

Summary of the 1st to 27th Nationwide Epidemiological Surveys of Kawasaki Disease in Japan

**Specified Non-profit Organization
Japan Kawasaki Disease Research Center
Yoshio Imada (Chairman of the Board of Directors)
Hiroshi Yanagawa (Editor-in-chief)**

March 2024

Greeting
Yoshio Imada
Chairman of the Board of Directors

The first nationwide survey on Kawasaki disease in Japan started by Professor Itsuzo Shigematsu (Director of the Department of Epidemiology of the Institute of Public Health) in 1970 with support of a Science and Technology Research Grant from the Ministry of Health and Welfare. Since then, it has been conducted once every two years, bringing the total number of 27 surveys over 50 years. This work has been passed on to Drs. Hiroshi Yanagawa and Yosikazu Nakamura (Both Professor of the Department of Public Health, Jichi Medical University). The surveys have clarified the epidemiological pictures of the disease, contributing greatly to the investigation of the causes and to the establishment of treatment methods as well.

Dr. Tomisaku Kawasaki repeatedly pointed, during his lifetime, that when considering the cause of a disease, the most important thing is not to contradict the epidemiological pictures. In 1992, the Japan Kawasaki Disease Research Center was established as a non-profit organization with the aim of investigating the cause of Kawasaki disease.

The center has supported the epidemiological surveys on Kawasaki disease as its main project, since the 16th Nationwide Epidemiological Survey. With the 27th survey, we have decided to conclude the current form of the nationwide survey, and have summarized the results of the survey to date. We hope that the results of the survey will be found this useful as a reference for the future research on Kawasaki disease. We would like to express our sincere gratitude to the pediatricians who took time out of their busy schedules to cooperate with the surveys.

Greeting
Yosikazu Nakamura
Professor Emeritus of Jichi Medical University
In compiling the Results of 27 Nationwide Surveys on Kawasaki disease in Japan

The nationwide surveys on Kawasaki disease, which have been conducted for more than half a century since 1970, ended with the 27th survey in 2023. In 1967, Dr. Tomisaku Kawasaki first reported a total of 50 cases, and three years later, consistent epidemiological survey focused on the epidemiology of new diseases and on the clinical medicine, including countermeasures and treatment. We believe that this survey has presented the ideal form of research as a foundation for epidemiology and countermeasures and treatment when a new disease emerges.

We have presented the ideal form of research as a foundation for research in medical fields. In addition, this research method has greatly influenced subsequent epidemiological studies of various diseases, especially descriptive epidemiological studies of chronic diseases with unknown etiologies.

The national survey would not have been possible without the cooperation of pediatricians across the country, as well as the Kawasaki disease patients and their families. I would like to express my sincere gratitude. We would also like to thank the "Parents Association of Children with Kawasaki Disease" for supporting this study, and the Japan Kawasaki Disease Research Center, a non-profit organization, for providing financial support after the research funds from the government were no longer available.

Finally, I would like to report on the completion of the nationwide epidemiological survey to three great seniors who have already passed away, Dr. Tomisaku Kawasaki, who first reported Kawasaki disease and led the survey, Dr. Itsuzo Shigematsu, who started the nationwide survey, and Mr. Mitsuru Asai, the first representative of the Association of Parents of Children with Kawasaki Disease. I sincerely wish for the soul to rest in peace.

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We welcome your comments on this report, such as your memories of Dr. Kawasaki, the Kawasaki disease epidemiological survey, and future prospects for the investigation of the cause of Kawasaki disease.

Please contact us below.

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Hiroshi Yanagawa

Professor Emeritus of Jichi Medical University

History of the 27 Nationwide Surveys of Kawasaki Disease to the Present

1. Motivation for conducting the Kawasaki disease nationwide survey

In February 1970, when Dr. Tomisaku Kawasaki visited the Ministry of Health and Welfare to apply for a medical research grant from the Ministry of Health and Welfare, Dr. Shunichi Kakurai, then Scientific Counselor, told him to conduct an epidemiological survey, and on the advice of the counselor, he visited Dr. Itsuzo Shigematsu, Director of the Department of Epidemiology, National Institute of Public Health. This led to Dr. Shigematsu undertaking the nationwide epidemiological survey of Kawasaki disease, and the Pediatric MCLS Research Group (led by Dr. Fumio Kosaki, Director of the Department of Pediatrics, Japan Red Cross (JRCS) Central Hospital*) was organized in 1970 with a medical research grant from the Ministry of Health and Welfare.

*Japan Red Cross (JRCS) Central Hospital is named JRCS Medical Center at present.

This was the beginning of a multicenter joint study and a nationwide epidemiological survey of Kawasaki disease, and Hiroshi Yanagawa was put in charge of the epidemiological investigation. In the first year of the research group, the main tasks of the research group were (1) preparation of a "Diagnostic Guidelines" for epidemiological investigations, (2) the implementation of a nationwide epidemiological survey, and (3) the clinical evaluation of fatal cases, and in January 1971, the first nationwide epidemiological survey of Kawasaki disease was conducted with close coordination and cooperation between epidemiologists and pediatricians.

2. 50-year history

Over the next 50 years, 27 national epidemiological surveys have been conducted uninterrupted. In 1977, Yanagawa was transferred from the National Institute of Public Health to Jichi Medical University, and the three surveys from the fifth survey (1979) to the seventh survey (1983) were conducted by Dr. Shigeo Shibata and Dr. Hidehiko Tamashiro of the Department of Epidemiology, National Institute of Public Health. From the 8th survey (1985) to the 15th survey (1999), Yanagawa was again in charge of the eight surveys at Jichi Medical University. In 1999, Yanagawa moved to Saitama Prefectural University, and from the 16th survey (2001), he asked his successor, Professor Yosikazu Nakamura, to conduct the survey, and he continued to conduct 12 surveys for 22 years until the 27th survey (2022).

Staff members, including Ms. Kazuko Takeuchi and Ms. Sumiko Ishikawa of the Department of Epidemiology of the National Institute of Public Health, Ms. Yoshie Terauchi, Ms. Hiroko Hasegawa, and Ms. Mayumi Yashiro of Jichi Medical University, and Ms. Michiko Kawashima of Saitama Prefectural University, cooperated as unsung heroes, so to speak, and successfully protected the data of a total of 445,688 Kawasaki disease patients. In particular, Ms. Mayumi Yashiro has been effectively responsible for 19 nationwide epidemiological surveys for 38 years since 1985, and has made

unreasonable requests to her in all aspects of the survey, including survey planning, liaison and coordination with medical institutions, data processing, statistical analysis, maintenance and updating of patient databases, and report preparation.

The clinical aspects of this study were supported by the cooperation and guidance of a large number of pediatricians. Dr. Fumio Kosaki, Dr. Tomisaku Kawasaki, Dr. Sanji Kusakawa, Dr. Hirohisa Kato, and Dr. Kensuke Harada, who have served as the heads of the Kawasaki Disease Research Group of the Ministry of Health and Welfare in various ways, as well as Dr. Sumio Okawa, Dr. Tomoyoshi Sonobe, Dr. Yoshio Imada, Dr. Seijiro Aso, Dr. Keiji Tsuchiya, and other pediatricians at the JRCS Medical Center, Dr. Shigehiko Kamoshita, who supported this survey from various aspects, I would like to express my gratitude to Dr. Kamoshita, Dr. Masayoshi Yanagisawa and other doctors in the Department of Pediatrics at Jichi Medical University. In addition, it must be noted that the fact that we have been able to conduct a nationwide epidemiological surveys of Kawasaki disease for 50 years is due to the extraordinary cooperation of pediatricians nationwide. I would like to express my gratitude and heartfelt respect to the doctors who filled out the troublesome questionnaire as a complete volunteer in between their busy medical treatments

In the early stages, the expenditures required for the nationwide epidemiological surveys of Kawasaki disease included research grants from the Ministry of Health and Welfare (Ministry of Health, Labour and Welfare) and scientific research funds from the Ministry of Education, Culture, Sports, Science and Technology (MEXT). However, it became difficult to continue for a long period of time, and from 1999 to 2023, it was taken up as a research project of the Japan Kawasaki Disease Research Center and was able to continue until now. I would like to express my deepest gratitude to the Japan Kawasaki Disease Research Center.

Over the past 50 years, information processing technology, especially computers, has made remarkable progress. The 1st to 3rd nationwide survey was conducted in the early 1970s, and I can not forget that at that time, I had to punch holes in 80-digit punch cards, carry heavy boxes of cards in 2,000 cases each, go to a private computer company, pay over tens of thousands of yen an hour, and struggle with the FOTRAN program. In addition, I experienced many critical situations, such as torn punch cards, unreadable data on magnetic tapes, and inability to convert data. With regard to updating past computer files, Dr. Takeshi Kawaguchi of the Saitama Prefectural Department of Health and Environment at the time cooperated with us to overcome the crisis.

Since then, generations of computers have changed one after another, and until the first half of the 1980s, we relied on the power of large computers, but since the 9th national epidemiological survey, personal computers have advanced rapidly, and it has become possible to work on a tabletop. However, we had to go through the generational changes of computers that came one after another, and the progress and selection of application programs.

3. Appearance on the international stage

In September 1974, the first paper on Kawasaki disease was published in the international journal *Pediatrics*, and the existence of Kawasaki disease was recognized internationally.

[Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H. A new infantile acute febrile

mucocutaneous lymph node syndrome (MLNS) prevailing in Japan (Pediatrics 1974; 54:271-276) (The contents of the paper was mainly epidemiology and clinical pictures)]

Later, in September 1980, the symposium on Kawasaki disease was taken up at the 16th International Congress of Pediatrics held in Barcelona, Spain. For the first time, Kawasaki disease was widely discussed at an international conference, and a large number of pediatricians gathered to make room for a standing cone, and it caused a great international reaction. All of this added up to make Kawasaki disease the world's Kawasaki disease.

4. Joint Research with China

The purpose of the Japan-China joint research is to clarify whether there are any differences in the epidemiology of Kawasaki disease between Japan and China, and second, to provide experience in the diagnosis and treatment of Kawasaki disease in Japan to Chinese pediatricians, and to contribute to the dissemination of early diagnosis and appropriate treatment methods. The person who played a central role in the realization of this joint research was Professor Zhang Tuohong of the School of Public Health at Peking University at the time.

In selecting the target areas, we listened to the opinions of the research teams of Japan and China and the Chinese government, and selected 10 regions in consideration of regional representativeness and economic development. These provinces are **Jiangsu, Shaanxi, Beijing, Guangdong, Heilongjiang (Harbin District), Liaoning (Dalian), Shanghai, Chongqing, Sichuan and Yunnan**. The subjects of the surveys were inpatients in the past five years at major hospitals in each region. In conducting the survey, we used questionnaires used in the national epidemiological survey in Japan and the "Diagnostic Guidelines".

5. Future Challenges

At this point, we believe that the goal of the nationwide survey has been almost achieved, and we have decided to conclude this survey with the 27th survey. In the future, when conducting a new form of Kawasaki disease epidemiological survey, it should not be a continuation of the nationwide survey that has been carried out so far, but should narrow down the purpose of the survey, select the survey subjects on the scale necessary to achieve the purpose, and determine the content of the survey.

[Note 1]

Epidemiology of Kawasaki Disease - A Summary of 30 Years (Editors: Hiroshi Yanagawa, Yoshikazu Nakamura, Mayumi Yashiro, Tomisaku Kawasaki, April 30, 2002, Diagnosis and Treatment)

[Tomisaku Kawasaki]

It can be said that the encounter with this patient was decisive in the author's subsequent fate. In other words, about a year later, in 1962, I encountered the second case, and I was convinced of the uniqueness of this disease, and as I experienced similar cases one after another, I was fascinated by its uniqueness, immersed myself in clinical research on this disease, and fell into its depths, and finally

could not get out of the abyss. At that time, I was aware that I was not a good fit with the bureaucratic JRCS, so I was secretly trying to choose the path of spiritual freedom.

Thus, in retrospect, the six years leading up to the submission of the original article to "Allergy (A journal)" in 1967 were the period in my life when I was most focused on a single purpose, both physically and mentally. At the beginning of 1967, there was a debate at the Tokyo Regional Assembly of the Japan Society of Pediatrics as to whether or not this disease was Stevens-Johnson syndrome, and its uniqueness was temporarily denied, but after a series of case reports at the level of each regional association, Director Fumio Kosaki ordered me to apply for research funds from the Ministry of Health and Welfare, but in 1969 it failed. The following year, in 1970, when I applied again, I caught the attention of Dr. Shunichi Kakurai, Scientific Counsellor in the Minister's Secretariat at the time, and introduced me to Dr. Itsuzo Shigematsu, and with his help, a research group of the Ministry of Health and Welfare was established with a scientific research grant, and the first nationwide survey was conducted under the leadership of Dr. Shigematsu, and new facts that pediatric clinicians had never imagined were demonstrated one after another, and the reality of Kawasaki disease was highlighted for the first time. The uniqueness of this disease was solidified. This is thanks in part to joint research between clinical practice and epidemiology. Since then, the Ministry of Health and Welfare research team has had some twists and turns, but epidemiological surveys have been passed down from Dr. Shigematsu to Dr. Yanagawa, and a total of 16 nationwide surveys have been conducted by the end of 2000

I am delighted to announce the publication of "The Epidemiology of Kawasaki Disease: A Review of 30 Years." However, research on Kawasaki disease is now at a critical juncture. First, it is necessary to elucidate the cause of Kawasaki disease and establish preventive methods. To do this, it is necessary to prove an etiology that satisfies the data of epidemiological studies in Japan. The second question is whether Kawasaki disease can be said to be a risk factor for juvenile arteriosclerosis in future patients. Pursuing this issue requires decades of long-term follow-up and intergenerational continuity of the epidemiologists in charge. Fortunately, Dr. Nakamura has succeeded Dr. Yanagawa in Kawasaki disease epidemiology research in Japan, and cohort studies of about 6,500 patients have been ongoing for 10 years. There is still a long way to go, but I hope that the final data will be compiled eventually.

[Yosikazu Nakamura]

The first time I became involved with Kawasaki disease was 20 years ago, in the fall of 1982. That spring, I had just graduated from university, and I was a student at the National Institute of Public Health in Tokyo at the time, but I was conducting research with Dr. Yanagawa. In an evening, while I was killing time at the medical office (I don't know if I can say that, but there is still an unofficial position such as "Acting Medical Director's Knowledge"), Dr. Yanagawa brought me the data of infectious disease surveillance, which was published for the first time at that time, and gave me the task of comparing it with the incidence trend in the national survey of Kawasaki disease.

When I was a student, I was an unserious medical student who rarely attended lectures. Naturally, therefore, the fledgling researcher who had grown hair on this uneducated student and passed the national examination for medical doctors by fluke, thought that the frequency of the occurrence of infectious

diseases was as self-evident as the incidence of other diseases, as was the case with ordinary people today. So, while wondering, "Why is I doing this research now?", I summarized the results and reported them at the research group meeting in January of the following year. After the group meeting, I had a drink with Dr. Kawasaki for the first time with Dr. Yanagawa at a yakitori restaurant in front of the station in Ueno (Mr. Kawasaki's personality is evident in a place that is not a high-end restaurant in Ginza).

At the yakitori restaurant, I was nervous with Mr. Dai, and Mr. Kawasaki asked, "Is Mr. Nakamura single?" "Actually, I'm thinking of getting married in the fall, and my partner works at the doctor's hospital (Red Cross Medical Center)," he confessed. As a result, I was able to have Mr. and Mrs. Kawasaki come as the guest of honor at the wedding on September 23, 1983, when I asked Mr. and Mrs. Yanagawa to serve as a mediator.

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The wedding was held at the Hongo Kaikan near Yotsuya Station. I didn't choose it because I was a railroad enthusiast, it was just that my wife had found a place. However, this "place" was a big hit. In his guest of honor, Dr. Kawasaki said, "Recently, I have been invited to doctors' weddings, but they are all luxury hotels. Compared to that, there are doctors like this who don't care about money (although they didn't say "I'm going to have a ceremony in a poor place")." He wept. Needless to say, after that, every time my friends had a wedding at a luxury hotel, the people around me commented that it was a venue that Dr. Kawasaki seemed to dislike.

I wanted to write it down somewhere, and it is my personal history in Kawasaki disease research.

[Mayumi Yashiro]

Finally, the publication of "The Epidemiology of Kawasaki Disease: A Summary of 30 Years," which can be said to be the culmination of the 30 years since the beginning of the history of Kawasaki disease, has been realized, and I am deeply moved.

My first encounter with Kawasaki disease dates back 17 years. It's 1985. The following year,

there was a third nationwide epidemic, and two years later, the ninth nationwide survey was conducted. Since then, I've been through as many as eight nationwide surveys. It took a considerable amount of time to complete the process (request questionnaires, collection, input, and aggregation) until each and every one was completed. In the beginning, there were no magnetic media that could store large amounts of data, so it was nerve-wracking to manage patient database files, and combining them with past patient data files was a series of data compatibility problems, the introduction of Windows, and the year 2000 problem. Therefore, I have a deep attachment to "Kawasaki disease", and my relationship with "Kawasaki disease" is directly connected to the history of the evolution of computers in my mind. I also feel that thanks to "Kawasaki disease", I have improved my computer a little.

