneurysms (diameter ≥ 6mm) and coronary stenosis, leading to ischemic heart disease. This study determined the long-term outcome for patients with Kawasaki disease complicated by significant coronary aneurysm.

**Methods and Results**
From the database in Seoul National University Children’s Hospital between December 1986 and December 2013, medical records of 83 patients (61 men and 22 women) with large coronary aneurysms (diameter ≥ 6mm) were retrospectively reviewed. Information on patient demographics, catheter or surgical interventions, and most recent status was collected. From these data, we calculated the survival rate, cumulative coronary intervention rate, coronary artery bypass graft surgery rate. The mean age at onset was 4.28 ± 2.62 years, and the mean observational period was 13.2 ± 6.5 years. The maximum coronary artery internal diameter ranged from 6.1 to 25mm (median 9mm). Giant coronary aneurysm was 57 patients (68.7%) and large coronary aneurysm (6-8mm) was 26 patients (31.3%). Coronary aneurysms had progressed to coronary artery stenosis and/or complete occlusion in 42 patients (50.6%). The overall freedom from coronary intervention, coronary artery bypass surgery, or coronary thrombi was respectively 85.5%, 85.5%, and 90.3%. Catheter and surgical coronary interventions (median 1 intervention; range 1 to 5 interventions) were performed in 20 patients (24.1%) at 9 month to 18 years after onset, resulting in 33.7% cumulative coronary intervention rates at 20 years after onset. There were no differences in cumulative coronary intervention rates between two coronary aneurysm groups (6-8mm vs ≥8mm). Myocardial infarction occurred in 8 (8.98 %) patients. During this study period, 1 patient died and 98% survival rates was seen in our patients group.

**Conclusion**
The long-term survival of patients with Kawasaki disease complicated by large coronary aneurysm is good even though a fourth of patients underwent multiple catheter or surgical interventions. Further research should focus on the indications for and effectiveness of percutaneous and surgical coronary interventions.
interventions in large coronary aneurysm (≥ 6mm).


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Magnetic Resonance Imaging in Children with Cardiac Complications of Kawasaki Disease: a Comparison with Echocardiography and Conventional Coronary Angiography

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Background: MRI is a potentially sensitive, specific, and non-invasive imaging modality that may be used in the detection and monitoring of KD cardiac complications. Its utility relative to the more commonly used imaging modalities of echocardiography and conventional coronary angiography has not been optimally established.

Methods: We compared concomitant clinical data, echocardiography, MRI, and angiography findings for children with coronary artery aneurysms.

Results: MRI and angiograms were performed within 1 month of each other for 15 patients (mean age 7 years, 80% male) at a mean of 4.2 years after diagnosis. Coronary artery bypass grafting (CABG) had been performed in 8 patients (53%). For 7 patients (47%), aneurysms were seen on MRI that were not seen on echocardiography. Wall motion abnormalities were reported in 7 subjects (47%). These were characterized on both echocardiography and MRI for all. MRI identified perfusion defects in 6 patients (40%) and evidence of myocardial scar in 9 patients (60%). Extra-cardiac aneurysms were identified in 5 patients (33%) on MRI. MRI showed strong correlation with angiograms regarding aneurysm location. MRI was limited in the assessment of bypass grafts in 4 of the 8 (50%) patients who had undergone CABG. Three patients (20%) had stenosis or thrombosis identified on angiography that were not appreciated on MRI. Angiograms provided added information regarding flow, stenoses, vascular morphology and/or calcification in 8 patients (53%). Collateral artery anatomy that was not appreciated on echo and MRI were reported on angiograms in 3 patients (20%).

Conclusions: MRI provides a valuable and comprehensive assessment of the cardiac sequelae of KD, though is limited in its assessment of CABG, stenoses, and thrombosis. MRI may be an important component of non-invasive imaging surveillance of children with important coronary artery involvement.


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Use of Statins in Patients with Coronary Artery Aneurysms: A Pilot Study from the North American Kawasaki Disease Registry

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Background: Statins have been considered as therapy for children with coronary artery aneurysms (CAA) after Kawasaki disease (KD), due to potential beneficial pleiotropic effects which might influence chronic vascular processes and inflammation.

Methods: The North American Kawasaki Disease Registry was queried to identify patients who have received statins in the first 6 months following the convalescent phase of KD. Each identified patient was matched by age, gender and CAA z score to 3 patients who were statin-naive (controls). Linear regression models adjusted for repeated measures and maximum coronary involvement were used to determine an association of statin use with longitudinal changes in coronary artery diameter z-score.
Kaplan-Meier analysis was used to compare freedom from angiographically-confirmed stenosis or interventions.

