KAWASAKI DISEASE RESEARCH CENTER
RADY CHILDREN'S HOSPITAL/UCSD

IN THIS ISSUE:

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WINTER 2024

Dear KD Families & Friends,

Welcome to the Winter 2024 edition of the KDRC newsletter!

First and foremost, the team at the KDRC hopes that this newsletter reaches you and your loved ones in good health and that you will enjoy some cozy "together time" over the holidays.

Our research continues to reveal new insights into Kawasaki Disease and we want to share some of the excitement with you!

We hope you have find this newsletter informative. If there are topics you would like to see covered or questions that you have, please contact us at kdresearch@ucsd.edu and we will include answers to your questions in our next newsletter.

Wishing you quiet moments of reflection and joyous time with your family over the holiday season.

With warmest regards,

The KDRC Team

2024 KDRC UPDATES

The Gordon and Marilyn Macklin Foundation

2024 started with a bang! The Gordon and Marilyn Macklin Foundation pledged $2 million to Rady Children's Hospital-San Diego to establish the Gordon and Marilyn Macklin Foundation Endowed Chair in Kawasaki Disease Care and Research, in Recognition of Brooke Dawn, KD Survivor with the goal of developing new treatments, pursuing promising discoveries, improving diagnosis and outcomes, and understanding the causes of KD.

On February 15th, a joyous celebration of the investiture was held and the Chair was bestowed on Dr. Jane Burns with Dr. Adriana Tremoulet named as her successor. This incredible gift ensures that the excellent care of KD patients and cutting edge research on KD will continue in perpetuity at the KDRC.

A Doctor's Lifelong Quest to Solve One of Pediatric Medicine's Greatest Mysteries

New York Times Article

More excitement was generated by a wonderful article by Emily Baumgartner of the New York Times about the work by our team at the KDRC. Emily spent two full days with us seeing patients in our clinic and engaging in conversation about our research. We hope you will enjoy this article that gives a sense of the broad scope of our research.

Click here to read the article

MORE EXCITEMENT!

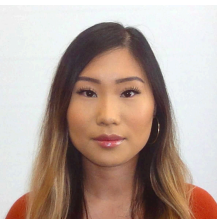
Clinton Global Initiative

As a result of the New York Times article, Dr. Burns was invited to become a Commitment Maker for the Clinton Global Initiative. She was invited by the Clintons to attend a two-day event showcasing projects from across the globe. President Clinton created the Clinton Global Initiative (CGI) to be a new kind of conference — one where every participant is required to take action. Defined by optimism and an unwavering belief in the power of cooperation, CGI members make Commitments to Action — new, specific, and measurable plans for addressing significant challenges. The KDRC Team made a commitment to create, test, and refine models that identify source regions for the aerosols associated with peaks in KD cases across three countries in Asia. Data will be analyzed to compare wind trajectories and source regions with extensive aerosol content databases maintained by the governments of each country to monitor pollutants, heavy metals, and other small molecules that are tracked by these systems. We are excited to be part of CGI!

Greetings & Goodbyes

After 9 years at the KDRC, our wonderful data manager, Emelia Bainto, opted to retire to spend more time with family. For many years, Emelia managed our REDCap database that supports our research on KD. As a phenomenal pastry chef, she also honored every team birthday with a wonderful cake. While she will be missed, we are delighted to welcome on board Jennifer Kim, our new data manager extraordinaire.

KDRC Team celebrating a milestone birthday with the cake Emelia (second from left) baked from scratch.



Jennifer graduated from University of Rochester with a Bachelor's in Psychology with a minor in Brain & Cognitive sciences and is currently pursuing her Masters of Science in Health Care Informatics. She joins us from UCLA Health where she was a Data Manager for clinical research focused on digital health. Her interests lie in using health informatics to deepen our scientific understanding about the etiology and clinical management of diseases.

14th International Kawasaki Disease Symposium (IKDS)

Another big event of the year was the 14th International Kawasaki Disease Symposium in Montreal, August 26-29, 2024. Dr. Adriana Tremoulet, Associate Director of our UCSD/RCHSD KD Research Center, was the co-president of this meeting.

Our team at 14th IKDS

Highlights from the meeting:

-269 participants from 23 countries and 6 continents – this embodied the theme of the meeting "***Fostering global collaborations to solve KD.***"

-It was a mix of students, trainees, basic scientists, clinical researchers, clinicians, patients/parents/advocates

-2.5 days full of content from panels addressing worldwide gaps in KD care, genetics, environmental science, artificial intelligence, cardiac imaging, novel therapies, and long term complications

-Breakout sessions addressed navigating difficult cases, discussion between experts and patient advocates, and understanding research careers related to KD. There was a live echocardiography session as well.

Happy reunion with former Japanese fellows at the KDRC (from left to right): Drs. Fujito Numano, Shinsuke Hoshino, Koichi Miyata, Jane Burns, Adriana Tremoulet, Kelly Han, Kirsten Dummer

-Over 250 scientific abstracts were featured and awards were given to 6 trainees who had the best science. We are proud to say that 3 of the 6 were either from our group (Hao Wang, Jonathan Lam) or collaborating with our group (Conor Loy)

-Our group gave 18 different presentations about our research and we enjoyed wonderful reunions with our colleagues and friends from India, UK, Japan, Korea, and the U.S.