These valuable assets of Kawasaki disease patient data are provided by pediatricians nationwide, and are the result of the support and cooperation of pediatricians. I would like to ask for the continued cooperation and understanding of all the doctors, and I am determined to make every effort to help investigate the cause of "Kawasaki disease" as soon as possible.

I would like to express my sincere gratitude to all the teachers who have supported me a lot, and to Dr. Yanagawa for giving me the opportunity to be involved in such a valuable work, and for always giving me words of gratitude and encouragement. Thank you very much..

[Hiroshi Yanagawa]

Omitted because it partially overlaps with the main text

[Note 2]

Summary of Kawasaki Disease Epidemiology Research (Slides)

Slides summarizing the history of the Kawasaki Disease National Epidemiological Survey and related international exchanges have been prepared (see Appendix (3) History of Kawasaki Disease and Epidemiological Research)

Yosikazu Nakamura

Professor Emeritus of Jichi Medical University

Summary of the Results of 27 Nationwide Surveys on Kawasaki disease in Japan

The nationwide surveys on Kawasaki disease, which began in 1970, have been conducted approximately once in every two years, and have continued until the 27th survey in 2023, clarifying the epidemiological and clinical pictures of Kawasaki disease in Japan. The summary of the results is as follows.

Table 1 shows the numbers of surveyed facilities, responding facilities, facilities with patients, and reported patients since the first survey. Targeted facilities were basically hospitals with 100 or more beds and with pediatric department, and pediatric specialty hospitals with less than 100 beds were also targeted.

Table 2 shows the yearly number of patients reported by diagnosis category. A total of 445,688 Kawasaki disease patients were reported. Based on various studies, it is estimated that the patient coverage rate was over 90%. **Figure 1** shows the yearly number of reported patients by sex. The number of patients gradually increased during the 1970s, and the first national epidemic was observed in 1979, followed by the second in 1982 and the third in 1985-1986. After that, no such nationwide epidemic was observed, but the number of patients showed an increasing trend from the mid-1990s, and in the mid-2010s, the number of patients reported exceeded the previous highest number in 1982. However, in 2020, the number of patients decreased by about two-thirds from the previous year, and this trend continued in 2021 and 2022. **Figure 2** shows the yearly incidence rate by sex (per 100,000 population aged 0-4 years). Due to the impact of the declining birthrate, the increase in incidence rate since the mid-1990s has exceeded the increasing trend in the number of patients.

Table 3 shows the number of patients and incidence rates by prefecture from 2019 through 2022. No regions were observed where prefectures with high incidence rates were concentrated.

Figure 3 shows the monthly number of reported patients by sex (2011-2012). The numbers of patients were usually high in January by the year 2019. This trend broke down in 2020, 2021 and 2022. The number of patients in August was higher than the number of patients in January (especially remarkable in 2021).

Figure 4 shows the age-specific incidence rate by sex in 2021 and 2022. As in the past, it was a unimodal distribution with a peak in the latter half of 0 years of age. The degree of certainty of the diagnosis (complete or incomplete) also depends on the revision of the diagnostic guide, but in recent years, approximately 20% of reported patients were diagnosed with the incomplete type.

Recurrent cases were less than 5%, and sibling cases are about 2%. Approximately 1% of the patients had one (or both) of their parents with a history of Kawasaki disease. One of the most serious problem with Kawasaki disease is damage to the heart (especially coronary arteries). Previously, nationwide surveys confirmed cardiac sequelae (coronary artery disorder [dilatation, aneurysm, stenosis],

myocardial infarction, and/or valvular lesions one month after the onset); In recent years, cardiac lesions (coronary artery disorder [dilatation, aneurysm, stenosis], myocardial infarction, and/or valvular lesions) confirmed at the time of initial diagnosis, most acute phase (the worst condition within one month from the onset) and cardiac sequelae (one month after the onset).

Figure 5 shows percentage of patients with cardiac impairment by sex and age (2021 and 2022) . It was more common in males than in females, and was also common in infancy. A slightly higher tendency is also observed for older children aged 5 and older. **Figure 6** shows the annual trends in the frequency of cardiac lesions and sequelae. The rate of cardiac sequelae, which was 15-20% before the establishment of acute-phase immunoglobulin therapy, has fallen to around 2% in recent years.

In recent years, more than 90% of patients received intravenous immunoglobulin therapy (2g/kg body weight) as acute treatment (96.0% in the 27th survey). We directly investigated whether the cases were non-responsive in the 27th survey, and 24.4% were reported as resistant cases for the first intravenous immunoglobulin therapy. Treatment methods listed in the guidelines included initial immunoglobulin administration in combination with steroids, booster immunoglobulin, steroids, cyclosporine, infliximab, ulinastatin, and plasma exchange for refractory cases,

The above are the results of the basic survey items in the nationwide surveys. In recent years, various items have been clarified by changing the items in each survey. The survey items for each survey are shown in a separate section (Summary of the 50-year Nationwide Survey of Kawasaki Disease and Information Processing), and for details on the results, please refer to the reports for each survey.

For other detailed results in recent reports are available online, so please refer to them (<http://www.jichi.ac.jp/dph/inprogress/kawasaki/>, in Japanese).

Table 1 The numbers of surveyed facilities, responding facilities, facilities with patients, and reported patients since the first survey

Survey	Surveyed facilities	Responding facilities	Facilities with patients	Reported patients
1st	1,466	631	415 *146	1,100
2nd	1,452	821	518 *385	2,826
3rd	1,638	620	379	2,597
4th	1,683	653	478	5,443
5th	1,688	943	643	6,257
6th	1,697 **1,199	1,199 **791	761 **474	10,799
7th	1,940	1,472	949	18,444
8th	2,315	1,433	966	15,933
9th	***2,336	1,514	1,058	20,458
10th	***2,247	1,443	949	10,473
11th	***2,679	1,789	1,087	11,297
12th	***2,652	1,826	1,086	11,221
13th	***2,639	1,730	1,063	11,458
14th	***2,626	1,777	1,059	12,531
15th	***2,663	1,825	1,071	12,966
16th	***2,619	1,741	1,077	15,314
17th	***2,413	1,642	1,052	16,952
18th	***2,308	1,618	1,058	19,138
19th	***2,183	1,543	993	20,475
20th	***2,102	1,540	972	23,337
21st	***2,033	1,445	925	23,730
22nd	***1,983	1,420	926	26,691
23rd	***1,943	1,456	950	31,675
24th	***1,881	1,444	965	31,595
25th	***1,804	1,357	924	32,528
26th	***1,745	1,345	904	28,520
27th	***1,723	1,286	821	21,930

* The numbers of facilities that hamd-in the personal data in the second survey.

** In the 6th survey, supplemental survey was conducted to the responding facilities.

*** The numbers of facilities excluding closing hispitals and so on.

Table 2 The yearly number of patients reported by diagnosis category

Nationwide survey		Total	Complete			Incomplete	Unknown
			Subtotal	Typical	Atypical		
Total		445,688	378,070	-	-	67,331	287
1st	-1964	88	66	-	-	22	-
	1965	61	47	-	-	14	-
	1966	79	57	-	-	22	-
	1967	101	77	-	-	24	-
	1968	310	260	-	-	50	-
	1969	461	379	-	-	82	-
2nd	1970	887	700	-	-	187	-
	1971	804	688	-	-	116	-
	1972	1,135	979	-	-	156	-
3rd	1973	1,524	1,320	-	-	204	-
	1974(1- 6)	1,073	939	-	-	134	-
4th	1974(7-12)	890	765	-	-	125	-
	1975	2,216	1,946	-	-	270	-
	1976	2,337	2,023	-	-	314	-
5th	1977	2,798	2,463	-	-	335	-
	1978	3,459	3,067	-	-	392	-
6th	1979	6,867	6,164	-	-	703	-
	1980	3,932	3,549	-	-	383	-
7th	1981	6,383	5,916	-	-	467	-
	1982(1- 6)	12,061	11,265	-	-	796	-
8th	1982(7-12)	3,458	3,162	-	-	296	-
	1983	5,961	5,416	-	-	545	-
	1984	6,514	5,924	-	-	590	-
9th	1985	7,611	6,997	-	-	614	-
	1986	12,847	11,833	-	-	1,014	-
10th	1987	5,256	4,714	-	-	542	-
	1988	5,217	4,696	-	-	521	-
11th	1989	5,591	5,028	-	-	563	-
	1990	5,706	5,192	-	-	514	-
12th	1991	5,677	5,112	4,889	223	565	-
	1992	5,544	5,011	4,819	192	533	-
13th	1993	5,389	4,755	4,550	205	634	-
	1994	6,069	5,369	5,111	258	700	-
14th	1995	6,107	5,416	5,198	218	691	-
	1996	6,424	5,650	5,430	220	774	-
15th	1997	6,373	5,643	5,416	227	730	-
	1998	6,593	5,763	5,513	250	830	-
16th	1999	7,047	6,109	5,819	290	938	-
	2000	8,267	7,092	6,759	333	1,175	-
17th	2001	8,113	7,041	6,800	241	1,072	-
	2002	8,839	7,675	7,410	265	1,164	-
18th	2003	9,146	8,003	7,678	325	1,143	-
	2004	9,992	8,540	8,262	278	1,452	-
19th	2005	10,041	8,564	8,191	373	1,405	72
	2006	10,434	8,807	8,458	349	1,530	97
20th	2007	11,581	9,588	9,251	337	1,975	18
	2008	11,756	9,633	9,322	311	2,094	29
21st	2009	10,975	8,960	8,666	294	2,001	14
	2010	12,755	10,338	10,014	324	2,409	8
22nd	2011	12,774	10,181	9,952	229	2,589	4
	2012	13,917	11,220	10,963	257	2,685	12
23rd	2013	15,696	12,624	12,312	312	3,069	3
	2014	15,979	12,860	12,560	300	3,116	3
24th	2015	16,323	12,842	12,591	251	3,477	4
	2016	15,272	12,248	11,984	264	3,017	7
25th	2017	15,164	12,194	11,945	249	2,964	6
	2018	17,364	14,032	13,716	316	3,325	7
26th	2019	17,347	14,276	14,072	204	3,071	-
	2020	11,173	9,057	8,906	151	2,116	-
27th	2021	11,597	9,439	9,300	139	2,156	2
	2022	10,333	8,396	8,292	104	1,936	1

1st-11th: "complete" and "incomplete"

12th-27th: "complete(typical)", "complete(atypical)", and "incomplete"

Table 3 The numbers of patients and incidence rates by prefecture
(per 100 thousands population of age 0-4) 2019-2022

Prefecture	2019				2020				2021				2022			
	No. of patients			Incidence rate	No. of patients			Incidence rate	No. of patients			Incidence rate	No. of patients			Incidence rate
	Total	Males	Females		Total	Males	Females		Total	Males	Females		Total	Males	Females	
All Japan	17,347	9,830	7,517	370.7	11,173	6,406	4,767	250.6	11,597	6,644	4,953	269.3	10,333	6,005	4,328	239.9
1: Hokkaido	654	355	299	387.0	391	232	159	231.4	362	214	148	232.1	312	175	137	200.0
2: Aomori	124	61	63	310.0	76	39	37	190.0	105	57	48	291.7	53	29	24	147.2
3: Iwate	93	50	43	232.5	40	24	16	100.0	58	36	22	161.1	42	22	20	116.7
4: Miyagi	256	149	107	308.4	136	71	65	163.9	140	80	60	184.2	131	76	55	172.4
5: Akita	82	48	34	303.7	54	35	19	200.0	66	37	29	275.0	55	37	18	229.2
6: Yamagata	187	100	87	519.4	96	49	47	266.7	108	59	49	327.3	70	44	26	212.1
7: Fukushima	236	131	105	357.6	135	76	59	204.5	130	64	66	220.3	134	79	55	227.1
8: Ibaraki	415	258	157	410.9	218	139	79	215.8	233	127	106	250.5	213	131	82	229.0
9: Tochigi	283	157	126	404.3	167	109	58	238.6	202	110	92	320.6	183	101	82	290.5
10: Gunma	281	151	130	425.8	178	100	78	269.7	196	114	82	321.3	153	86	67	250.8
11: Saitama	1,114	647	467	415.7	693	415	278	258.6	711	405	306	283.3	696	413	283	277.3
12: Chiba	910	528	382	402.7	615	344	271	272.1	644	369	275	302.3	599	350	249	281.2
13: Tokyo	2,010	1,174	836	382.1	1,262	739	523	239.9	1,274	745	529	260.5	1,110	656	454	227.0
14: Kanaagwa	1,246	715	531	367.6	701	397	304	206.8	810	451	359	254.7	668	388	280	210.1
15: Niigata	314	166	148	418.7	213	127	86	284.0	220	130	90	318.8	203	120	83	294.2
16: Toyama	107	72	35	305.7	76	44	32	217.1	75	53	22	227.3	46	29	17	139.4
17: Ishikawa	164	84	80	381.4	132	77	55	307.0	125	65	60	312.5	93	54	39	232.5
18: Fukui	104	58	46	358.6	60	29	31	206.9	90	48	42	333.3	59	30	29	218.5
19: Yamanashi	106	54	52	378.6	53	33	20	189.3	37	20	17	137.0	29	18	11	107.4
20: Nagano	268	141	127	362.2	162	87	75	218.9	177	119	58	260.3	137	70	67	201.5
21: Gifu	257	138	119	356.9	182	97	85	252.8	196	112	84	301.5	149	90	59	229.2
22: Shizuoka	512	288	224	393.8	300	160	140	230.8	274	164	110	230.3	210	118	92	176.5
23: Aichi	1,132	615	517	371.1	691	397	294	226.6	738	401	337	258.9	715	422	293	250.9
24: Mie	195	127	68	304.7	150	93	57	234.4	146	89	57	247.5	91	54	37	154.2
25: shiga	257	142	115	435.6	180	112	68	305.1	161	101	60	292.7	139	85	54	252.7
26: Kyoto	336	191	145	365.2	241	137	104	262.0	248	155	93	291.8	231	125	106	271.8
27: Osaka	1,201	688	513	367.3	794	450	344	242.8	800	468	332	258.1	812	482	330	261.9
28: Hyogo	728	413	315	350.0	483	281	202	232.2	477	272	205	247.2	498	289	209	258.0
29: Nara	214	112	102	455.3	132	63	69	280.9	117	65	52	272.1	112	67	45	260.5
30: Wakayama	161	93	68	503.1	88	43	45	275.0	110	54	56	366.7	68	39	29	226.7
31: Tottori	92	43	49	438.1	58	31	27	276.2	65	37	28	325.0	65	40	25	325.0
32: Shimane	84	53	31	323.1	68	32	36	261.5	67	40	27	279.2	47	25	22	195.8
33: Okayama	259	138	121	350.0	220	130	90	297.3	243	142	101	352.2	194	114	80	281.2
34: Hiroshima	416	249	167	381.7	316	182	134	289.9	311	164	147	307.9	284	163	121	281.2
35: Yamaguchi	177	113	64	376.6	97	42	55	206.4	122	69	53	283.7	77	39	38	179.1
36: Tokushima	124	61	63	496.0	69	39	30	276.0	74	36	38	321.7	71	41	30	308.7
37: Kagawa	95	55	40	263.9	71	41	30	197.2	69	37	32	209.1	49	27	22	148.5
38: Ehima	181	104	77	385.1	146	87	59	310.6	144	87	57	327.3	110	76	34	250.0
39: Kochi	96	61	35	417.4	47	25	22	204.3	51	27	24	231.8	42	23	19	190.9
40: Fukuoka	672	359	313	314.0	491	292	199	229.4	557	337	220	275.7	589	342	247	291.6
41: Saga	82	54	28	241.2	65	40	25	191.2	75	42	33	234.4	57	29	28	178.1
42: Nagasaki	154	89	65	296.2	101	61	40	194.2	113	68	45	235.4	105	59	46	218.8
43: Kumamoto	245	139	106	335.6	182	102	80	249.3	192	108	84	282.4	171	91	80	251.5
44: Oita	166	103	63	395.2	127	67	60	302.4	108	53	55	276.9	85	54	31	217.9
45: Miyazaki	130	68	62	295.5	95	55	40	215.9	73	40	33	178.0	90	43	47	219.5
46: Kagoshima	218	123	95	330.3	165	86	79	250.0	168	99	69	271.0	138	81	57	222.6
47: Okinawa	204	109	95	255.0	156	95	61	195.0	135	74	61	177.6	147	78	69	193.4
48: Outside Japan	5	3	2	—	0	0	0	—	0	0	0	—	1	1	0	—
Unknown	0	0	0	—	0	0	0	—	0	0	0	—	0	0	0	—

*Prefectural incidence rates were calculated using the 2020 Basic Resident Registration Population for 2019-2020, and the 2022 for 2021-2022).