**Results:** Of 29 patients with KD and CAA (maximum coronary artery z-score >10) who received statins at any time (of n=621, 5%), 10 (9 males) patients were started within 6 months of the acute KD episode. The mean age at KD was 6.3±3.4 years (5.4±3.5 for controls, p=0.57). Mean maximum CAA z-score was 36±14 (vs. 29±16, p=0.20); 90% of statin patients and 87% of matched controls had CAAs in 3 or more branches. Linear regression analysis of 442 serial echocardiograms showed that maximum CAA z-score decreased by -1.5 (95%CI: -2.7; -0.4) SD/year (p=0.008) for control patients compared to -2.9 (95%CI: -4.4; -1.4) SD/year (p<0.001) for statin treated patients. The difference between the rate of change of CAA z-score for statin vs. control patients did not reach statistical significance (controls vs. statins: +1.4 SD/year, 95%CI: -0.6; +3.4, p=0.18). n=7 patients (3 on statin, 4 controls) developed stenosis or had revascularization, with no significant difference between groups (HR for statin group: 2.2 (0.4-11.4), p=0.41).

**Conclusions:** This underpowered pilot study suggests that equipoise likely exists with regards to statin therapy in children with KD and CAA, and that a formal registry-nested trial might be considered.


**Background:** Clinical research in children with Kawasaki disease (KD), particularly those with coronary artery aneurysms (CAA), is challenging due to the limited number of patients available at any single institution. This has resulted in imperfect evidence for optimal management and considerable practice variation.

**Methods:** The North American Kawasaki Disease Registry (NAKDR) was started in July 2013 to determine the prevalence, patient-level and pharmacological risk factors for outcomes of CAA after KD. The NAKDR enrolls KD patients diagnosed from 1999-2013 with CAA (defined as any segment with a z-score >2.5). The NAKDR and its internet-based data entry portal are maintained at The Hospital for Sick Children in Toronto. Local ethics approvals and bilateral data sharing agreements are necessary for participation. Participation in the NAKDR is currently unfunded and voluntary. In September 2014, a survey on the future of the NAKDR was sent to all participating centers (response rate: 54%).

**Results:** 45 sites have been invited, of which 37 (82%) agreed to participate. As of September 2014, 20 sites are actively submitting data; 17 are still being initiated; 706 cases have been submitted. The majority (90%) of members indicated that they wished to continue enrolling newly diagnosed patients and continue follow-up on patients already enrolled. Members were split (45% for, 55% against) as to whether the NAKDR should be expanded to include all KD patients, regardless of CAA status. Finally, while most NAKDR members (60%) indicated that site reimbursement was not an absolute condition for future participation, most members suggested that potential funding sources should be sought to expand/facilitate activities. At term, the NAKDR is expected to comprise ~1,400 patients and, if moving forward, add ~120 new KD patients with CAA per year.

**Conclusions:** The NAKDR is an important tool for clinical research in children with CAAs after KD, and its success represents broad support from clinicians. The next step will be to formalize the NAKDR leadership structure, create standard operating procedures, and pursue prospective studies and funding.

B.W. McCrindle: None.

**Background:** Surgical resolution of coronary artery obstruction in incomplete Kawasaki disease is challenging due to the limited number of patients available at any single institution. This has resulted in imperfect evidence for optimal management and considerable practice variation.

**Methods:** The North American Kawasaki Disease Registry (NAKDR) was started in July 2013 to determine the prevalence, patient-level and pharmacological risk factors for outcomes of CAA after KD. The NAKDR enrolls KD patients diagnosed from 1999-2013 with CAA (defined as any segment with a z-score >2.5). The NAKDR and its internet-based data entry portal are maintained at The Hospital for Sick Children in Toronto. Local ethics approvals and bilateral data sharing agreements are necessary for participation. Participation in the NAKDR is currently unfunded and voluntary. In September 2014, a survey on the future of the NAKDR was sent to all participating centers (response rate: 54%).

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**Conclusions:** The NAKDR is an important tool for clinical research in children with CAAs after KD, and its success represents broad support from clinicians. The next step will be to formalize the NAKDR leadership structure, create standard operating procedures, and pursue prospective studies and funding.