Click here for more details

16TH ANNUAL KD PARENT SYMPOSIUM

Brought to you in partnership by:

2024 KD Parent Symposium Panelists

Jane C. Burns, MD
Director
UCSD Kawasaki Disease Research Center

Kirsten Dummer, MD
Pediatric Cardiologist
Rady Children's Hospital San Diego

Koichi Miyata, MD
Pediatric Cardiologist
Keio University, Japan

Lucia Acosta
(*Spanish Interpreter*)

Adriana Tremoulet, MD, MAS
Associate Director
UCSD Kawasaki Disease Research Center

Angie Rodriguez-Verdin, BS
Adult KD Study Coordinator
UCSD Kawasaki Disease Research Center

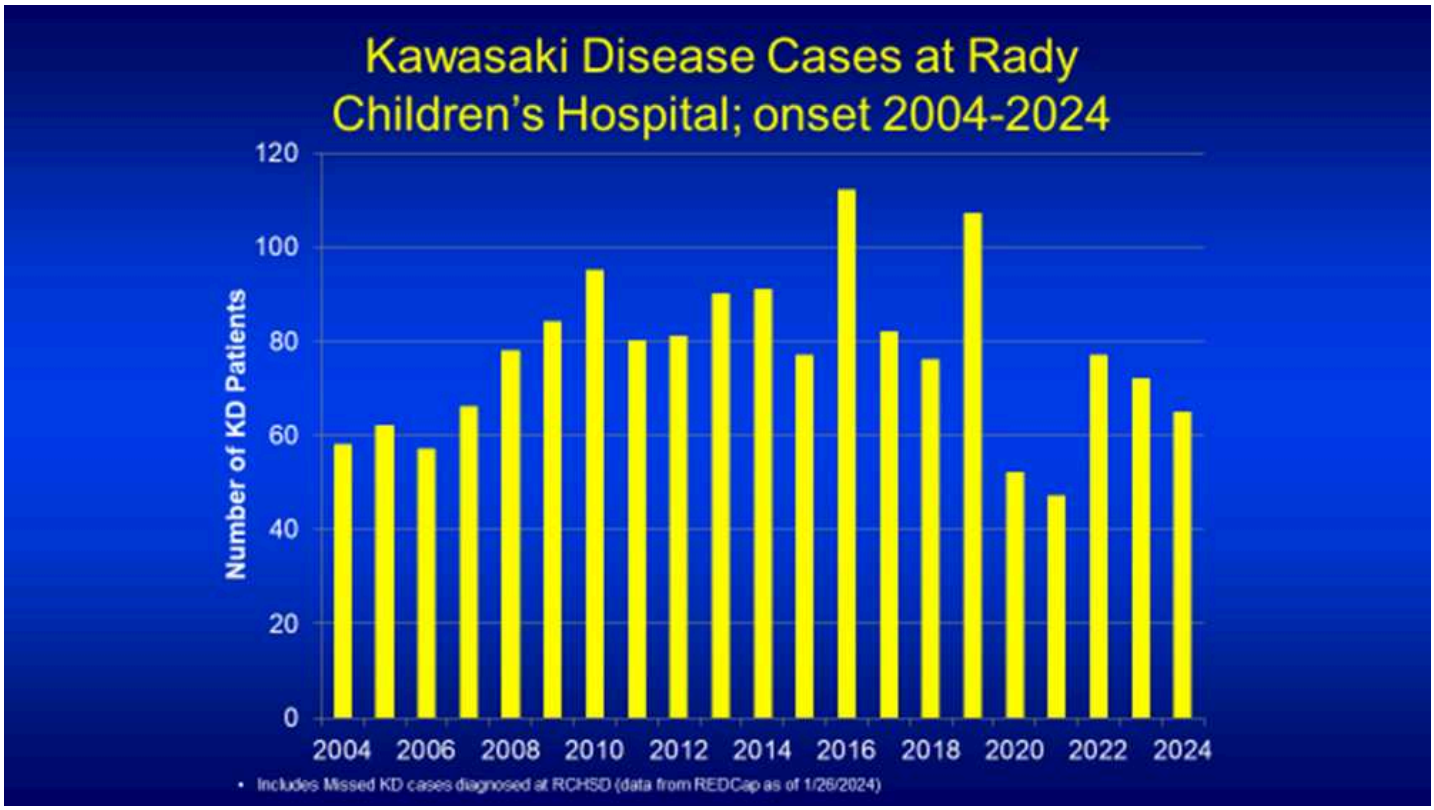
Nadia Copeland, BS
Research Data Analyst
UCSD Kawasaki Disease Research Center