**National Incidence rates were calculated using the estimated population for each year (with the exception of 2020, which was revised; for 2022, the estimated

Figure 1 Yearly number of reported patients by sex

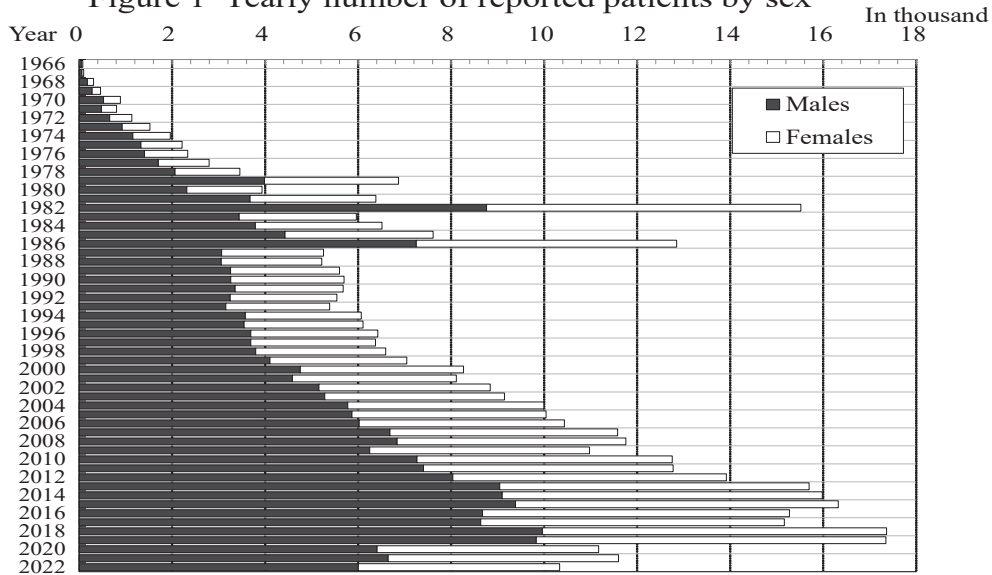


Figure 2 Yearly incidence rate by sex

Rate per 100 thousands of age 0-4 y.o.

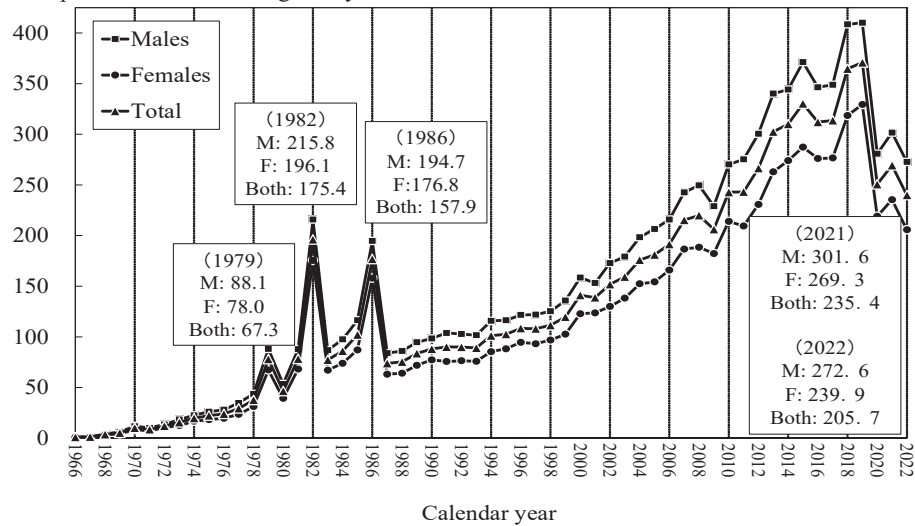


Figure 3 Monthly number of reported patients by sex (2011-2022)

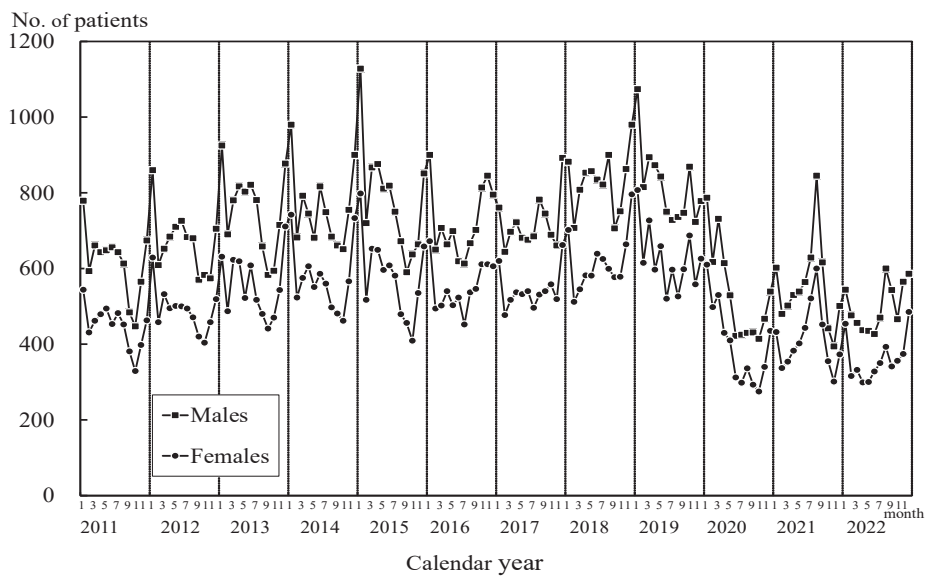


Figure 4 Age-specific incidence rate by sex (2021 and 2022)

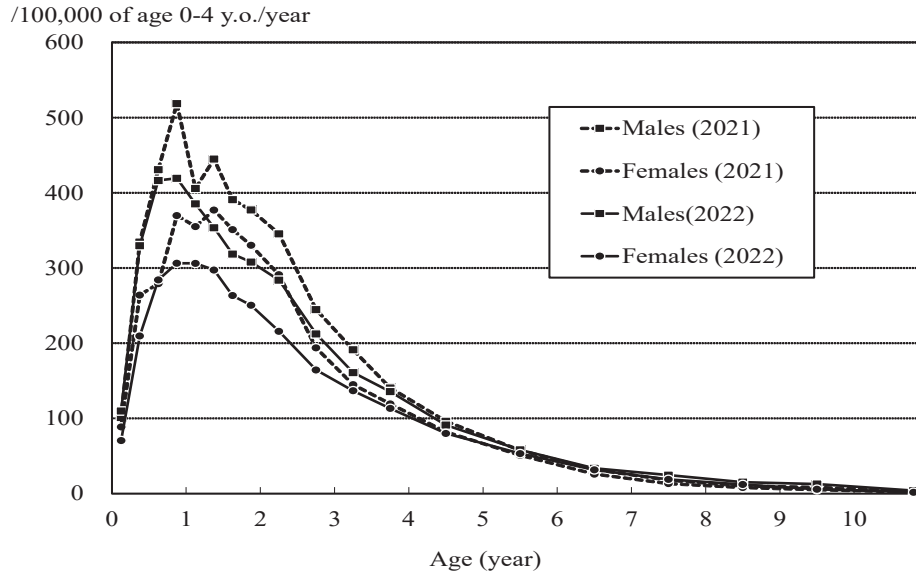


Figure 5 Proportion of patients with cardiac impairment by sex and age (2021 and 2022)

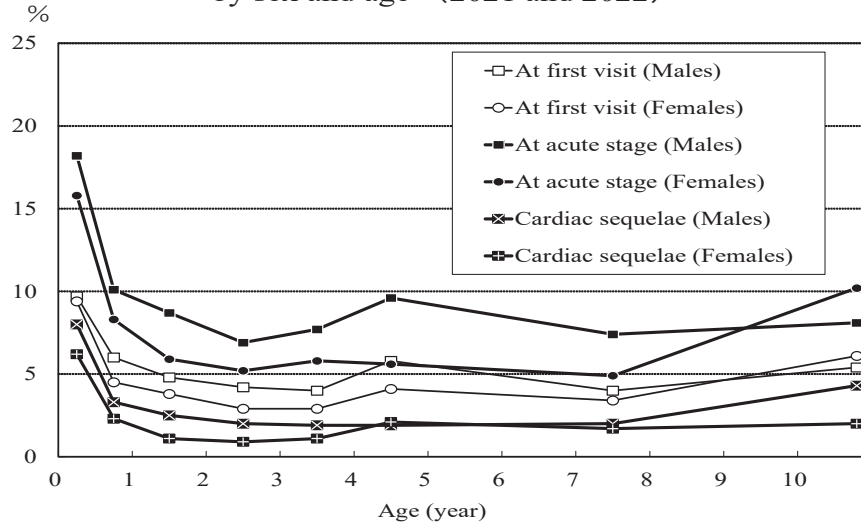
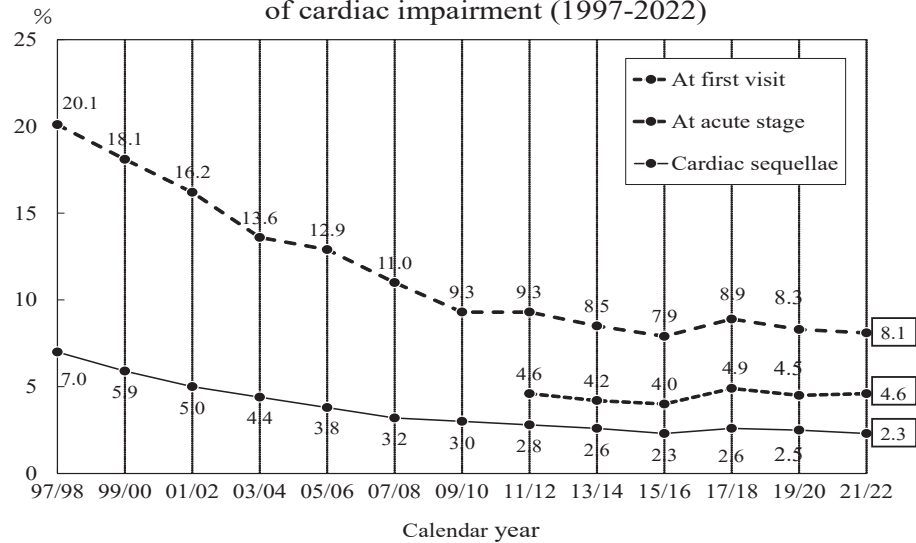


Figure 6 Annual trends in the frequency of cardiac impairment (1997-2022)



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Overview of the data processing system in 50-year nationwide surveys of Kawasaki disease in Japan

I. Data processing of the reported Kawasaki disease patients

Table 1 shows the database creation and data processing for the 1st to 27th nationwide surveys of Kawasaki disease in Japan. The database creation procedure in each survey is shown step by step.

1. Database creation for the 1st to 8th nationwide surveys

By the year 2000, we created a database of all patients over the 30 years since the Kawasaki Disease Research Group was first established in 1970. Fujitsu's computer system FACOM 270-30 was used for the 1st to 3rd nationwide surveys and FACOM 230-25 for the 4th and 5th, Hitachi's computer system HITAC 20 was used for the 6th and 7th nationwide surveys, and HITAC M-220H for the 8th.

The records for the patients reported in the 1st to 7th nationwide surveys were stored as separate data sets on punch cards or magnetic tapes. They were consolidated in September 1984 for the first time using a Hitachi's HITAC M-220H system. The records for the patients reported in the 8th nationwide survey were also included in 1985. At this stage, a summary of the patient data was created and published in a book entitled "Kawasaki Disease - All Epidemiological Data" (Edited by the Study Committee on Cause of Kawasaki Disease, Japan Heart Foundation, Published by Soft Science Publications).

2. Database creation for the 9th to 12th nationwide surveys

For the 9th and 10th nationwide surveys, patient data was entered using the Dos-Basic program and saved as text data. For the 11th and 12th nationwide surveys, an input program was created using the commercially available software dBase III PLUS, and all of the questionnaire data was inputted. This became the basis for patient database registration since then to present time. During this period, all the information for patients including items (name, date of birth, date of initial consultation, facility number) that were not included in the registration records for the 1st to 10th nationwide surveys, was entered into the survey form. The patient database for the 1st to 12th nationwide surveys was completed. All of this procedure was carried out using dBase III PLUS. At that time, computers were not as widespread as they are now, so it was difficult to handle large amounts of data, and it took a lot of effort to save and manage it.

3. Database creation for the 13th to 17th nationwide surveys

From the 13th nationwide survey onwards, data entry work was outsourced to a contractor. For

the 13th to 15th nationwide surveys, patient files were created from fixed-length text files using dBase III PLUS. For the 16th and 17th nationwide surveys, data from CSV format text files were entered by vendors. A database was created using the Microsoft Office spreadsheet software Excel (hereinafter referred to as Excel).

With the widespread of Windows, DOS files such as dBase III PLUS are difficult to handle, and it has become necessary to convert past registered data to Windows files. Data from the 1st to 15th nationwide surveys were converted from the Microsoft Office database software Access to files such as Excel. Initially, there was a problem with data size limitations (maximum 65,536 rows) and it was difficult to store large amounts of data.

4. Database creation after the 18th nationwide survey

From the 18th nationwide survey, a database was created by inputting patient data into an Excel format from the time of vendor input. From the 20th nationwide survey, we have adopted a method of additionally inputting the necessary survey items to the Excel data in which the basic patient items have already been registered, targeting facilities that cooperate with internet surveillance, so we have included the survey form (entered by the vendor). In the end, three ways of combining Excel data were added.

Thereafter, logical checks and corrections were performed on the necessary items (sex, age in days, year of first diagnosis, treatment method, test findings, etc.). At the same time, Access was used to check for duplicate consultations for the same patient (at the same facility or at other facilities). Because the secretariat was fully aware of the contents of the series of work, highly accurate survey results were obtained.

Table 1 Data processing methods for the 1st to the 27th nationwide surveys

Survey No.	Year of diagnosis	Method of data processing	Application	Database integration	Confirm duplicate cases
1st- 8th	1984 or before	Data entry using 80-digit punch card Program with Fortran IV Private large computer rental (hourly)			
9th-10th	1985-1988	Dos-Basic program Text data storage	Dos-Basic		
11th-12th	1989-1992	dBase III PLUS program (Basics of patient database)	Dos-Basic	1st-12th surveys integration dBase III PLUS	
13th-15th	1993-1998	Fixed length text file (Input entrusted to a private company) dBase III PLUS	Dos-Basic		
16th-18th	1999-2004	CSV format text file (Input entrusted to a private company) Excel, Access	F-Basic	1st-15th surveys integration Access	Access
19th-27th	2005-2022	Excel format file (Input entrusted to a private company) Excel, Access	F-Basic	1st-27th surveys integration Excel2007	Access

Information collection method: The basic method is to mail questionnaires, but from the 18th survey, Excel data processing methods have been introduced.

5. Tabulation for analysis file for each survey

For tabulations for each survey, items used for tabulation were selected from the database file and a text file was created. This was converted to Basic data for tabulation using the Basic conversion program. We checked the logic on the program and created additional processing codes as needed. Basic simple tabulation and further cross-tabulation were performed for analysis. To create this tabulation program, Dos-Basic was used until the 15th nationwide survey. Windows F-Basic was used from the 16th nationwide survey onwards. Thankfully, this software is still working. This program is used to perform tabulation and analysis when creating each report.

Although the nationwide survey data was plagued by compatibility issues, the introduction of Windows, and the year 2000 problem, it can be said that it has survived the waves of the computer age and has been completed.

Taking the 26th nationwide survey as an example, we show an overview of the work order and information processing for about one year from survey preparation to completion of the database (**Table 2**).