B.W. McCrindle: None.
Infantil de Mexico Federico Gomez, Mexico city, Mexico

Case Report 8 months old male, who presented with 7 days fever, hematuria, conjunctival injection and limb edema; treated as a post infectious glomerulonephritis. Twenty days later, desquamation at the tip of the fingers and in palms and soles plus thrombocytosis were found. Considering Kawasaki disease (KD), an echocardiogram was performed, finding a 5mm aneurysm in right coronary artery and 4mm ectasia in the left coronary artery. The patient was on the subacute therefore IVIG was not administered; aspirin however in antiplatelet dose range was begun. He continued on surveillance by Cardiology Department without signs of cardiac malfunction. At two years follow up a new echocardiogram was performed, showing a left coronary aneurism of 6mm and a right coronary artery of 2.0mm which was difficult to identify. Left ventricular function was preserved with an ejection fraction of 72%. Four years later, posterior myocardial necrosis, without acute ischemia on electrocardiography was found. A perfusion myocardial scan showed an uptake defect in apical region, both during stress and rest phase, suggesting an old apical infarction. Cardiac catheterization reported a tortuous right coronary artery with diffuse obstruction and left coronary artery aneurysm of 6.1mm. Due to findings above, heart transplant was considered. On a second perfusion scan a large perfusion defect on the inferior and septal wall, which improved during the rest phase was seen. The finding above correlates with inferior and septal myocardial infarction and residual ischemia. The PET-CT scan showed viable tissue in the left ventricle wall. Recently, the patient underwent revascularization surgery of right coronary artery with coronary artery bypass graft. Postsurgical echocardiogram reported a left coronary giant aneurysm of 8mm, ejection fraction of 40%, and a compromised posterior and inferior left ventricular wall function. We report the first case of surgical resolution of a coronary artery obstruction due to KD in our medical center. Because of patient’s age and coronary arteries abnormalities, a surgically intervention was the best approach in order to preserve patient’s life, cardiac function, improve the prognosis and mainly to gain time for future treatment decisions. 


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Repeat Coronary Artery Bypass Grafting in an Adult Case of Kawasaki Disease

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[Background]
The incidence of giant coronary artery aneurysm as a complication of Kawasaki disease is approximately 0.35%. Kawasaki disease was first described in 1967. However, only a few studies have reported on adult cases of cardiovascular sequelae in Kawasaki disease. Adult cases of coronary stenosis due to Kawasaki disease shows a predilection for the age range of late teens to the twenties; elderly onset, such as around the age of 60 years, is rare. [Case report] A 62-year-old woman with a history of coronary artery bypass grafting (two-vessel bypass) was diagnosed with a coronary artery aneurysm and concomitant Kawasaki disease at another hospital at the age of 48 years. A reoperation was recommended owing to re-strangulation, but the patient opted for progress observation. At the age of 53 years, the patient experienced respiratory pain during laborious work, and coronary angiography was indicated. We therefore performed coronary artery bypass grafting (four-vessel bypass) for there to base Kawasaki disease, calcification of advanced, restenosis, coronary flow was observed. The postoperative course was good, and the patient has remained without restenosis for 9 years after the surgery. [Conclusion] The progress of patients with a history of Kawasaki disease in adulthood has not been established; these patients therefore require periodical follow-up examinations. Moreover, because coronary artery involvement in Kawasaki disease is a risk factor for myocardial infarction, careful attention should be paid to lifestyle-related diseases. 

Variations in Pharmacological Management of Children with Coronary Artery Aneurysms after Kawasaki Disease: A Study from the North American Kawasaki Disease Registry

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Background: The pharmacological management of coronary artery aneurysms (CAA) associated with Kawasaki disease (KD) is based on imperfect evidence, which may lead to considerable practice variation.

Methods: Pharmacological management of patients included in the North American Kawasaki Disease Registry was reviewed. The Registry included data for 621 patients with CAA after KD (280 patients with maximum CAA z-score between 2.5-5.0, 139 with z-score 5.0-10.0 and 202 with z-score >10.0) followed at 20 medical centers. Practice variation regarding acute treatment, anti-inflammatory agents, statins, beta-blockers, antiplatelet therapy and anticoagulation were assessed.

Results: Considerable practice variation existed between centers. During the acute phase, 93% of patients received at least one dose of IVIG (range: 80-100%), with 23% (range: 12-50%) receiving additional immunomodulatory treatment (22% additional IVIG, 17% steroids, 4% infliximab). Use of a 3rd course of IVIG was infrequent (2%). All centers reported using additional IVIG or steroids for IVIG-resistant patients, but only 6 centres reported any experience with infliximab (2 commonly, 4 infrequent). Routine use of non-steroidal anti-inflammatory agents was limited to 2 centres, with 4 additional sites reporting infrequent use (10% of patients). Statins (5%), beta blockers (4%) and abciximab (3%) were mostly used by a single centre and was limited to patients with giant CAAs. Aspirin was the primary antiplatelet modality for 97% of patients, clopidogrel (10% of all patients, 23% in giant CAA) was routinely prescribed to patients with giant CAAs at 6 centres, with 2 more centres reporting infrequent use and the remainder not reporting any use. For patients with giant CAA (z-score>10.0), 46% were maintained on an antiplatelet agent alone, 17% additionally were on low molecular weight heparin(LMWH), 12% on warfarin and 25% had initially received LMWH and were later switched to warfarin.

Conclusions: Given the important variations in management between centres and the poor evidence base, randomized controlled trials examining outcomes and nested in a high-quality collaborative registry may be an efficient strategy to address this gap.

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<td>Genetics/Kawasaki</td>
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<td>Disease</td>
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