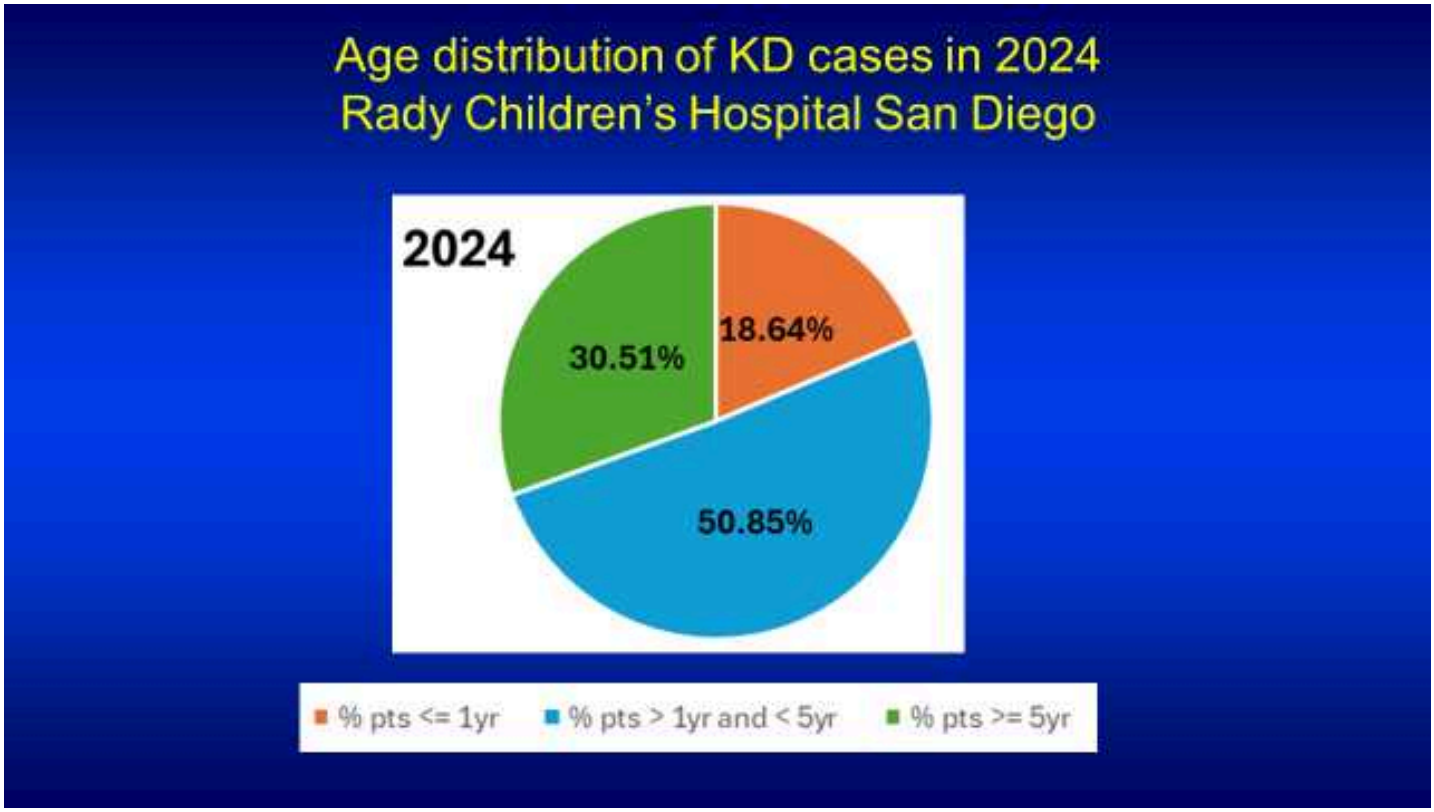
The symposium was held in October 2024 with 85 participants from 27 different countries joining through live-streaming. We were delighted to have Lucia Acosta, one of our KD parents, as our Spanish translator. The recording of the live-stream video has had more than 258 views since then. A huge thank you to the KD Foundation in Boston for facilitating the live-streaming and supporting the event!