Table 2 Overview of the flow and information processing of the nationwide Kawasaki disease survey

Step No.	Processing steps	Description of the step	Month of implementation
1	Creating a patient list	Create a patient list to be enclosed with the survey request (for each facility where a patient was reported in the previous survey)	Oct (Previous)
2	Finalizing questionnaire items and creating forms	Change of the layout of the previous survey and addition of new items	Oct (Previous)
3	Selection of survey target facilities	Pediatric departments of the hospitals with over 100 beds and pediatric specialized hospitals with less than 100 beds	Oct (Previous)
4	Announcement of survey forms and Excel input forms	Posted on the Jichi Medical University Department of Public Health website	Oct (Previous)
5	Printing a set of survey forms	Printing and preparing for shipping request letters, survey forms, diagnostic guidelines, document sending envelopes, and return envelopes	Nov (Previous)
6	Send email to surveillance participating facilities	Request for cooperation in the nationwide survey and guidance on creating an Excel file for inputting registered data	Dec (Previous)
7	Sending a set of survey forms (an email will also be sent to facilities participating in the surveillance)	Send request letter, survey form, diagnostic guide, return envelope, and patient list (only to facilities with previous patients)	Jan
8	Responding to inquiries from surveyed facilities	Creating manuals for responding to inquiries	Jan-May
9	Inquiry/confirmation to survey target facilities	Creating a manual to confirm inspection items (prioritize inquiries to email addresses; if there is no response, request in writing; as a last resort, request by phone)	Jan-May
10	Inspection, confirmation, and coding of survey forms	Inspection of omissions and incorrect entries in survey forms, confirmation of inquiries to facilities, entry of city/ward/town/village codes, etc.	Feb-Jul
11	Inspection, confirmation, and coding of data submitted in Excel	Inspection of data submitted on magnetic media, confirmation of inquiries to facilities, entry of city/ward/town/village codes, etc.	Feb-Jul
12	Facility data entry	Input facility data for survey form (facility code, number of patients, facility questions, etc.)	Feb-Jul
13	Re-request/re-request to non-responding facilities	Conducted twice. Re-request by mail in early March (documents, questionnaire, diagnosis guide, and return envelope are enclosed) A repeat request will be made in mid-April (as a general rule, a postcard will be sent, documents, questionnaires, and diagnostic guides will be enclosed for facilities with a large number of patients in the previous survey, and requests will also be made by email to facilities participating in the surveillance)	Mar-Apr
14	Confirm survey responses to non-responding facilities	Facilities that received a large number of patient reports in the previous survey will be sent a return postcard to confirm whether they can submit submissions, the number of patients, and when they will respond	Jun
15	Patient data entry (requested to vendor)	Create an Excel format for vendor input and outsource input to the vendor	Jun-Jul
16	Unification of Excel submission data	Unify Excel data for facilities subject to surveillance and facilities that submit downloaded Excel files	Jun-Jul
17	Unification of vendor data	Unify the Excel patient data that was created in step 16 and the Excel patient data entered by the vendor	Jun-Jul
18	Logical check and correction using computer	Logical check of unified data. If you find any deficiencies in important items, please check with the facility (reconfirm)	Jun-Jul
19	Duplicate check, correction and deletion of duplicated patient data	Check for duplication of unified data (confirm corrections to remaining data)	Jun-Jul
20	Add new code	Creation of new data on sibling cases, Kawasaki disease in parents (by parent), coronary artery aneurysm, and enlargement	Jul-Aug
21	Completing the database	Complete data with new code added	Aug
22	Correction of number of reported cases by facility	Confirmation of response rate and number of patients	Aug-Sep
23	Data return to collaborators (Database completed)	Creating a data file for distribution (personal information removed)	Sep

III. Flow of creating a Kawasaki disease nationwide survey report

The flow of creating a Kawasaki disease nationwide survey report is shown using the 26th nationwide survey as an example (**Table 3**) The Kawasaki disease nationwide survey office analyzes registered data and creates a report at the same time as every survey is completed. . After completion, we upload them to our website, deliver them to partner organizations, present them at academic conferences, and publish them in the press.

Table 3 Flow of creating report on nationwide epidemiological survey on Kawasaki disease

Steps	Items	Description of the step	Month of implementation
1	Creating data for the report	Regional code creation, reclassification of cardiac disorders (first visit, acute phase, sequelae) Calculation of recovery rate and morbidity rate	Aug-Sep
2	Preparation for report manuscript	Creation of manuscript, tables, figures and list of collaborating facilities	Aug-Sep
3	Report printing	Submit the manuscript to the printer (PDF + original)	Sep-Oct
4	Publication and distribution of reports	Send report to cooperating facility, announce to the press and publish on Jichi Medical University Public Health website	Sep-Oct
5	Presented at academic conferences	Publish at the meeting of Japanese Kawasaki Disease Society, International Kawasaki Disease Symposium, etc.	Oct-Nov
6	Submitted to a pediatric and epidemiological journal	Journal of Pediatric treatment (in Japanese)	Nov

IV. Flow of survey items

The first survey consisted of (1) presence or absence of case experience (if yes, number of cases), (2) year of first case experience, and (3) diagnosis at that time. Next, we conducted a secondary investigation on several items, including the patient's name, sex, date of birth, date of first diagnosis, certainty of diagnosis (certain, suspected), and dead or alive (whether or not an autopsy was performed).

The second survey was conducted with the same content as the secondary investigation of the first survey. From the third survey onwards, we stopped using the two-stage survey method and used a continuous list method to determine the name, address, sex, date of birth, date of initial diagnosis, date of illness at initial diagnosis, certainty of diagnosis, presence or absence of referral, and death. The survey was conducted in almost the same way up to the 7th nationwide survey, with requests for information on whether there was an autopsy or not.

Items related to treatment were introduced in the 4th nationwide survey and after. Sibling occurrence and recurrence were taken up from the 5th nationwide survey. From the 8th nationwide survey, items regarding the presence of cardiac sequelae, whether echocardiography was performed, and the use of other drugs were added. The 9th to 11th nationwide surveys were conducted using the same method as the previous ones, but γ -globulin was included in the drug category. Starting with the 12th survey, items related to diagnosis, γ -globulin treatment, and recurrence were expanded in detail. In the

13th to 16th nationwide surveys, several test findings were added due to advances in diagnostic technology and treatment. Furthermore, starting with the 16th nationwide survey, from the perspective of protecting personal information, names were changed to initials only, and addresses were changed to municipal code on city, ward, town, and village. An item has been added regarding parents' history of Kawasaki disease. The 17th nationwide survey included information on the presence of major symptoms, the 18th nationwide survey included additional treatment with γ -globulin, and the 19th nationwide survey included additional treatment with steroids and BCG vaccination. The 20th and 21st nationwide surveys included non-cardiac complications, additional treatments, and cases of failure. The 22nd to 24th nationwide surveys covered several test findings, and from the 22nd nationwide survey, heart disorders at the time of initial examination were also added. The 25th nationwide survey focused on antibiotics taken before the first visit. Furthermore, new survey items related to the new coronavirus infection were added in the 26th and 27th nationwide surveys, and the 27th nationwide survey also investigated the presence or absence of testing for the new coronavirus infection and the multisystem inflammatory syndrome in children (MIS-C) was investigated (**Table 4**) .

Table 4 Changes in the items in the nationwide survey on Kawasaki disease

Survey No.	Description of survey items
1st	Primary survey: Case experience (if yes, No. of cases, Year of first case experience and its diagnosis) Secondary survey: Name, Sex, Date of birth, Date of first examination, Certainty of diagnosis (definite, suspect), Alive or death(Autopsy), Tertiary survey: Main symptoms, laboratory findings and treatments as indicated in the "Kawasaki Disease Diagnostic Guideline"
2nd	Experience with cases (if yes, how many?), The year of the first experience, and its diagnosis
3rd	Name, address, sex, date of birth, date of the first hospital visit, day of illness at first visit, certainty of diagnosis, referral from other facilities, dead(autopsy) or alive,

○ common items for the past surveys(3rd-12th)

Name, address, sex, date of birth, date of the first hospital visit, day of illness at first visit, certainty of diagnosis, referral from other facilities, dead(autopsy) or alive	
Survey No.	Description of survey items
4th	steroids, antibiotics
5th	Sibling case
6th	Relapse, Aspirin treatment
7th	Same as 6th survey
8th	Cardiac sequelae, echocardiography, other medications (γ -globulin, flurbiprofen, vitamin E, etc.)
9th	γ -globulin
10th	Same as 9th survey
11th	Same as 10th survey
12th	Diagnosis(1. Definite A, 2. Definite B, 3. Suspicious), Cardiac sequelae (1. Giant aneurysm, 2. aneurysm/enlargement, 3. stenosis, 4. myocardial infarction, 5. valvular lesion) , γ -globulin treatment (date of start, daily dose, duration, product name)

○ Past to recent nationwide surveys (13th to 27th): Additional items

Survey No.	Description of survey items
13th	Laboratory findings (highest values) include white blood cell count and CRP
14th	Laboratory findings (minimum values): platelet count, serum albumin
15th	laboratory findings (at the initial visit); Ht, WBC count, Neutrophil count

○ Recent nationwide surveys (16th-27th): Common Items

Name initials, Patient address (Prefecture and Municipality), Date of birth, Date of first medical exam, sex, Day of illness at first exam, Certainty of diagnosis, γ -globulin treatment, Recurrence, Siblings, Previous history of parents, Cardiac disorder, Dead or alive	
Survey No.	Description of survey items
16th	Laboratory findings (at the time of initial examination) include Hb, ALT (GPT), serum Na, and parents' past history of Kawasaki disease.
17th	Day of illness at discharge, Presence of major 6 symptoms, Duration of fever
18th	Antipyretic days, Additional γ -globulin treatment, Patient referral
19th	Details of additional treatment (steroids), Changes in BCG vaccination site
20th	Suspected cases (number of major symptoms), Other treatments (steroids, infliximab, immunosuppressive drugs), Non-cardiac complications
21st	Conditions at birth, IGG refractory case, initial facility treated with IGG, Additional treatment: plasma exchange Complications: 1. Encephalitis/encephalopathy 2. Severe myocarditis 3. Tachyarrhythmia 4. Vomiting/diarrhea 5. Bronchitis/pneumonia 6. Gross hematuria
22nd	Add transfer information, use of concomitant steroids at initial IG treatment and whether pulse or otherwise, and White blood cell count, platelet count, albumin, CRP, and heart failure (abnormalities at first visit) were added as laboratory findings (at first visit).
23rd	Hb, ALT (GPT), and serum Na were added as laboratory findings (at initial visit).
24th	Platelet counts (initial, highest, and lowest) and the date at the highest and lowest platelet counts
25th	Presence or absence of antibiotics administered within 1 week prior to initial visit and drug name
26th	BCG vaccination history and vaccination site status, presence of 6 major symptoms, novel coronavirus PCR test, coronary Z-score or measured coronary artery diameter
27th	Details of acute phase treatment divided into 1st line, 2nd line, and 3rd line and beyond; refractory in the 1st line; details of the status of testing for novel coronavirus infection; and the possibility of novel coronaviruses and MIS-C.

V. Progress in revisions of the “Diagnostic Guidelines”

In 1970, the first edition of the Diagnostic Guidelines of Kawasaki Disease" was produced in advance of the first nationwide survey. Subsequently, the first revised edition was published in September 1972, the second revised edition in April 1974, the third revised edition in August 1978, the fourth revised edition in September 1984, the fifth revised edition in February 2002, and the sixth revised edition in May 2019. It has been revised six times (**Table 5**).

Table 5 Flow of revision of "Diagnostic guidelines of Kawasaki disease"

<p>1st revision (1972) 2nd Survey</p> <p>[Addition] The fatality rate was about 1.5%, and the primary autopsy finding was vasculitis with thrombotic occlusion of the coronary arteries.</p>
<p>2nd revision (1974) 3rd and 4th surveys</p> <p>[Change] Non-purulent lymphadenopathy was moved from a reference item to a major symptom (6 major symptoms).</p> <p>[Addition] ECG findings (myocarditis-like or ischemic changes), autopsy findings (coronary artery aneurysm, mitral valve insufficiency), and later development (myocardial infarction-like symptoms, mitral regurgitation)</p>
<p>3rd revision (1978) 5th to 7th surveys</p> <p>[Change] Expression of fever (from antibiotic refractory fever to unexplained fever)</p> <p>[Addition] "Kawasaki disease" is used as the common name for the disease, and the clinical features (increased platelets, enlarged gallbladder, etc.) are also noted.)</p>
<p>4th revision (1984) 8th to 16th surveys</p> <p>[Change] When a coronary artery aneurysm is confirmed by echocardiography or angiography, Kawasaki disease was diagnosed even with only 4 main symptoms. Fever of unexplained (unexplained → deleted)</p> <p>[Addition] Clinical symptoms (paralytic ileus, enlarged gallbladder, convulsions, and disturbance of consciousness)</p>
<p>5th revision (2002) 17th to 25th surveys</p> <p>[Change] Expression of fever (Addition: including fever resolution of less than 5 days due to treatment), Order of description of major symptoms</p> <p>[Addition] There are cases in which coronary artery aneurysms are identified even if the main symptoms are not met.</p>

Revision is necessary due to the need to revise the diagnostic method for suspect cases (failure type), the evaluation of coronary artery lesions (Z-score determination), and the need to revise the content of the reference clause to make it more suitable for the current situation.



<p>6th revision (2019) 26th and 27th surveys</p> <p>[A. Major Symptoms] The six major symptoms are well recognized by clinicians, and the basic policy was not to make major changes, but some points were revised to meet the requirements of clinical practice.</p> <p>[B. Reference] The format has been changed from the conventional listing by organ to one in which each item is categorized and listed according to its significance in terms of medical treatment.</p>
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VI. Patient file contents

1. 1st to 27th nationwide surveys common file

An analysis file consisting of basic common items was created in Excel from the database of each survey. Starting with the 14th nationwide survey, some items specific to each survey were added. There are also fields such as patient address region, facility region, patient age classification, survey period classification, survey time, etc. If you use this file, you can easily access all reported patients from the 1st to 27th nationwide surveys (approximately 440,000 patients). Tabulation and epidemiological analysis can be performed on basic items. This patient file is a valuable database that can be used to investigate the cause of Kawasaki disease and investigate the prognosis of cardiac sequelae. If necessary, the data can be returned to collaborating facilities or researchers by selecting items.

2. 11th to 27th nationwide surveys common file

Starting from the 12th nationwide survey, detailed items on γ -globulin treatment and cardiac sequelae were added, and the 11th to 27th nationwide surveys included these additional items. By performing tabulation using this data, detailed observations can be made regarding γ -globulin treatment, cardiac sequelae, etc.

3. 14th to 27th nationwide surveys file for distribution to collaborators

Since the 14th nationwide survey, all patient data excluding personal information has been created in Excel files every time. It was mainly distributed to research collaborators, and it has also been used for student practical training.

4. 1st to 27th nationwide surveys death information file (Including those not registered)

Regarding deceased patients ascertained by the Kawasaki disease nationwide surveillance office, we can see whether (1) they died at the time of the investigation, (2) they died at a later date (there is a Kawasaki disease nationwide surveillance registration), or (3) only deaths are reported (there is no Kawasaki disease nationwide surveillance registration). Death information has been registered. Currently, 542 people have been confirmed to have died at a later date (registered in the Kawasaki disease nationwide survey).

VII. Additional resources

1. Number of reported patients, number of survey facilities, and response rate

We created the number of reported patients, number of surveyed facilities, number of responding facilities, and response rate from the 1st to 27th nationwide surveys. To be close with the spread of new coronavirus infection, the number of reported patients in 2020 decreased to two-thirds of the previous year, and this trend was seen in 2021 and 2022 as well (**Figure 1**). Although the number of surveyed facilities has decreased in recent years due to the closure of pediatric departments, the response rate has continued to be over 70% (**Figures 2 and 3**).

Figure 1 Number of patients reported for each survey

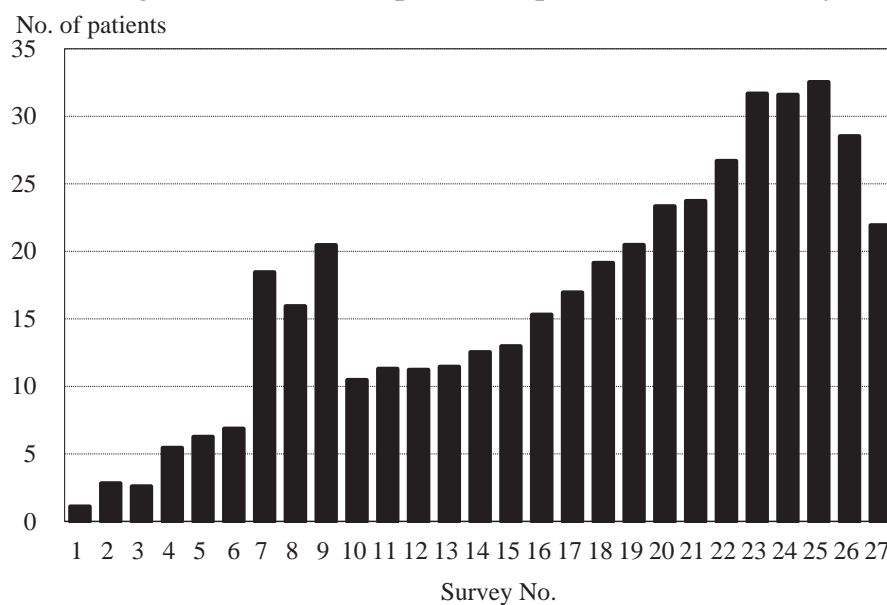


Figure 2 No. of facilities surveyed and responded for each survey

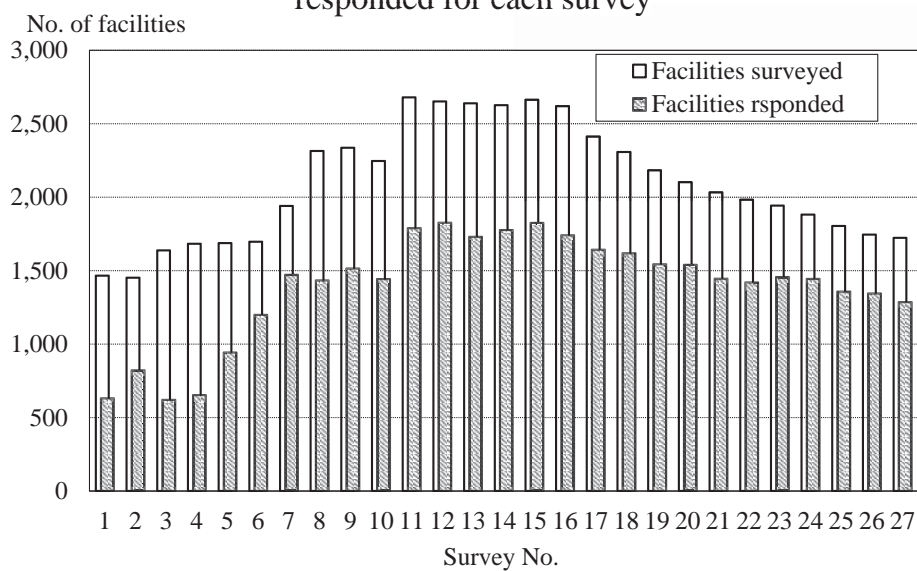
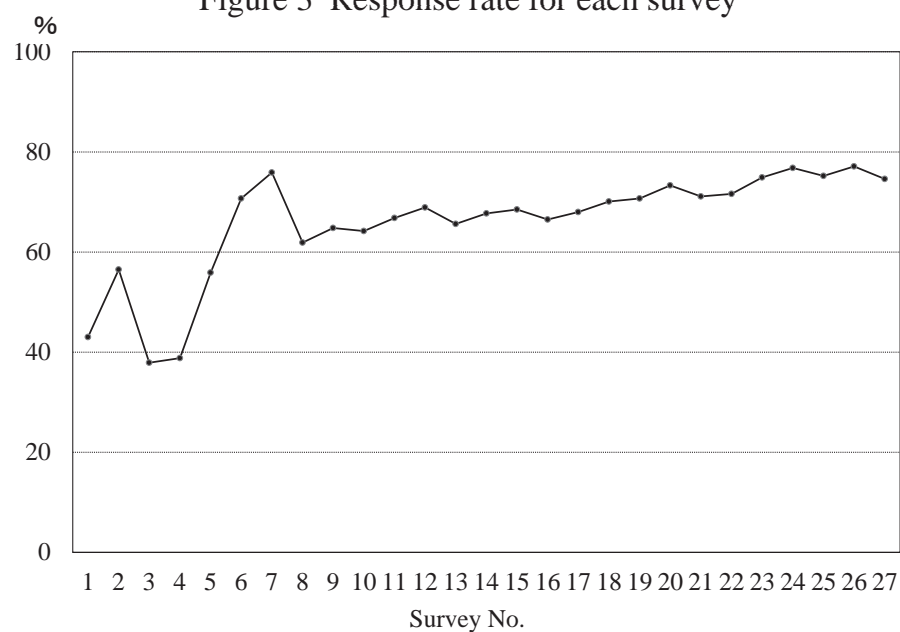