Click here to watch the video

@TheKDFoundation **www.kdfoundation.org** **Kdresearch@ucsd.edu**

2024 KD CASES





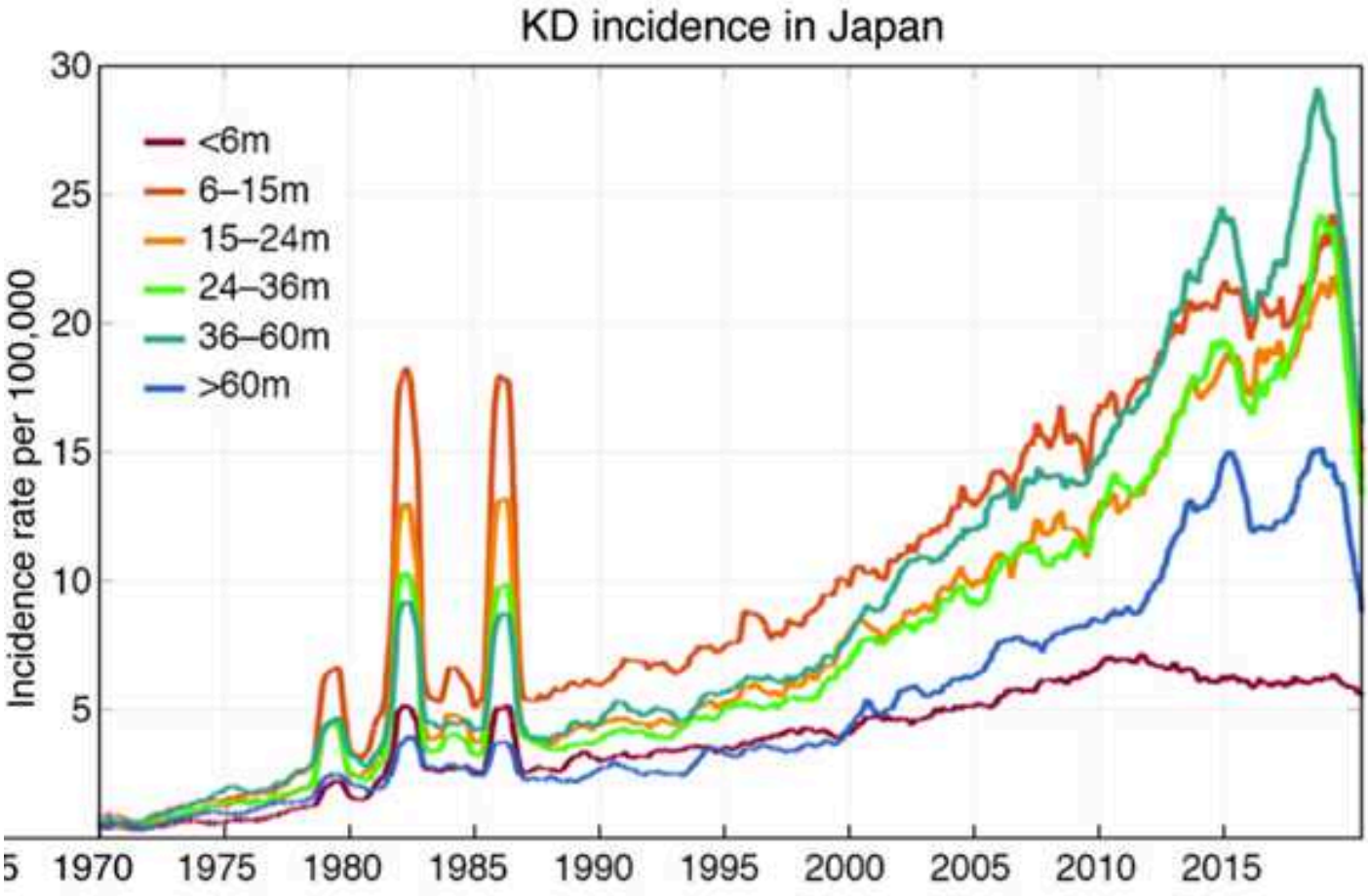
READ ABOUT OUR RESEARCH PUBLICATIONS

1. New insights into KD epidemiology in Japan

Original Investigation | Pediatrics

Age-Dependent Variations in Kawasaki Disease Incidence in Japan

Laurel L. DeHaan, MS; Charles D. Copeland, BA; Jennifer A. Burney, PhD; Yosikazu Nakamura, MD; Mayumi Yashiro, BS; Chisato Shimizu, MD; Koichi Miyata, MD; Jane C. Burns, MD; Daniel R. Cayan, PhD



The 4.5-fold increase in cases in older children occurring from the mid-1990s to 2019 suggests increasing exposure of large populations to an environmental trigger, possibly a wind-borne aerosol. Incidence in infants remained essentially unchanged over three decades, suggesting a different mode of exposure to the KD trigger in this youngest age group. In 2020, reduced exposure due to isolation measures taken during the COVID-19 pandemic resulted in a decrease in KD incidence that was mirrored by other countries around the globe.

DeHaan LL, Copeland CD, Burney JA, et al. Age-Dependent Variations in Kawasaki Disease Incidence in Japan. JAMA Netw Open. 2024;7(2):e2355001. doi:10.1001/jamanetworkopen.2023.55001

Click here to read the article

READ ABOUT OUR RESEARCH PUBLICATIONS

KAWASAKI DISEASE RESEARCH CENTER
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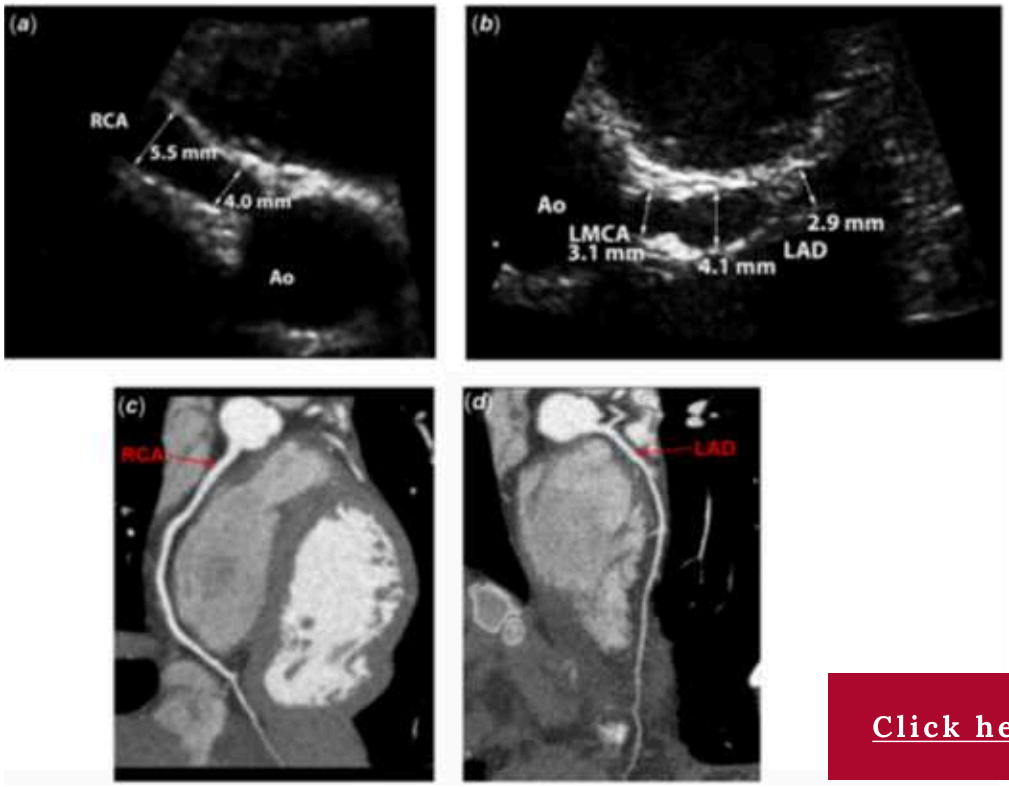
2. Giant aneurysms can heal!

The long-term vascular and myocardial outcomes in selected Kawasaki disease patients with regression of giant coronary artery aneurysms

Samuel C. Kung[1], Koichi Miyata[1], Gabrielle M. Colvert[2], Andrew M. Kahn[3], Lori B. Daniels[3], Shinsuke Hoshino[1], Kirsten B. Dummer[1,4], Ian Fraser Golding[1,4], Samantha Roberts[1,4], Chisato Shimizu[1], Adriana H. Tremoulet[1,4], Elliot R. McVeigh[2], John B. Gordon[5] and Jane C. Burns[1,4]

Kung SC, Miyata K, Colvert GM, et al. The long-term vascular and myocardial outcomes in selected Kawasaki disease patients with regression of giant coronary artery aneurysms. Cardiology in the Young. Published online 2024:1-8. doi:10.1017/S104795112403614X



Imaging of the coronary artery aneurysms by echocardiography during acute KD with paired coronary artery CT images performed 13 years later.

Echocardiography was performed during the acute phase of KD at age 3 months.

CT images show complete regression of his right CAA (C) and LAD CAA (D) 13 years later.

Click here to read the article

READ ABOUT OUR RESEARCH PUBLICATIONS

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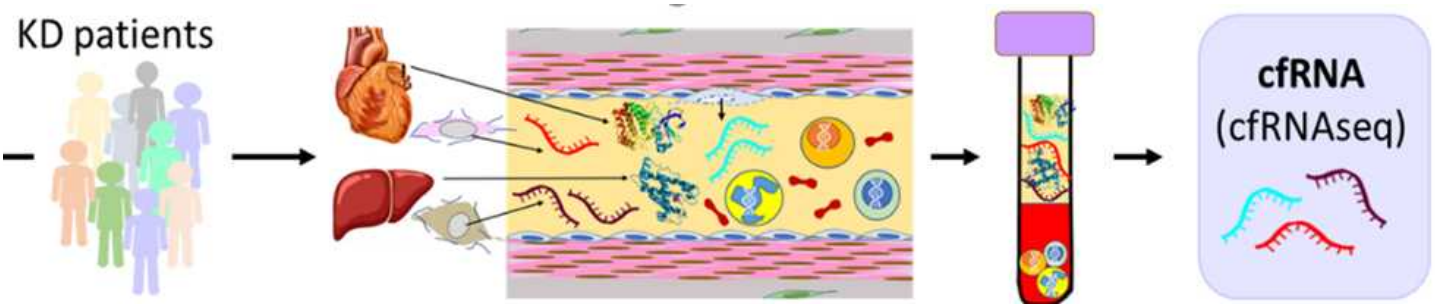
3. Cell-free RNA provides hope for a robust diagnostic test for KD

PNAS RESEARCH ARTICLE | MEDICAL SCIENCES OPEN ACCESS

Plasma cell-free RNA signatures of inflammatory syndromes in children

Conor J. Loy[a], Venice Servellita[b], Alicia Sotomayor-Gonzalez[b], Andrew Bliss[a], Joan S. Lenz[a], Emma Belcher[a], Will Suslovic[c], Jenny Nguyen[b], Meagan E. Williams[c], Miriam Oseguera[b], Michael A. Gardiner[d,e], P.E.M.K.D.R.G.[1], the C.H.A.R.M.S. the Study Group[1], Jong-Ha Choi[f,g], Hui-Mien Hsiao[f,g], Hao Wang[e], Jihoon Kim[h], Chisato Shimizu[e], Adriana H. Tremoulet[d,e], Meghan Delaney[c,i], Roberta L. DeBiasi[c,i], Christina A. Rostad[f,g], Jane C. Burns[d,e,2], Charles Y. Chiu[b,j,k,2], and Iwijn De Vlaminck[a,2]



Cell-free RNA is released into the bloodstream when cells are injured or dying and thus provides a window on tissue injury. We are working with a fabulous team at Cornell University led by Prof. Iwijn De Vlamink and his post-doc, Conor Loy, to develop cfRNA as a potential diagnostic test for KD. This work is being funded through the generous support of the Macklin Foundation.

This study provides a proof of concept that circulating RNA in blood plasma can be used to differentiate multiple inflammatory syndromes in children that are difficult to diagnose clinically, as well as provide evidence that circulating RNA in blood plasma can also be used to characterize organ damage using the same assay.

Loy, C. J., Servellita, V., Sotomayor-Gonzalez, A., Bliss, A., Lenz, J., Belcher, E., Suslovic, W., Nguyen, J., Williams, M. E., Oseguera, M., Gardiner, M. A., Pediatric Emergency Medicine Kawasaki Disease Research Group (PEMKDRG), CHARMS Study Group, Choi, J. H., Hsiao, H. M., Wang, H., Kim, J., Shimizu, C., Tremoulet, A., Delaney, M., ... Vlaminck, I. (2024). Plasma Cell-free RNA Signatures of Inflammatory Syndromes in Children. medRxiv : the preprint server for health sciences, 2024.03.06.24303645. https://doi.org/10.1101/2024.03.06.24303645

Click here to read the article

JOIN THE ADULT KD STUDY

KAWASAKI DISEASE RESEARCH CENTER
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Longitudinal Study On Long-term Effects of KD