Figure 3 Response rate for each survey



2. Registered patient designation date age calculation

We calculated the age as of January 1, 2023 of the 445,146 people currently registered alive who were reported in the 1st to 27th nationwide surveys (death information does not include those who fall into this category). As a result, three people over the age of 70 were confirmed to have Kawasaki disease (**Table 6**).

Table 6 Age groups of patients registered for Kawasaki disease
(As of January 1, 2023)

Age	No. of patients	Age	No. of patients
0-4	30,746	50-59	9,100
5-9	72,155	60-69	292
10-15	85,636	70	1
16-19	44,952	73	1
20-29	80,952	74	1
30-39	64,152	Age unknown*	821
40-49	56,337	Total**	445,146

*Age at registration not known

**542 confirmed deaths among those registered as patients were excluded

Material (1-1) List of academic papers on Kawasaki disease nationwide surveys in Japanese				
No.	Title	Name of Journal	Volume and No.	Authors
1	急性熱性皮膚粘膜リンパ節症候群と急性死.	日児誌	1971; 75(6):433-434.	川崎富作.
2	急性熱性皮膚粘膜リンパ節症候群(MCLS)の疫学.	日児誌	1972; 76(11):695-696.	重松逸造.
3	指趾の特異的落屑を伴う急性熱性皮膚粘膜リンパ節症候群(略称:MCLS).	日赤中央病院医報	1972; 1(2):73-83.	川崎富作.
4	小児MCLS(いわゆる川崎熱病)の臨床疫学的研究: その1 昭和47年度第2回全国実態調査成績.	日公誌	1973; 20(10, 特別附録):378.	柳川洋, 志毛ただ子, 重松逸造.
5	急性熱性皮膚粘膜リンパ節症候群(MCLS).	感染・炎症・免疫	1974; 4(2):55-66.	川崎富作.
6	最近のMCLSを語る(臨床座談会).	小児科	1974; 15(3):204-214.	濱島義博, 川崎富作, 草川三治, 重松逸造, 篠塚輝治, 神前章雄.
7	いわゆる川崎病について.	日衛誌	1975; 22(6):306-312.	重松逸造, 柳川洋.
8	MCLS発生数の全国調査成績.	小児科	1975; 16(8):786-790.	重松逸造, 柳川洋.
9	MCLS全国調査例の臨床所見.	小児科	1975; 16(8):790-795.	川崎富作, 大川澄男.
10	急性熱性皮膚粘膜リンパ節症候群(MCLS)死亡例の検討.	小児診	1975; 38:608-614. 38:608-614.	大川澄男, 川崎富作, 神前章雄, 柳川洋, 志毛ただ子, 重松逸造.
11	川崎病の実態.	公衆衛生情報	1975; 5(12):22-29.	柳川洋.
12	最近における川崎病の実態(第3回全国調査成績より).	日衛誌	1975; 22(10, 特別附録):188.	柳川洋, 竹内和子, 重松逸造, 川崎富作, 福富和夫.
13	川崎病(MCLS)における病因追求の動向.	日本臨牀	1976; 34(2):284-189.	重松逸造.
14	いわゆる川崎病について.	日本医事新報	1976; No.2722:3-8.	川崎富作, 窪田誠一.
15	川崎熱発見とその後の研究動向.	日本臨牀	1976; 34(2):222-227.	川崎富作.
16	川崎病の疫学.	日本臨牀	1976; 34(2):275-283.	柳川洋.
17	小児急性熱性皮膚粘膜リンパ節症候群の診断基準・臨床像と最近の知見.	臨牀看護	1977; 3:1406-1414.	川崎富作.
18	MCLS(川崎病).	日本臨牀	35(Suppl 1):746-747.	川崎富作.
19	急性熱性皮膚粘膜リンパ節症候群.	医学のあゆみ	100(1):216.	川崎富作.
20	MCLSの同胞発生に関する疫学的研究.	小児科	1977; 18(1):59-63.	富永真琴, 大島健次郎, 柳川洋, 重松逸造, 川崎富作.
21	原因不明疾患の疫学:川崎病を例として.	公衆衛生	1978; 42(9):545-548.	安西定, 柳川洋, 高原亮治, 川口毅.
22	いわゆる川崎病(急性熱性皮膚粘膜リンパ節症候群)の疫学的研究.	日医大誌	1978; 45(5):321-337.	窪田誠一.
23	川崎病(MCLS).	内科	1978; 41(6):1048-1055.	川崎富作.
24	最近(1977~78年)におけるMCLS(川崎病)の実態:第5回全国調査結果の速報.	小児科	1979; 20(7):755-757.	川崎病研究班.
25	川崎病の疫学的研究について.	小児科臨床	1979; 32(7):1415-1420.	浅井利夫, 草川三治.
26	川崎病(MCLS)死亡例の検討:5回にわたる全国調査成績より.	日衛誌	1980; 35(1):347.	玉城英彦, 柴田茂男, 重松逸造, 柳川洋.
27	「川崎病」:特にその公衆衛生的側面.	日衛誌	1980; 27(10,特別附録):133-136.	川崎富作.
28	川崎病発生の時間集積性について.	日衛誌	1981; 28(6):257-263.	横山英明, 橋本勉, 柳川洋, 玉城英彦, 柴田茂男.
29	MCLS(川崎病)の多発(1979年):第6回全国調査成績の速報.	小児科	1981; 22(1):53-58.	川崎病研究班.
30	疫学(川崎病).	小児内科	1981; 13(3):371-380.	柳川洋, 玉城英彦, 柴田茂男, 重松逸造.
31	川崎病のあゆみ.	治療	1982; 64(10):1609-1612.	川崎富作.
32	川崎病の最新の知見と展望.	小児看護	1982; 5(8):897-903.	川崎富作.
33	川崎病疫学の新しい知見.	小児診	1982; 45(9):1323-1328.	草川三治.
34	川崎病の疫学:現状と今後の課題.	治療	1982; 64(10):1613-1619.	柳川洋, 橋本勉.
35	症候学および年齢別罹患率の推移から見た川崎病病因の考察:溶連菌感染症説の可能性をめぐって.	日本臨牀	1983; 41:1994-2004.	山本高治郎.
36	川崎病発症時の気象医学的検討について:第1報 石川県下発生例を中心に.	小児臨	1983; 36:1289-1294.	森田正人, 浅井利夫.
37	最近(1981年1月~82年6月)におけるMCLS(川崎病)の実態:第7回全国調査結果の速報.	小児科	1983; 24(1):53-58.	川崎病研究班.

No.	Title	Name of Journal	Volume and No.	Authors
38	川崎病の研究史と展望.	日本臨牀	1983;41(9):1964-1969.	川崎富作.
39	川崎病(MCLS)の本態と治療.	日本医師会雑誌	1983;89(10):1695-1702.	川崎富作.
40	川崎病.(本邦臨床統計集)	日本臨牀	1983;41(春期増刊 Suppl):1482-1497.	川崎富作.
41	川崎病の現状と展望.	こども医療セン ター医学誌	1983;12(2):71-77.	川崎富作.
42	厚生省研究班.(川崎病各研究班の指向と成果)	日本臨牀	1983;41(9):1970-1977.	草川三治.
43	川崎病研究最近の動向.(総説)	島根医学	1983;6(8):721-735.	草川三治.
44	川崎病と主要感染症の週別発生状況の解析.	日児誌	1983;87(11):2149- 2157.	中村好一, 永井正規, 柳川洋, 草川三治.
45	川崎病研究の進歩.	日本臨牀	1983;41:180-190.	柳瀬義男, 川崎富作.
46	川崎病病因への接近:疫学的立場から.	小児科	1983;24(3):271-280.	柳川洋, 柴田茂男, 重松逸造.
47	川崎病の地域集積性と時間集積性の意味するもの: 1979年, 1982年流行例を中心に.	日本臨牀	1983;41(9):1987-1993.	柳川洋, 大金央子, 永井正規.
48	川崎病(MCLS, 小児急性熱性皮膚粘膜リンパ節症候 群)診断の手引き:改訂4版.	日児誌	1984;88:2693-2694.	厚生省川崎病研究班.
49	川崎病同胞発生例の臨床疫学的研究.	昭和医会誌	1984;44(5):605-625.	今田義夫.
50	昭和57年北陸地方における川崎病流行状況の概要.	小児臨	1984;37:1337-1341.	森田正人, 浅井利夫, 中川秀昭, 河野俊 一, 谷口昂, 舘孔三, 中田慶子.
51	川崎病: その概説と研究史.	小児医学	1984;17(6):887-909.	川崎富作.
52	川崎病.	綜合臨牀	1984;33(5):1004-1006.	川崎富作.
53	小地域単位に観察した川崎病罹患率の疫学的特性.	日衛誌	1984;31(10):539-547.	中村好一, 大金央子, 柳川洋.
54	川崎病死亡の推移をたどる.	厚生指標	1984;31(3):3-8.	柳川洋, 橋本勉.
55	川崎病の疫学像.	小児医学	1984;17(6):910-925.	柳川洋, 大金央子, 橋本勉.
56	川崎病死亡例の臨床的検討.	小児科	1985;26:1017-1021.	加藤裕久, 一ノ瀬英世, 柳川洋, 川崎富 作.
57	第8回川崎病全国調査成績.	小児科	1985;26(9):1049-1053.	厚生省川崎病研究班.
58	疫学的見地からみた川崎病の病因.	Prog Med	1985;5(1):29-34.	重松逸造.
59	川崎病(MCLS)発見の歴史と経緯.	小児内科	1985;17(5):639-642.	重松逸造.
60	川崎病(MCLS).(注目の感染症)	日本臨牀	1985;43(春期増刊 Suppl):1017-1025.	川崎富作.
61	川崎病のサーベイランス:昭和59年1年間のまとめ.	小児内科	1985;17:653-658.	柳川洋, 永井正規, 川崎富作.
62	川崎病再発例, 同胞例の疫学像.	日衛誌	1985;32(1):3-7.	柳川洋, 永井正規, 大金央子, 橋本勉, 中 村好一.
63	川崎病サーベイランス事業の現状.	Prog Med	1985;5:7-12.	柳川洋, 川崎富作.
64	川崎病疫学像の総括.	小児内科	1985;17(5):647-652.	柳川洋.
65	同胞発生例.	Prog Med	1986;6(1):15-20.	今田義夫, 柳川洋.
66	川崎病についての話題.	保健の科学	1986;28(7):452-458.	川崎富作.
67	サーベイランスにもとづく疾病流行の予測:福岡県にお ける川崎病を例に.	日衛誌	1986;41(5):836-842.	中村好一.
68	川崎病: 疫学データのすべて.	ソフトサイエンス社 (東京)		日本心臓財団川崎病原因究明委員会編 (代表:重松逸造, 柳川洋, 川崎富作).
69	第9回川崎病全国調査成績.	小児科	1987;28(9):1059-1066.	厚生省川崎病研究班.
70	川崎病流行時の気象医学的検討:第2報 国内での流 行を中心に.	小児臨	1987;40(3):537-543.	森田正人, 浅井利夫.
71	川崎病概論.	日赤医学	1987;39(4):183-193.	川崎富作.
72	川崎病の地域集積性および時間集積性に関する記述 疫学的研究.	日児誌	1987;91(4):896-910.	中村好一.
73	流行時における川崎病患者および家族の健康調査(6 施設共同研究).	小児診	1987;50:1207-1210.	藤田委由, 中村好一, 柳川洋, 草川三治, 野間清司, 福田睦夫, 渡部誠一, 大國真 彦, 原田研介, 川崎富作, 麻生誠二郎, 浅 井利夫, 豊田貢一, 今田義夫.
74	川崎病サーベイランス成績-三年間のまとめ-.	日本医事新報	1987;3282:32-34.	柳川洋, 屋代真弓, 中村好一, 麻生誠二 郎, 今田義夫, 川崎富作, 重松逸造.