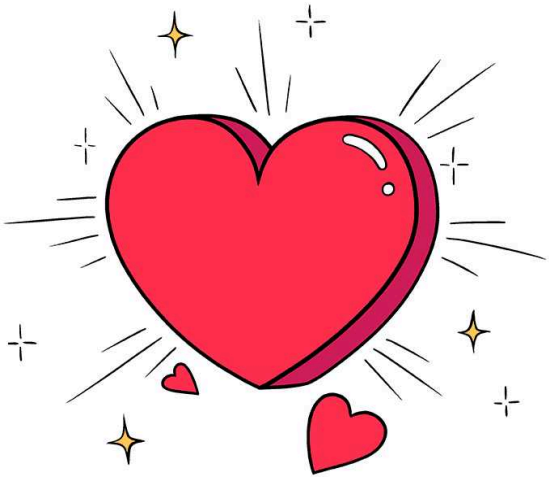
At the KDRC, thanks to funding and support from the Gordon and Marilyn Macklin foundation, our team of researchers continues to work toward a greater understanding about the short- and long-term health outcomes of Kawasaki Disease patients through the AKD study.

If you or a loved one had KD in childhood and would like to help our team gain more insight into the long-term effects of KD in adults, we invite YOU to participate in the study!

To learn more about the study and how to participate, email us at adultkd@health.ucsd.edu. We hope you join the study today and become part of something bigger!

What Is The AKD Study?

Longitudinal questionnaire survey to learn about the cardiovascular and general health of individuals who experienced KD in childhood



What Does The Study Involve?

•An online, detailed health questionnaire

•A follow-up health questionnaire every 2 years

•An optional blood sample for subjects in San Diego

Visit our website

Why A Health Questionnaire?

•Comparison of adults with a history of Kawasaki Disease to other adults

•Insights about the long-term outcomes for KD patients

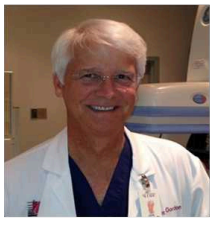
Who Can Participate?

•KD Participants: Adults who had KD in childhood

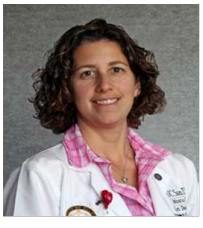
•Control participants: Adults who NEVER had KD in childhood.