No.	Title	Name of Journal	Volume and No.	Authors
75	川崎病の最近の疫学について.	Prog Med	1987;7(1):7-12.	柳川洋, 藤田委由, 中村好一.
76	疫学からみた川崎病の病因論.	小児診	1987;50(6):1144-1150.	柳川洋.
77	川崎病. (疾病発生要因へのmultidisciplinary approach).	現代医学	1987;34(3):363-369.	柳川洋.
78	川崎病全国調査対象施設の医療状況:断層心エコーを中心に.	Prog Med	1988;8:7-12.	菌部友良, 今田義夫, 麻生誠二郎, 川崎富作, 浅井利夫, 多田羅勝義, 草川三治, 原田研介, 柳川洋, 屋代真弓, 中村好一.
79	全国調査による川崎病心後遺症の解析.	日児誌	1988;92(8):1736-1741.	藤田委由, 中村好一, 永井正規, 柳川洋, 今田義夫, 麻生誠二郎, 川崎富作.
80	川崎病はうつる病気か?その流行像と疫学像.	医学のあゆみ	1988;144(3):199-200.	母里啓子.
81	サーベイランスによる川崎病患者発生数の推定.	日児誌	1988;92(8):1754-1759.	柳川洋, 中村好一, 藤田委由, 永井正規, 麻生誠二郎, 今田義夫, 川崎富作.
82	川崎病に関する研究.	日本医師会雑誌	1989;101(1):91-97.	川崎富作.
83	第10回川崎病全国調査成績.	小児科	1990;31(5):569-576.	厚生省川崎病研究班.
84	川崎病の歴史.	小児内科	1990;22(12):1757-1761.	川崎富作.
85	川崎病の生い立ちとその展望.	Prog Med	1990;10(7):1451-1470.	川崎富作.
86	六年間にわたる川崎病サーベイランス成績.	日本医事新報	1990;No 3472:27-30.	柳川洋, 屋代真弓, 中村好一, 川崎富作, 大川澄男.
87	10回にわたる全国調査による川崎病疫学像の特徴.	Prog Med	1990;10(1):113-117.	柳川洋, 屋代真弓, 中村好一, 藤田委由, 永井正規, 川崎富作.
88	川崎病死亡例.	Prog Med	1991;11:19-21.	大川澄男.
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No.	Title	Name of Journal	Volume and No.	Authors
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182	全国調査成績からみた最近の川崎病の動向.	小児内科	2009;41(1):9-13.	中村好一.
183	川崎病の出生年コホート別心後遺症累積罹患率.	日児誌	2009;113(8):1212-1218.	河合邦夫, 屋代真弓, 中村好一, 柳川洋.
184	疫学からみたガンマグロブリン不応例.(川崎病:最近の進歩と課題)	小児内科	2009;41(1):66-68.	上原里程.
185	川崎病容疑例(狭義の不全型)の疫学的特徴.	日児誌	2010;114(3):497-502.	上原里程, 屋代真弓, 中村好一, 柳川洋, 藺部友良.
186	出生年コホート別にみた川崎病心後遺症の種類別の累積罹患率.	小児保健研究	2010;69(3):380-386.	河合邦夫, 屋代真弓, 中村好一, 柳川洋.
187	川崎病急性期にステロイド投与を受けた症例の冠動脈障害発生の頻度.	日児誌	2010;114(5):853-857.	鈴木啓之, 荻野廣太郎, 中村好一, 上原里程, 屋代真弓, 柳川洋.
188	第20回川崎病全国調査成績.	小児診	2010;73(1):143-156.	屋代真弓, 中村好一, 上原里程, 柳川洋.
189	疫学からみた成人期の川崎病を考察する.(成人期における川崎病冠動脈瘤を考える)	Vascular Medicine	2010;6(1):2-6.	上原里程.
190	増大する「川崎病」の今を知る.	月刊地域保健	2010;41(4):62-69.	中村好一.
191	冠動脈疾患「下」一診断と治療の進歩一XV. 川崎病の診断・治療の現状 川崎病全国調査成績の概要.	日本臨床	2011;69(9):525-528	上原里程.
192	疫学からみた川崎病死亡例.	循環器内科	2011;69(4):412-420	中村好一, 屋代真弓.
193	公衆衛生アーカイブ:君たちへ.	公衆衛生情報	2011;40(10):6-18.	重松逸造, 多田羅浩三.
194	疫学から.(川崎病の本態にせまる:古くて新しい研究から)	小児診	2011;74(8):1097-1102.	上原里程.
195	第21回川崎病全国調査成績.	小児診	2012;75(3):507-523.	屋代真弓, 上原里程, 中村好一, 柳川洋.
196	川崎病疫学調査よりわかってきたこと.	京都府立医科大学雑誌	2012;121(2):55-59.	小澤誠一郎.
197	最近10年における川崎病巨大冠動脈瘤の実態全国調査:第1報.	心臓	2012;44(11):1440-1441.	深澤隆治, 濱岡建城, 佐地勉, 津田悦子, 鮎沢衛, 鈴木啓之, 松裏裕行, 三浦大, 小林徹, 賀藤均, 屋代真弓, 中村好一, 阿部淳, 小川俊一.
198	川崎病研究の将来.	小児科	2012;53(13):1803-1812.	川崎富作, 直江史郎.
199	川崎病全国調査からみた川崎病疫学の特徴とその変遷.	日本小児循環器学会雑誌	2012;28(3):148-156.	中村好一, 屋代真弓, 上原里程.
200	川崎病の疫学:現状と課題.	小児科	2012;53(13):1777-1784.	中村好一.
201	第10届国际川崎病研讨会概述.	中华儿科杂志	2012;50(9):714-717.	陈树宝, 黄美容.
202	血管炎一基礎と臨床のクロストーク一Ⅲ. 川崎病の病因・病理・診断・治療.	日本臨床	2013;71(増刊1):113-117.	中村好一, 屋代真弓, 上原里程.
203	最近10年における川崎病巨大冠動脈瘤の実態全国調査.	心臓(第30回関東川崎病研究会)	2013;45(5):604-605	深澤隆治, 濱岡建城, 佐地勉, 津田悦子, 鮎沢衛, 鈴木啓之, 松裏裕行, 三浦大, 小林徹, 賀藤均, 屋代真弓, 中村好一, 阿部淳, 小川俊一.
204	巨大冠動脈瘤全国調査における死亡例の検討.	Prog Med	2013;33(7):1506-1512.	深澤隆治, 津田悦子, 佐野哲也, 坂崎尚徳, 寺口正之.
205	川崎病発見の経緯とその後.(我が国で命名された血管炎)	日本臨床	2013;71(増刊1):35-39.	川崎富作, 直江史郎.
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207	川崎病50年の歴史.	循環器内科	2014;75(1):123-128.	小川俊一.
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210	川崎病疫学とその変遷.	日本臨床	2014;72(9):2014-2019.	中村好一.
211	川崎病の白血球数の解析一第22回川崎病全国調査成績から一.	小児診	2015;78(12):1837-1840.	山下真穂, 屋代真弓, 青山泰子, 牧野伸子, 中村好一.
212	疫学からみた川崎病の原因.	小児科	2015;56(8):1099-1104.	中村好一, 牧野伸子.
213	川崎病免疫グロブリン不応例の疫学.	小児科	2015;56(7):995-1000.	牧野伸子.
214	最新冠動脈疾患学(下)一冠動脈疾患の最新治療戦略一川崎病の疫学像の推移とデータベース構築.	日本臨床	2016;74(増刊6):497-502.	牧野伸子, 屋代真弓
215	第23回川崎病全国調査成績.	小児診	2016;79(2):273-292.	屋代真弓, 牧野伸子, 中村好一, 柳川洋.

No.	Title	Name of Journal	Volume and No.	Authors
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217	川崎病の発見. (日本で発見された疾患概念)	循環器専門医	2016;24(1):129-133.	川崎富作.
218	川崎病の疫学と病態.	臨床検査	2016;60(6):586-591.	中村好一, 牧野伸子.
219	川崎病の最近の動向:川崎病全国調査成績を中心に.	皮膚病診療	2017;39(5):464-469.	高橋啓.
220	膠原病の発症・増悪における季節性. (リウマチ・膠原病とアレルギー疾患)	アレルギーの臨床	2017;201737(5):426-430.	小倉剛久.
221	川崎病50年. (川崎病の現況)	臨床免疫・アレルギー科	2017;68(6):612-616.	川崎富作.
222	川崎病の疫学:Yamaguchi Studyの結果から. (川崎病の現況)	臨床免疫・アレルギー科	2017;68(6):617-622.	長谷川俊史, 鈴木康夫, 木畑鉄弘, 守分正, 大淵典子, 大賀正一, 中村好一.
223	第24回川崎病全国調査成績.	小児診	2018;81(2):271-274.	屋代真弓, 牧野伸子, 中村好一, 柳川洋.
224	川崎病の疫学:第24回川崎病全国調査成績の概要. (川崎病アップデート:病因・病態論の推移と展望)	アレルギー・免疫	2018;25(11):1374-1382.	中村好一.
225	川崎病の最近の話題ー疫学を中心にー.	東京小児科医会報	2018;36(3通巻121):21-25.	柳川洋, 中村好一, 屋代真弓.
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227	日本における川崎病の疫学的所見. (Inflammation & Immunology Focus on Kawasaki disease)	臨床のあゆみ	2019;No. 107:7-8.	牧野伸子, 中村好一.
228	川崎富作(1925-):川崎病発見の奇跡的偉業. (現代医学・生物学の先駆者たち:臨床医学)	生体の科学	2019;70(5):472-473.	濱岡建城.
229	第25回川崎病全国調査成績.	小児診	2020;83(2):269-273.	小佐見光樹, 屋代真弓, 牧野伸子, 中村好一.
230	疫学. (川崎病:原因究明・診断・治療の進歩)	小児科	61(7) 946-952.	牧野伸子, 中村好一.
231	川崎病診断の手引きとガイドラインの変遷.	小児診	2021;84(9):1233-1237.	中村好一.
232	川崎病全国調査データベースからみえる患者動向.	小児内科	2021;53(1):10-16	牧野伸子, 中村好一.
233	川崎病全国調査にみるガイドラインが与えた急性期治療への影響. (おさえた川崎病ガイドラインのツボ ガイドラインの変遷と影響)	小児診	2021;84(9):1239-1243.	阿江竜介.
234	成人期に移行した川崎病. (川崎病の今:急性期以降の治療)	小児内科	2021;53(1):141-146.	三谷義英.
235	川崎病の疫学:近年の動向(特集:川崎病ー基礎と臨床の最前線).	医学と薬学	2021;78(8):911-916.	牧野伸子, 中村好一.
236	第26回川崎病全国調査成績.	小児診	2022;85(3):391-396.	阿江竜介, 屋代真弓, 松原優里, 小佐見光樹, 牧野伸子, 中村好一.
237	川崎病の発生状況:全国調査成績から. (特集:川崎病)	日本医師会雑誌	2022;151(2):204-207.	阿江竜介, 中村好一.
238	難病の疫学研究.	日本医師会雑誌	2022;150(10):1819-1822.	中村好一.
239	【川崎病の子どもと家族への看護ケア】基礎知識 川崎病の疫学と歴史.	小児看護	2023;46(8):906-913.	鮎澤衛.

Material (1-2) List of academic papers on Kawasaki disease nationwide surveys in English				
No.	Title	Name of Journal	Volume and No.	Authors
1	A new infantile acute febrile mucocutaneous lymph node syndrome (MLNS) prevailing in Japan.	Pediatrics	1974;54(3):271-276.	Kawasaki T, Kosaki F, Okawa S, Shigematsu I, Yanagawa H.
2	Epidemiology of Kawasaki disease (MCLS).	Jpn J Med Sci Biol	1979;32(4):241-243.	Yanagawa H.
3	Epidemiology of Kawasaki disease in Japan.	Acta Paediatr Jpn	1979;21(1):1-10.	Yanagawa H, Shigematsu I, Kusakawa S, Kawasaki T.
4	Kawasaki disease continues to increase in Japan.	Pediatrics	1979;64(3):386	Shigematsu I, Shibata S, Tamashiro H, Kawasaki T, Kusakawa S.
5	Kawasaki disease: a worldwide survey. (letter)	Lancet	1979;2(8135):193.	Shigematsu I, Tamashiro H, Shibata S, Kawasaki T, Kusakawa S.
6	Kawasaki Disease (MCLS).	Asian Med J	1980;23(12):927-930.	Kawasaki T.
7	Epidemiological features of Kawasaki disease in Japan.	Acta Paediatr Jpn(Overseas Ed.)	1983;25(2):94-107.	Yanagawa H, Shigematsu I.
8	An analysis on weekly incidence of Kawasaki disease and selected infectious disease.	Acta Paediatr Jpn	1984;26(1):107.	Nakamura Y, Nagai M, Yanagawa H, Kusakawa S.
9	Nationwide epidemic of Kawasaki disease in Japan during winter of 1985-86.	Lancet	1986;2(8516):1138-1139	Yanagawa H, Nakamura Y, Kawasaki T, Shigematsu I.
10	Epidemiology of Kawasaki disease in Japan.	Prog Clin Biol Res	1987;250:5-17.	Yanagawa H.
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12	Nationwide survey on Kawasaki disease in Japan.	Pediatrics	1987;80(1):58-62.	Yanagawa H, Kawasaki T, Shigematsu I.
13	Temporal and geographical clustering of Kawasaki disease in Japan.	Prog Clin Biol Res	1987;250:19-32.	Nakamura Y, Yanagawa H, Kawasaki T.
14	A nationwide incidence survey of Kawasaki disease in 1985-1986 in Japan.	J Infect Dis	1988;158(6):1296-1301.	Yanagawa H, Nakamura Y, Yashiro M, Fujita Y, Nagai M, Kawasaki T, Aso S, Imada Y, Shigematsu I.
15	Kawasaki disease in families.	Pediatrics	1989;84(4):666-669.	Fujita Y, Nakamura Y, Sakata K, Hara N, Kobayashi M, Nagai M, Yanagawa H, Kawasaki T.
16	Kawasaki disease.	Asian Medical Journal	1989;32(9)p497-506	Kawasaki T.
17	Cardiac sequelae of Kawasaki disease in Japan: statistical analysis.	Pediatrics	1991;88(6):1144-1147.	Nakamura Y, Fujita Y, Nagai M, Yanagawa H, Imada Y, Okawa S, Kawasaki T, Kato H.
18	Mortality among children with Kawasaki disease in Japan.	N Engl J Med	1992;326(19):1246-1249.	Nakamura Y, Yanagawa H, Kawasaki T.
19	Incidence rate of recurrent Kawasaki disease in Japan.	Acta Paediatr	1994;83(10):1061-1064.	Nakamura Y, Hirose K, Yanagawa H, Kato H, Kawasaki T.
20	Incidence rate, cumulative incidence, and cohort effect of Kawasaki disease in Japan.	J Epidemiol	1994;4(1):13-16.	Nakamura Y, Yanagawa H, Hirose K, Kawasaki T.
21	Iv gamma globulin treatment of Kawasaki disease in Japan: results of a nationwide survey.	Acta Paediatr	1995;84:765-768.	Yanagawa H, Yashiro M, Nakamura Y, Sakata K, Kawasaki T.
22	Cardiac sequelae of Kawasaki disease in Japan over 10 years.	Acta Paediatr Jpn	1995;37(6):667-671.	Hirose K, Nakamura Y, Yanagawa H.
23	Epidemiologic pictures of Kawasaki disease in Japan: from the nationwide incidence survey in 1991 and 1992.	Pediatrics	1995;95(4):475-479.	Yanagawa H, Yashiro M, Nakamura Y, Kawasaki T, Kato H.
24	General review and problems in Kawasaki disease.	Jpn Heart J	1995;36(1):1-12.	kawasaki T.
25	Intravenous gammaglobulin treatment of Kawasaki disease In Japan.	Elsevier Science B.V.	1995;321-327.	Hirose K, Yanagawa H, Nakamura Y, Yashiro M.
26	Iv gamma globulin treatment of Kawasaki disease in Japan: results of a nationwide survey.	Acta Paediatr	1995;84(7):765-768.	Yanagawa H, Yashiro M, Nakamura Y, Sakata K, Kawasaki T.
27	Kawasaki disease. (review)	Acta Paediatr	1995;84(7):713-715.	Kawasaki T.
28	Nationwide surveillance of Kawasaki disease in Japan, 1984 to 1993.	Paediatr Infect Dis J	1995;14(1):69-71.	Yanagawa H, Yashiro M, Nakamura Y, Hirose K, Kawasaki T.
29	Results of 12 nationwide epidemiological incidence surveys of Kawasaki disease in Japan.	Arch Paediatr Adolesc Med	1995;149(7):779-783.	Yanagawa H, Yashiro M, Nakamura Y, Kawasaki T, Kato H.
30	Results of 12 nationwide surveys of Kawasaki disease.	Elsevier Science B.V.	1995;3-14.	Yanagawa H, Nakamura Y, Yashiro M, Hirose K.
31	Surveillance of Kawasaki disease in Japan, 1984-1994.	Elsevier Science B.V.	1995;15-21.	Yashiro M, Nakamura Y, Hirose K, Yanagawa H.
32	A case-control study of recurrent Kawasaki disease using the database of the nationwide surveys in Japan.	Eur J Paediatr	1996;155(4):303-307.	Nakamura Y, Yanagawa H.
33	Epidemiology of infant Kawasaki disease with a report of the youngest neonatal case ever reported in Japan.	Acta Paediatr	1996;85(8):995-997.	Tsuchida S, Yamanaka T, Tsuchida R, Nakamura Y, Yashiro M, Yanagawa H.