The Adult KD Team

Jane C. Burns,
MD
Director
Principal Investigator



John B. Gordon,
MD
Cardiologist



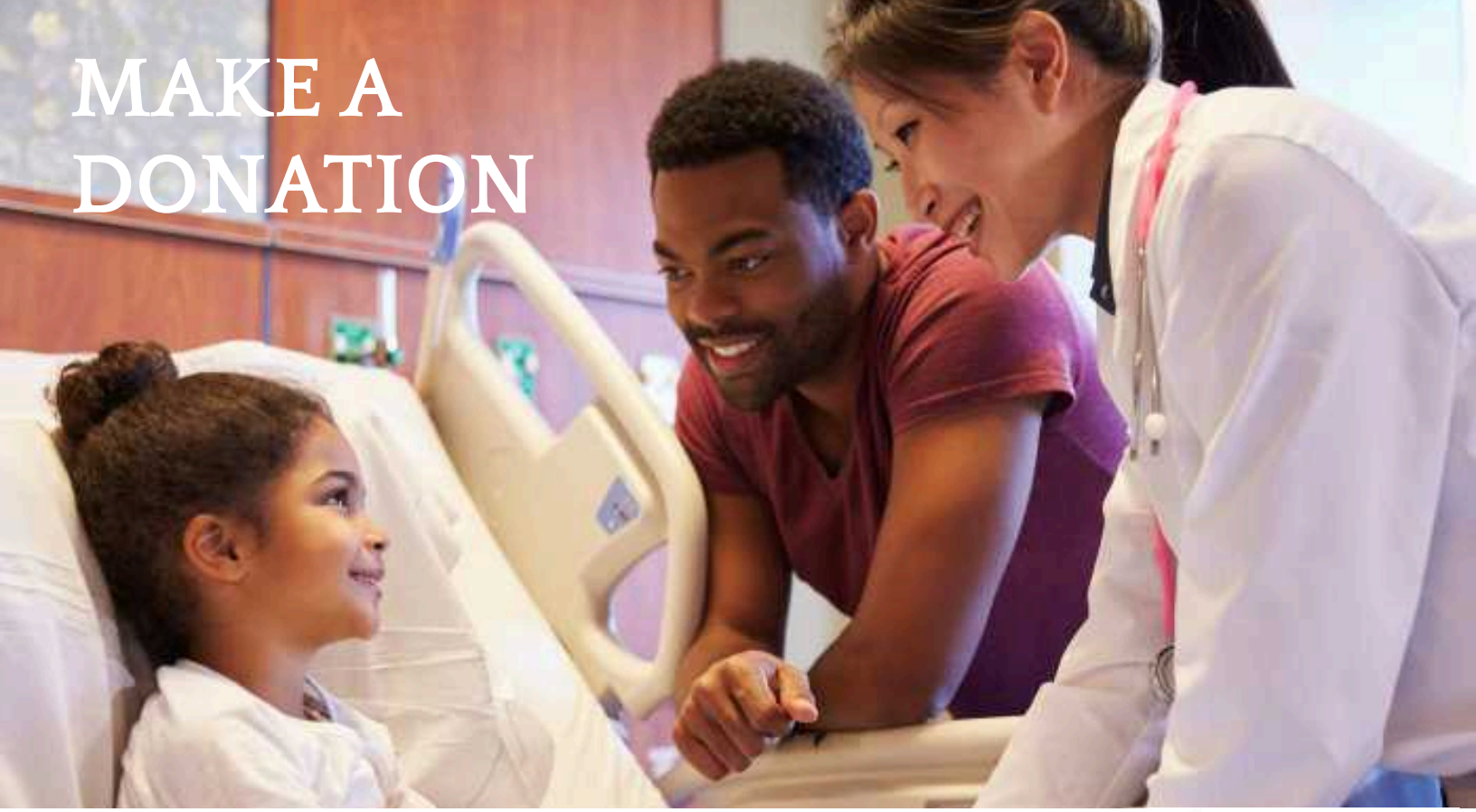
Lori B. Daniels,
MD, MAS
Cardiologist

Jiken Bhatt,
MD
Cardiologist

Kirsten Dummer,
MD
Cardiologist

Angie R. Verdin,
BS
Clinical
Research Coordinator

MAKE A DONATION



SHOW YOUR SUPPORT THIS HOLIDAY SEASON

We are so grateful to the wonderful families whose donations have made all the research progress possible. Our challenge going forward is to continue to support our important research. Our team at the KDRC relies entirely on grant support and donations to understand the disease and improve outcomes for KD patients here in San Diego and worldwide. We hope you will consider a gift to support KD research this holiday season.

THE GORDON AND MARILYN MACKLIN FOUNDATION is supporting Rady Children's groundbreaking research to improve the diagnosis and treatment of Kawasaki Disease (KD). The Foundation will match donations up to $862,225 over the next three years to fund two key projects:

- RAPID BLOOD TEST: Developing a quick and accurate blood test to diagnose KD early.
- CLINICAL DECISION SUPPORT TOOL: Creating a tool to help doctors identify KD more efficiently.

These innovations have the potential to significantly improve outcomes for children with KD.

To make a gift online, visit: **Donate to Rady Children's Hospital**. Select **"Other"** in the Gift Designation drop down box and type **"KD research"** in the text box labeled "Designation of your choice".

Or, contact Amy Weeks, Assistant Vice President of Philanthropy, aweeks@rchsd.org or (858) 966-8116.

Thank you for helping to fund life-saving discoveries for children with Kawasaki disease.

DONATE NOW

KAWASAKI DISEASE RESEARCH CENTER
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Late features of Kawasaki Disease

Peeling of fingers or toes

{Periungual Desquamation)

Keep an eye out for peeling on your child's fingertips and toes! Patients with Kawasaki disease may develop this type of thick peeling around the fingernails or toenails, usually two weeks after the start of their illness.

Nail indentations

(Beau's Lines)

Search for horizontal nail grooves appearing six weeks after the onset of Kawasaki disease.

If your child develops **peeling** under the nailbed or **grooves across the nail** following an illness that involved **fever, rash,** and **red eyes,** please contact your doctor and ask about Kawasaki disease. If there are concerns for missed Kawasaki disease, your doctor can contact the hospital page operator at 858-576-1700, ext. 0 between 9am and 5pm and ask to speak to the Kawasaki disease doctor on call.

To learn more about Kawasaki disease, watch **"Kawasaki disease: A Parent Guide"** on YouTube and visit the KD Research Center website at **https://medschool.ucsd.edu/som/pediatrics/research/centers/kawasaki-disease**

Rady Children's Hospital San Diego

KAWASAKI DISEASE RESEARCH CENTER
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I was diagnosed with Kawasaki Disease when I was __ years old.

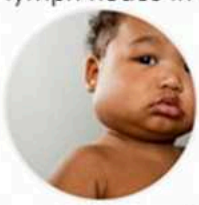
What is Kawasaki Disease?

Kawasaki Disease (KD) is an inflammatory disorder that can affect the heart and the coronary arteries. Some signs of KD are:

- Fever
- Rash
- Swollen lymph nodes in the neck

Bloodshot eyes

Red lips and tongue



Swollen hands and feet

When left untreated, up to 25% of patients can develop swelling of the small arteries in the heart named coronary arteries. If the swelling is significant (aneurysm), there is a risk of a blood clot and heart attack.

Echocardiogram results

Z-scores of the coronary arteries indicate the size of your coronary artery compared to normal values based on body size. For those who have a persistently abnormal Z-score, it is important to follow up with an adult cardiologist after your last visit in KD clinic at Rady Children's Hospital.

Z-Score	Evaluation
< 2	Normal
2.0 - 2.4	Dilated
2.5 – 4.9	Small aneurysm
5.0 – 9.9	Large Aneurysm
> 10	Giant Aneurysm

My Z–scores:

☐ My Z-scores were always in the normal range
☐ My Z-scores were dilated but resolved.
Max : _____
☐ My Z-scores are persistently abnormal.
Max : _____ Current : _____

Other changes on the echo

☐ Patent Foramen Ovale (PFO) is a natural hole between the top chambers of the heart. About 20% of people still have a PFO as an adult. If you have a PFO, you should avoid deep scuba diving and discuss with your PCP.

Things I should know

Things to consider for heart healthy lifestyle

Good for Heart

- **Exercise**
- **Maintain ideal weight for height :**

Current percentile for height : _____
weight : _____

- **Maintain normal blood pressure :**

My blood pressure today : _____

- **Maintain a heart healthy diet**
- **Maintain normal blood values for lipids**

My recent total cholesterol, HDL, and LDL value :
Date : _____
Cholesterol : _____ (Heart Healthy : < 200)
HDL : _____ (Heart healthy : > 60)
LDL : _____ (Heart healthy : <100)

Avoidance of the following are very important to keep your heart healthy:

- **Tobacco/Cigarettes**
- **Amphetamines**
- **Cocaine**

Medications for my heart recommended by my Kawasaki Doctor:

☐ None
☐ Aspirin
☐ Plavix
☐ Statin _____
☐ Direct oral anticoagulant _____

Why did I have Kawasaki Disease?