No.	Title	Name of Journal	Volume and No.	Authors
34	Hospital facilities available to patients with Kawasaki disease: results of a national survey of Kawasaki disease in Japan.	Acta Paediatr Jpn	1996;38(6):562-566.	Koyanagi H, Nakamura Y, Yashiro M, Yanagawa H.
35	Kawasaki Disease Follow-up Group. Mortality rates for patients with a history of Kawasaki disease in Japan.	J Pediatr	1996;128(1):75-81.	Nakamura Y, Yanagawa H, Kato H, Kawasaki T.
36	Update of the epidemiology of Kawasaki disease in Japan: from the results of 1993-94 nationwide survey.	J Epidemiol	1996;6(3):148-157.	Yanagawa H, Nakamura Y, Yashiro M, Ojima T, Koyanagai H, Kawasaki T.
37	Epidemiology of Kawasaki disease in the United States and worldwide.	Prog Pediatr Cardiol	1997;6(3):181-185.	Taubert KA.
38	Leukocyte counts in patients with Kawasaki disease: from the results of nationwide surveys of Kawasaki disease in Japan.	Acta Paediatr	1997;86(12):1328-1332.	Koyanagi H, Yanagawa H, Nakamura Y, Yashiro M.
39	Serum C-reactive protein levels in patients with Kawasaki disease: from the results of nation-wide surveys of Kawasaki disease in Japan.	Acta Paediatr	1997;86(6):613-619.	Koyanagi H, Yanagawa H, Nakamura Y, Yashiro M.
40	Use of intravenous γ -globulin for Kawasaki disease: effects on cardiac sequelae.	Pediatr Cardiol	1997;18(1):19-23.	Yanagawa H, Nakamura Y, Sakata K, Yashiro M.
41	Cardiac sequelae in recurrent cases of Kawasaki disease: a comparison between the initial episode of the disease and a recurrence in the same patients.	Pediatrics	1998;102(6):e66.	Nakamura Y, Oki I, Tanihara S, Ojima T, Yanagawa H
42	Cardiac sequelae of Kawasaki disease among recurrent cases.	Arch Dis Child	1998;78(2):163-165.	Nakamura Y, Yanagawa H, Ojima T, Kawasaki T, Kato H.
43	Lower level of serum potassium and higher level of C-reactive protein as an independent risk factor for giant aneurysms in Kawasaki disease.	Acta Paediatr	.1998;87(1):32-36.	Koyanagi H, Nakamura Y, Yanagawa H.
44	Results of the nationwide epidemiologic survey of Kawasaki disease in 1995 and 1996 in Japan.	Pediatrics	1998;102(6):e65.	Yanagawa H, Nakamura Y, Yashiro M, Ojima T, Tanihara S, Oki I, Zhang T.
45	The Kawasaki Disease Follow-up Group. Mortality among patients with a history of Kawasaki disease: the third look.	Acta Paediatr Jpn	1998;40(5):419-423.	Nakamura Y, Yanagawa H, Kato H, Harada K, Kawasaki T.
46	Changes in epidemic patterns of Kawasaki disease in Japan.	Pediatr Infect Dis J	1999;18(1):64-66.	Yanagawa H, Nakamura Y, Ojima T, Yashiro M, Tanihara S, Oki I.
47	Effects of gamma-globulin on the cardiac sequelae of Kawasaki disease.	Pediatr Cardiol	1999;20(4):248-251.	Yanagawa H, Zhang T, Oki I, Nakamura Y, Yashiro M, Ojima T, Tanihara S.
48	Factors related to cardiac sequelae of Kawasaki disease.	Eur J Pediatr	1999;158:694-697.	Zhang T, Yanagawa H, Oki I, Nakamura Y, Yashiro M, Ojima T, Tanihara S.
49	A multicenter collaborative study on the risk factors of cardiac sequelae due to Kawasaki disease: a one-year follow-up study.	Acta Paediatr	2000;89: 1435-1438.	Oki I, Tanihara S, Ojima T, Nakamura Y, Yanagawa H.
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52	Incidence rate of recurrent Kawasaki disease and related risk factors: from the results of nationwide surveys of Kawasaki disease in Japan.	Acta Paediatr	2001;90(1):40-44.	Hirata S, Nakamura Y, Yanagawa H.
53	Incidence survey of Kawasaki disease in 1997 and 1998 in Japan.	Pediatrics	2001;107(3):e33.	Yanagawa H, Nakamura Y, Yashiro M, Oki I, Hirata S, Zhang T, Kawasaki T.
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No.	Title	Name of Journal	Volume and No.	Authors
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No.	Title	Name of Journal	Volume and No.	Authors
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90	Risk of coronary arterial lesions in immunoglobulin resistant Kawasaki disease.	Open Journal of Pediatrics	2012;2:38-41.	Ogino H, Kaneko K, Uchiyama T, Yoshimura K, Teraguchi M, Nakamura Y.
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101	Cumulative incidence of Kawasaki disease in Japan.	Pediatr Int	60(1):19-22.	Nakamura Y, Yashiro M, Yamashita M, Aoyama N, Otaki U, Ozeki Y, Sano T, Kojo T, Ae R, Aoyama Y, Makino N, Kotani K.
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No.	Title	Name of Journal	Volume and No.	Authors
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112	Global epidemiology of vasculitis.	Nat Rev Rheumatol	2022;18(1):22-34.	Watts RA, Hatemi G, Burns JC, Mohammad AJ.
113	Incidence of Kawasaki disease before and after the COVID-19 pandemic in Japan: Results of the 26th nationwide survey, 2019 to 2020.	JAMA Pediatr	2022;176(12):1217-24. doi: 10.1001/jamapediatrics.2022.3756.	Ae R, Makino N, Kuwabara M, Matsubara Y, Kosami K, Sasahara T, Nakamura Y.

Material (2) Copies of the diagnostic guidelines

First edition (1970) First nationwide survey

小児急性熱性皮膚粘膜リンパ節症候群 (Muco-Cutaneous Lymphnode Syndrome, 略称MCLS)

昭和45年度厚生省医療研究助成補助金によるMCLS研究班 (班長：神前章雄) 作成

診断の手びき

本症は主として4才以下の乳幼児に好発する原因不明の疾患で、その症候は以下
の必発症状と参考症状とに分けられるが、必発症状(5症状)のうち、1を
含む4つ以上の症状を伴うものを本症として取扱う。

A 必発症状

1. 抗生物質に不応の5日以上続く発熱
2. 両側眼球結膜の充血
3. 四肢末端の変化：①硬性浮腫(急性期)②掌蹼紅斑または末端紅斑(急性期)③爪皮膚移行部からの膜様落屑(回復期)
4. 口唇、口腔所見：①口唇の乾燥、紅潮、き裂 ②舌乳頭腫大(毒舌様変化) ③口腔、咽頭粘膜のびまん性発赤
5. 体幹の不定形発疹(ただし、水疱、痂皮は伴わない)

B 参考症状(必発症状と併せて、診断上大切である)

1. 拇指頭大以上の急性頸部リンパ節腫脹(ただし、決して化膿しない)
2. 下痢
3. 蛋白尿、尿沈渣中の白血球増多
4. 検査所見：①核左方移動を伴なう白血球増多 ②赤沈促進 ③CRP陽性など
5. 時にみられる症状：①無菌性髄膜炎 ②軽度の黄疸、血中トランスアミン一ゼ値軽度上昇 ③心炎、心筋炎 ④関節痛、関節炎
6. 4才以下に好発し、後遺症を残さず、同胞発生をみない

お願い

本症に合致する症例をご覧になりましたら、本研究班にご連絡下さい。
連絡先 東京都渋谷区広尾4-1-22(〒150) 日赤中央病院小児科MCLS研究班
(TEL: 400-1311)

(裏面に本症のカラー写真を掲載してあります。)



▲本症の全身像



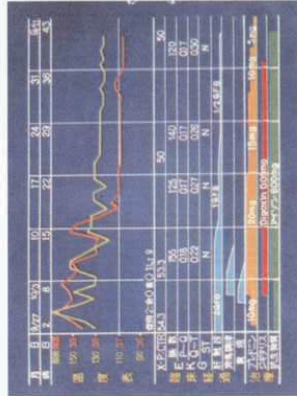
▲眼球結膜充血



▲定型的な指先の落屑



▲手掌紅斑および硬性浮腫(急性期)



▲本症の熱型(東京女子医大第2病院症例)

小児急性熱性皮膚粘膜リンパ節症候群 (Muco-Cutaneous Lymphnode Syndrome, 略称MCLS)

診断の手びき

昭和47年度厚生省特別研究費によるMCLS研究班 (班長: 神前章雄) 作成

(昭和45年度作成の手びきのうち、今回はB-6. の一部を削除、B-7. を追加した。)

本症は主として4才以下の乳幼児に好発する原因不明の疾患で、その症候は以下の必発症状と参考症状とに分けられるが、必発症状 (5症状) のうち、1を含む4つ以上の症状を伴うものを本症として取扱う。

A 必発症状

1. 抗生物質に不応の5日以上続く発熱
2. 両側眼球結膜の充血
3. 四肢末端の変化: ①硬性浮腫 (急性期) ②掌趾紅斑または末端紅斑 (急性期) ③爪皮膚移行部からの膜様落屑 (回復期)
4. 口腔、口腔所見: ①口腔の乾燥、紅潮、き裂 ②舌乳頭腫大 (莓舌様変化) ③口腔、咽頭粘膜のびまん性発赤
5. 体幹の不定形発疹 (ただし、水疱、痂皮は伴わない)

B 参考事項 (必発症状と併せて、診断上大切である)

1. 拇指頭人以上の急性頸部リンパ節腫脹 (ただし、決して化膿しない)
2. 下痢
3. 蛋白尿、尿沈渣中の白血球増多
4. 検査所見: ①核左方移動を伴う白血球増多 ②赤沈促進 ③CRP陽性など
5. 時にみられる症状: ①無菌性髄膜炎 ②軽度の黄疸、血中トランスアミナーゼ値軽度上昇 ③心炎、心筋炎 ④関節痛、関節炎
6. 4才以下に好発し、同胞発生をみない
7. 本症の致死率は約1.5%で、主な剖検所見は冠動脈の血栓性閉塞を伴った血管炎である

お願い

本症に合致する症例をご覧になりましたら、本研究班にご連絡下さい。
連絡先 東京都渋谷区区尾4-1-22(〒150) 日赤医療センター小児科MCLS研究班
または 東京箱根地区白台4-6-1(〒108) 国立公衆衛生院疫学部MCLS研究班
(TEL: 03-441-7111 内線243)

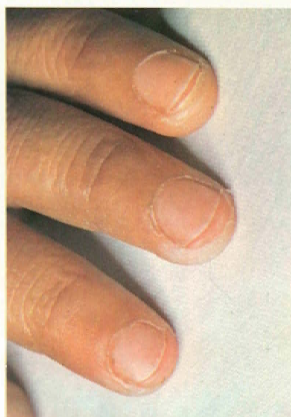
(裏面に本症のカラー写真を掲載してあります。)



▲本症の全身像



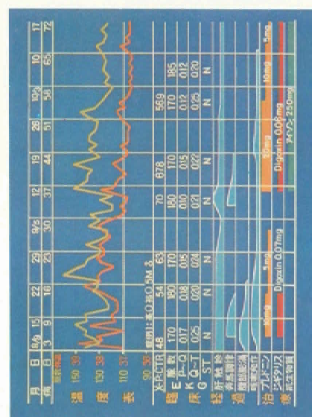
▲眼球結膜充血



▲典型的な指尖の落屑



▲手掌紅斑および硬性浮腫(急性期)



▲本症の熱型(東京女子医大第2病院症例)

Revised second edition (1974) 3rd and 4th nationwide surveys

小児急性熱性皮膚粘膜リンパ節症候群 (略称MCLS)診断の手びき 改訂2版

MCLS研究班作成 (昭和45年9月初版、47年9月改訂1版、49年4月改訂2版)

本症は主として4才以下の乳幼児に好発する原因不明の疾患で、その症候は以下の主要症状と参考条項とに分けられるが、6つの主要症状のうち、5つ以上の症状を伴うものを本症として取扱う。

A 主要症状

1. 抗生物質に不応の5日以上続く発熱。
2. 四肢末端の変化：〔急性期〕手足の硬性浮腫、掌蹼ないしは指趾先端の紅斑。
〔回復期〕爪皮膚移行部からの膜様落屑。
3. 水疱、痂皮を形成しない不定形発疹（体幹に多い）。
4. 両側眼球結膜の充血（一過性のことがある）。
5. 口唇、口腔所見：口唇の紅潮、舌舌、口腔咽頭粘膜のびまん性発赤。
6. 急性期における非化膿性頸部リンパ節腫脹（一過性のことがある）。

B 参考条項

しばしばみられる症状または所見

1. 心血管系：心電図の変化（PQ、QTの延長、低電位傾向、ST、Tの変化、不整脈）。異常聴診所見（頻脈、心雑音、奔馬調律、微弱心音）。
 2. 消化器：下痢、嘔吐、腹痛。
 3. 尿：蛋白尿、沈渣の白血球増多。
 4. 血液：①核左方移動を伴う白血球増多。②軽度の貧血。③赤沈値の促進。④CRP陽性。⑤ α_2 グロブリンの増加。⑥ASLO値は上昇しない。
- 時にみられる症状または所見
5. 呼吸器：咳嗽、鼻汁。
 6. 関節：疼痛、腫脹。
 7. その他：①髄膜刺激症状、髄液の単核球、蛋白などの増多。②軽度の黄疸あるいは血清トランスアミナーゼ値の上昇。

備考

1. 本症候群の性比は1.5:1で男児に多く年齢分布は4才以下が80%を占め、致死率は1~2%である。
2. 再発は2%内外にみられる。
3. 心電図所見としては心筋炎様、心外膜炎様または虚血性変化を示し、いままでの報告例ではほぼ全例に冠動脈増大と血行性閉塞および心筋炎を認める。
4. 本症経過後に冠動脈狭窄症や僧帽弁閉鎖不全の発生をみることもある。
5. この診断の手びきに合致する症例で敗血症を伴うもの、若年性関節リウマチに移行したもの、結節性動脈周囲炎と病理診断されたもの、その他疑問点はそのむね付記された。

本症に合致する症例をご覧になりましたら、本研究班にご連絡下さい。

連絡先 東京都渋谷区広尾4-1-22(〒150) 日赤医療センター小児科MCLS研究班
(TEL: 03-409-2211)

(裏面に本症のカラー写真を掲載しております。)



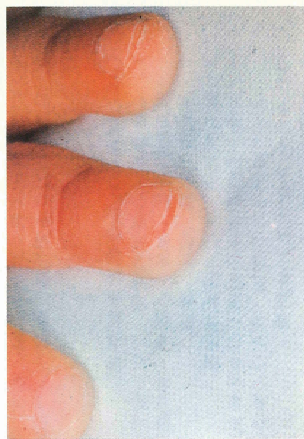
▲MCLSの発疹 (男10月、第4病日)



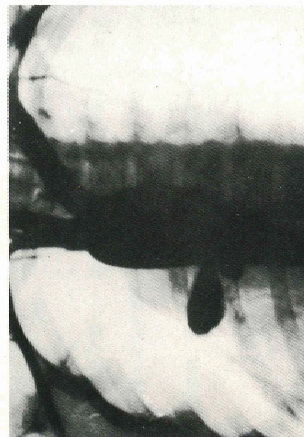
▲口唇の変化と眼球結膜の充血 (女4才、第5病日)



▲足の紅腫と硬性浮腫 (女1才6月、第6病日)



▲指先の落屑 (男1才、第11病日)



▲MCLS罹患児の冠動脈造影像：左冠動脈強と右冠動脈閉塞 (男5才、発病7月後に心筋梗塞様発作)



▲冠動脈の血行性閉塞 (男10月、第31病日に急性死)

Revised third edition (1978) 5th-7th nationwide surveys

小児急性熱性皮膚粘膜リンパ節症候群 (略称MCLS)診断の手びき 改訂3版

MCLS研究班作成
(昭和45年9月初版, 47年9月改訂1版, 49年4月改訂2版, 53年8月改訂3版)
*フアンダーブインの箇所を変更または追加。

本症は主として4才以下の乳幼児に好発する原因不明の疾患で、その症候は以下の主要症状と参考条項とに分けられるが、6つの主要症状のうち、5つ以上の症状を伴うものを本症として取扱う。

A 主要症状

1. 原因不明の5日以上続く発熱。
2. 四肢末端の変化：〔急性期〕手足の硬性浮腫、掌蹼ないしは指趾先端の紅斑。
〔回復期〕爪皮膚移行部からの膜様落屑。
3. 水泡、痂皮を形成しない不定形発疹（体幹に多い）。
4. 口唇、咽頭粘膜の充血（一過性のあることがある）。
5. 口唇、口腔所見：口唇の紅潮、歯舌、口腔咽頭粘膜のびまん性発赤。
6. 急性期における非化膿性頸部リンパ節腫脹（一過性のあることがある）。

B 参考条項

しばしばみられる症状または所見

1. 心血管系：心電図の変化（PQ、QTの延長、低電位傾向、ST、Tの変化、不整脈）。
異常聴診所見（頻脈、心雑音、奔馬調律、微弱心音）。
 2. 消化器：下痢、嘔吐、腹痛。
 3. 尿：蛋白尿、沈渣の白血球増多。
 4. 血液：①尿左方移動を伴う白血球増多。②軽度の貧血。③赤沈値の促進。④CRP陽性。
⑤α₂グロブリンの増加。⑥血小板増多。⑦ASO値は上昇しない。
- 時にみられる症状または所見
5. 呼吸器：咳嗽、鼻汁。
 6. 関節：疼痛、腫脹。
 7. その他：①髄膜刺激症状、髄液の単核球、蛋白などの増多。②軽度の黄疸あるいは血清トランスアミナーゼ値の上昇。③胆嚢腫大。

備考

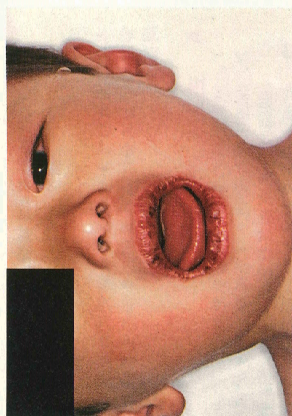
1. 本症発症の性比は1.5:1で男児に多く、年齢分布は4才以下が80%を占め、致死率は1~2%である。
2. 再発は2%内外にみられる。
3. 心電図所見としては心筋炎様、心外膜炎様または虚血性変化を示し、いままでの剖検例ではほぼ全例に冠動脈炎と血栓性閉塞および心筋炎を認める。
4. 本症発症後心筋梗塞様症状や肺動脈閉塞不全の発生をみることがある。
5. この診断の手びきに合致する症例で敗血症を伴うもの、右心性閉塞性肺動脈移行したもの、結節性動脈周囲炎と病理診断されたもの、その他疑難症例はそこの付記されたい。
6. 本症の通称名としては川崎病を用いられる。
7. 英文略称は原著通り“MCLS”を用いるべきで、第9回修正WHO国際疾病分類(446.1)でも、これが採用されている。“MLNS”という略称は、Pediatricsの編集者が原著に無断で変更したもの。

連絡先 東京都渋谷区広尾4-1-22(〒150) 日赤医療センター小児科MCLS研究班
(TEL:03-400-1311)

(裏面に本症のカラー写真を掲載しております。)



▲MCLSの発疹 (男10月、第4病日)