You had Kawasaki Disease because:

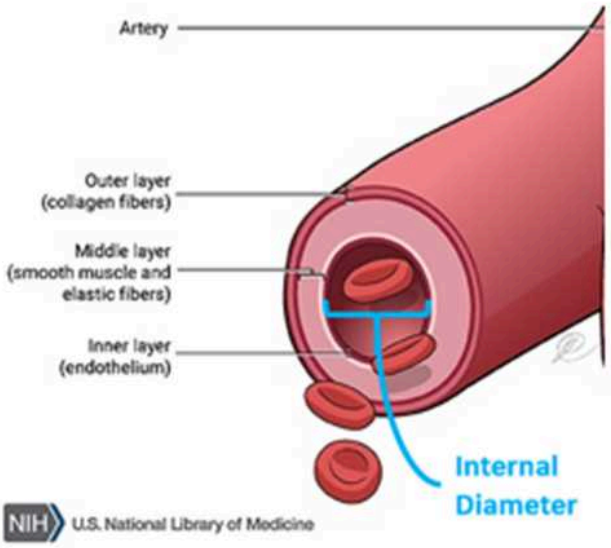
1. You have a pattern of genes which made you susceptible to KD and
2. You breathed in something from the air that triggered KD (the exact agent is not yet known)

Because you carry the genetic pattern for KD, if you have children in the future, they may inherit this pattern and be at slightly greater risk of developing KD.

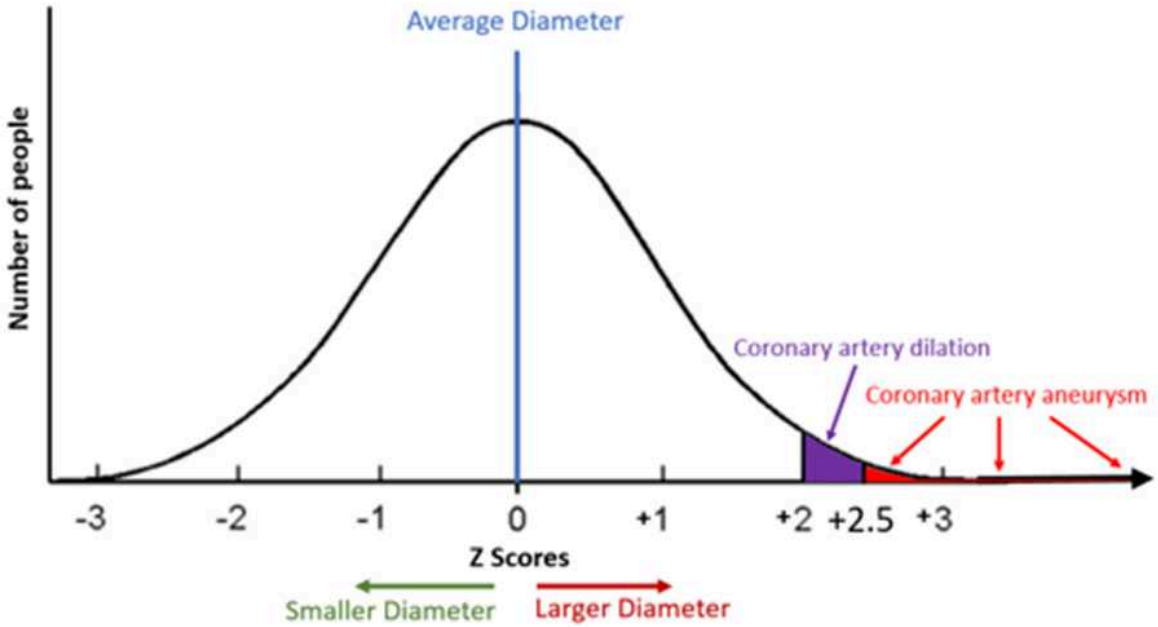
Kawasaki Disease: Z Scores

WHAT IS A Z SCORE?

A Z score normalized for body surface area represents how much larger (or smaller) a *measured* coronary artery internal diameter is compared to the average coronary artery diameter for a child of the same size (body surface area includes both height and weight). The average diameter is assigned a Z score of 0. Positive Z scores reflect larger diameters, while negative Z scores reflect smaller diameters.



Most individuals (~95%) have coronary artery Z scores between -2 and +2, and are considered to have normal coronary arteries (see figure below). A coronary artery Z score **between +2.0 and less than +2.5** (i.e., 2 to less than 2.5 standard deviations above the average normalized for body surface area) is considered **dilated**. A coronary artery with a Z score **between +2.5 and less than +5.0** is considered a **small aneurysm**. A Z score **between +5.0 and less than +10.0** is considered a **large aneurysm**. A Z score of **+10.0 or greater** is considered a **giant aneurysm**.



WHY DO WE USE Z SCORES WHEN MEASURING CORONARY ARTERY INTERNAL DIMENSIONS?

Coronary artery aneurysms can be measured in millimeters (mm). However, this measurement does not account for body size. How big the coronary artery should be depends on the size of the child. For instance, a 4-mm aneurysm in a 1 year-old patient carries more severe long-term cardiovascular risks compared to a 4-mm aneurysm in a 10 year-old patient. In contrast, Z scores normalized for body surface area account for body size. This allows us to accurately assess and track aneurysm size over time (i.e., as the patient grows).