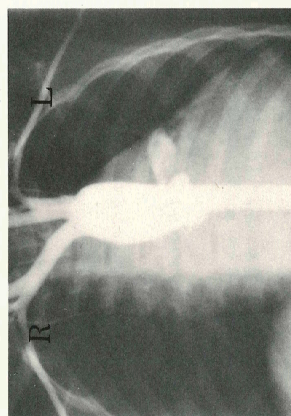
▲口唇の変化と咽頭粘膜の充血 (男3才、第5病日)



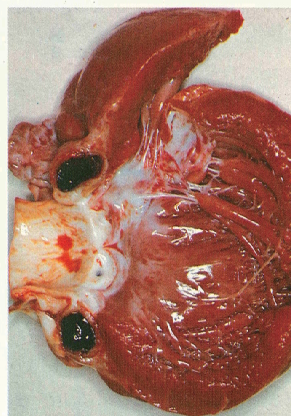
▲足の紅斑と硬性浮腫 (女1才6月、第6病日)



▲指先の蒼白 (男2才、第12病日)



▲MCLS罹患児の冠動脈造影像：左冠動脈と右冠動脈閉塞 (男5才、発病7月後に心筋梗塞様発作)



▲冠動脈の血栓性閉塞 (男10月、第58病日に急性死)

Revised 4th edition (1984) 8th-16th nationwide surveys

川崎病 (MCLS, 小児急性熱性皮膚 粘膜リンパ節症候群) 診断の手引き

厚生省川崎病研究班作成 改訂4版

(1970年9月初版, 1972年9月改訂1版, 1974年4月改訂2版,
1978年8月改訂3版, 1984年9月改訂4版)

本症は、主として4歳以下の乳幼児に好発する原因不明の疾患で、その症候は以下の主要症状と参考条項とに分けられる。

A 主要症状

1. 5日以上続く発熱
2. 四肢末端の変化：(急性期) 手足の硬性浮腫、掌蹠ないしは指趾先端の紅斑 (回復期) 指先からの脱屑落屑
3. 不定形発疹
4. 両側眼球結膜の充血
5. 口唇、口腔所見：口唇の紅潮、いちご舌、口腔咽頭粘膜のびまん性発赤
6. 急性期における非化膿性頸部リンパ節腫大

6つの主要症状のうち5つ以上の症状を伴うものを本症とする。
ただし、上記6主要症状のうち、4つの症状しか認められなくても、経過中に断層心エコー法もしくは、心血管造影法で、冠動脈瘤 (いわゆる拡大を含む) が確認され、他の疾患が除外されれば、本症とする。

B 参考条項

以下の症候および所見は、本症の臨床に、留意すべきものである。

1. 心血管：聴診所見 (心雑音、奔馬調律、微弱心音)、心電図の変化 (PR・QTの延長、異常Q波、低電位差、ST Tの変化、不整脈)、胸部X線所見 (心陰影拡大)、断層心エコー図所見 (心臓液貯留、冠動脈瘤)、狭心症状、束梢動脈瘤 (脱臼など)
2. 消化器：下痢、嘔吐、腹痛、胆嚢腫大、麻痺性イレウス、軽度の黄疸、血清トランスアミナーゼ値上昇
3. 血液：血小板減少を伴う白血球増多、血小板増多、赤沈値の促進、CRP陽性、低アルブミン血症、α₂グロブリンの増加、軽度の貧血
4. 尿：蛋白尿、沈渣の白血球増多
5. 皮膚：BCG接種部位の発赤・痂皮形成、小膿疱、爪の縦溝
6. 呼吸器：咳嗽、鼻汁、肺野の異常陰影
7. 関節：疼痛、腫脹
8. 神経：髄液の単核球増多、けいれん、意識障害、顔面神経麻痺、四肢麻痺

備考 1. 主要症状Aの2は、回復期所見が重要視される。

2. 本症の性比は、1.3-1.5；1で男児に多く、年齢分布は4歳以下が80-85%を占め、致死率は0.3-0.6%である。

3. 再発率は2-3%に、再発率は1-2%にみられる。

連絡先 東京都渋谷区広尾4-1-22 (〒150-8835) 日赤医療センター小児科気付 川崎病研究班
(TEL: 03-3400-1311)

(裏面に本症のカラー写真を掲載してあります。)



▲口唇の変化と眼結膜の充血 (女2歳、第4病日)



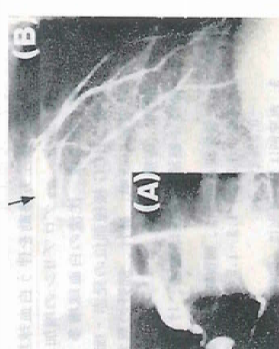
▲川崎病の発疹 (男7月、第4病日)



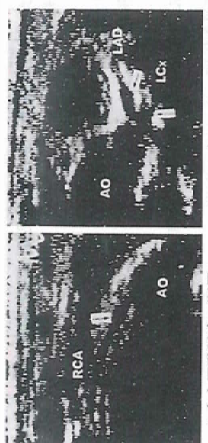
▲指先の浮腫 (男3歳、第12病日)



▲手の紅腫と硬性浮腫 (女1歳6月、第6病日)



(A) 右多発冠動脈瘤 (男9月、第60病日)
(B) 左前下行枝の冠動脈瘤と狭窄性狭窄 (男5歳、発症後3年) 矢印は狭窄を示す。



▲左右冠動脈瘤の断層心エコー図所見 (男2歳、第12病日)
RCA: 右冠動脈
AO: 大動脈
LAD: 左冠動脈前下行枝
LCx: 左冠動脈回旋枝
矢印は冠動脈瘤を示す。

川崎病 (MCLS, 小児急性熱性皮膚 粘膜リンパ節症候群) 診断の手引き

厚生労働省川崎病研究班作成 改訂5版
(1970年9月初版、1972年9月改訂1版、1974年4月改訂2版、1978年8月改訂3版、
1984年9月改訂4版、2002年2月改訂5版)

本症は、主として4歳以下の乳幼児に好発する原因不明の疾患で、その症候は以下の主要症状と参考症状とに分けられる。

A 主要症状

1. 5日以上続く発熱 (ただし、治療により5日未満で解熱した場合も含む)
 2. 両側眼球結膜の充血
 3. 口唇、口腔内、口唇の紅潮、いちご舌、口腔咽頭粘膜のびまん性発赤
 4. 不定形発疹
 5. 四肢末端の変化: (急性期) 手足の硬性浮腫、掌蹠ないしは指趾先端の紅腫 (回復期) 指先からの脱皮落屑
 6. 急性期における非化膿性頸部リンパ節腫脹
- 6つの主要症状のうち5つ以上の症状を伴うものを本症とする。
ただし、上記6主要症状のうち、4つの症状しか認められなくても、経過中に断層心エコー法もしくは、心血管造影法で、冠動脈瘤 (いわゆる拡大を含む) が確認され、他の疾患が除外されれば本症とする。

B 参考症状

以下の症候および所見は、本症の臨床に、留意すべきものである。

1. 心血管: 肺動脈 (心雑音、奔馬調律、微弱心音)、心電図の変化 (P-R-Q-Tの延長、異常Q波、低電位差、S-T-Tの変化、不整脈)、胸部X線所見 (心陰影拡大、断層心エコー図所見 (心腔液貯留、冠動脈瘤)、狭心症状、未相対脈瘤 (狭窄など))
2. 消化器: 下痢、嘔吐、腹痛、胆嚢腫大、麻痺性イレウス、軽度の黄疸、血清トランスアミナーゼ値上昇
3. 血液: 軽度左方移動を伴う白血球増多、血小板増多、赤沈値の促進、CRP陽性、低アルブミン血症、 α_2 グロブリンの増加、軽度の貧血
4. 尿: 蛋白尿、沈渣の白血球増多
5. 皮膚: BCG接種部位の発赤・痂皮形成、小膿疱、爪の増殖
6. 呼吸器: 咳嗽、鼻汁、肺野の異常陰影
7. 関節: 疼痛、腫脹
8. 神経: 髄液の単核球増多、けいれん、意識障害、顔面神経麻痺、四肢麻痺

備考 1. 主要症状Aの5は、回復期所見が重要視される。

2. 急性期における非化膿性頸部リンパ節腫脹は他の主要症状に比べて発現頻度が低い (約65%)。

3. 本症の性別比は、1.3~1.5:1で男児に多く、年齢分布は4歳以下が80~85%を占め、致死率は0.1%前後である。

4. 再発率は2~3%に、回復例は1~2%にみられる。

5. 主要症状を満たさなくても、他の疾患が否定され、本症が疑われる管腔病が約10%存在する。この中には冠動脈瘤 (いわゆる拡大を含む) が確認される例がある。

連絡先 〒150-8535 東京都渋谷区広尾 4-1-22 日赤医療センター小児科 川崎病研究班
電話 03-3400-1311, FAX 03-3400-1394



眼球結膜充血



口唇の紅潮といちご舌



顔部リンパ節腫脹



脱皮



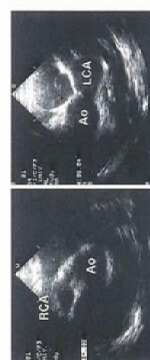
手の紅斑



脱皮 (回復期)



BCG接種部位の発赤



冠動脈瘤の心エコー図
(Ao: 大動脈, RCA: 右冠動脈, LCA: 左冠動脈)

Revised 6th edition (2019) 26th and 27th nationwide surveys

川崎病診断の手引き 改訂第 6 版

日本川崎病学会、特定非営利活動法人日本川崎病研究センター
厚生労働科学研究 難治性血管炎に関する調査研究班

初版 1970 年 9 月、改訂 1 版 1972 年 9 月、改訂 2 版 1974 年 4 月、改訂 3 版 1978 年 8 月
改訂 4 版 1984 年 9 月、改訂 5 版 2002 年 2 月、改訂 6 版 2019 年 5 月

本症は、主として 4 歳以下の乳幼児に好発する原因不明の疾患で、その症候は以下の主要症状と参考
項とに分けられる。

【主要症状】

1. 発熱
2. 両側眼結膜の充血
3. 口唇、口腔所見：口唇の紅潮、いちご舌、口腔咽頭粘膜のびまん性発赤
4. 発疹 (BCG 接種痕の発赤を含む)
5. 四肢末端の変化：
(急性期) 手足の硬性浮腫、手掌足底または指趾先端の紅斑
(回復期) 指先からの糠疹落屑
6. 急性期における非化膿性頸部リンパ節腫脹

- a. 6 つの主要症状のうち、経過中に 5 症状以上を呈する場合は、川崎病と診断する。
- b. 4 主要症状しか認められなくても、他の疾患が否定され、経過中に断層心エコー法で冠動脈病変 (内径の Z スコア+2.5 以上、または実測値で 5 歳未満 3.0mm 以上、5 歳以上 4.0mm 以上) を呈する場合は、川崎病と診断する。
- c. 3 主要症状しか認められなくても、他の疾患が否定され、冠動脈病変を呈する場合は、不全型川崎病と診断する。
- d. 主要症状が 3 または 4 症状で冠動脈病変を呈さないが、他の疾患が否定され、参考条項から川崎病がもつとも考えられる場合は、不全型川崎病と診断する。
- e. 2 主要症状以下の場合には、特に十分な鑑別診断を行ったうえで、不全型川崎病の可能性を検討する。

【参考条項】

以下の症候および所見は、本症の臨床に、留意すべきものである。

1. 主要症状が 4 つ以下でも、以下の所見があるときは川崎病が疑われる。
 - 1) 病初期のトランスアミン値の上昇
 - 2) 乳児の尿中白血球増加
 - 3) 回復期の血小板増多
 - 4) BNP または NT pro BNP の上昇
 - 5) 心臓超音波検査での僧帽弁閉鎖不全・心腔液貯留
 - 6) 胆嚢腫大
2. 低アルブミン血症・低ナトリウム血症
 - 1) 心腔炎
 - 2) 血圧低下 (ショック)
 - 3) 麻痺性イレウス
 - 4) 意識障害

3. 下記の要因は免疫グロブリン抵抗性に強く関連するとされ、不応例予測スコアを参考にすることが望ましい。

- 1) 核の左方移動を伴う白血球増多
- 2) 血小板数低下
- 3) 低アルブミン血症
- 4) 低ナトリウム血症
- 5) 高ビリルビン血症 (黄疸)
- 6) CRP 高値
- 7) 乳児

4. その他、特異的ではないが川崎病で見られることがある所見 (川崎病を否定しない所見)

- 1) 不機嫌
- 2) 心血管：心音の異常、心電図変化、肺動脈などの末梢動脈瘤
- 3) 消化器：腹痛、嘔吐、下痢
- 4) 血液：赤沈値の促進、軽度の貧血
- 5) 皮膚：小膿疱、爪の横溝
- 6) 呼吸器：咳嗽、鼻汁、咽後水腫、肺野の異常陰影
- 7) 関節：疼痛、腫脹
- 8) 神経：髄液の単核球増多、けいれん、顔面神経麻痺、四肢麻痺

【備考】

1. 急性期の致死率は 0.1%未満である。
2. 再発率は 3〜4%に、同胞例は 1〜2%にみられる。
3. 非化膿性頸部リンパ節腫脹 (超音波検査で多房性を呈することが多い) の頻度は、年少児では約 65%と他の主要症状に比べて低いが、3歳以上では約 90%に見られ、初発症状になることも多い。

連絡先：日本川崎病学会事務局
〒150-8935 東京都渋谷区広尾 4-1-22
E-mail jskd-office@umt.n.org

川崎病全国疫学調査事務局 造記

川崎病全国調査の「診断の確実度」の定義について
裏面【主要症状】の a から e のうち

確実 A:

- a. 6 つの主要症状のうち、経過中に 5 症状以上を呈する場合は、川崎病と診断する。

確実 B:

- b. 4 主要症状しか認められなくても、他の疾患が否定され、経過中に断層心エコー法で冠動脈病変 (内径の Z スコア+2.5 以上、または実測値で 5 歳未満 3.0mm 以上、5 歳以上 4.0mm 以上) を呈する場合は、川崎病と診断する。

不全型:

- c. 3 主要症状しか認められなくても、他の疾患が否定され、冠動脈病変を呈する場合は、不全型川崎病と診断する。
- d. 主要症状が 3 または 4 症状で冠動脈病変を呈さないが、他の疾患が否定され、参考条項から川崎病がもつとも考えられる場合は、不全型川崎病と診断する。
- e. 2 主要症状以下の場合には、特に十分な鑑別診断を行ったうえで、不全型川崎病の可能性を検討する。

患者症例写真については、日本川崎病学会ホームページの川崎病関連情報を参考にしてください

<http://www.jskd.jp/info/photo.html>

English version of the first edition (1970) and 5th edition (2002)

First edition

Table 1. First edition of the Diagnostic Guidelines

MCLS is a disease of unknown etiology affecting most frequently infants and young children under 5 years of age. The symptoms can be classified into two categories, indispensable symptoms and other significant symptoms.

A. INDISPENSABLE SYMPTOMS

1. Fever continuing 5 days or more not responding to antibiotics
 2. Congestion of bilateral ocular conjunctivas
 3. Changes of peripheral extremities: (1) indurative edema (initial stage), (2) erythema of palms and soles (initial stage), (3) membranous desquamation at the transitional part of nails/skin (convalescence stage)
 4. Changes in lips and oral cavity: (1) dryness, redness and fissuring of lips, (2) swelling of tongue papillae (strawberry-like), (3) diffuse reddening of the oral and pharyngeal mucosa
 5. Polymorphous exanthema of body trunk without vesicles or crusts
- Item 1 and at least three items of 2-5 are indispensable for diagnosis of MCLS

B. OTHER SIGNIFICANT SYMPTOMS

1. Acute nonpurulent swelling of cervical lymph nodes of thumb-tip or bigger size
2. Diarrhea
3. Proteinuria and an increase in leukocytes in urine sediment
4. Blood examination: (1) leukocytosis with nuclear shift to the left, (2) acceleration of blood sedimentation rate, (3) positive CRP, etc.
5. Changes occasionally observed: (1) aseptic meningitis, (2) mild jaundice or slight increase in the serum transaminase level, (3) carditis, myocarditis, (4) arthralgia, arthritis
6. Most prevalent under 5 years of age. Usually favorable prognosis without sequelae. No familial occurrence.

The official English translation of the diagnostic guidelines of the first to 5th versions have been publicized, but the 6th version not yet.

Source:

Yanagawa H et al. (Edit) Epidemiology of Kawasaki disease –A 30-year achievement, Shindan-to-chiryosha Co, Ltd, 2004.

5th edition

Table 5. The fifth revised edition of the Diagnostic Guidelines

This is a disease of unknown etiology affecting most frequently infants and young children under 5 years of age. The symptoms can be classified into two categories, principal symptoms and other significant symptoms or findings.

A. PRINCIPAL SYMPTOMS

1. Fever persisting 5 days or more (inclusive of those cases in whom the fever has subsided before the 5th day in response to therapy)
2. Bilateral conjunctival congestion
3. Changes of lips and oral cavity: Reddening of lips, strawberry tongue, diffuse injection of oral and pharyngeal mucosa
4. Polymorphous exanthema
5. Changes of peripheral extremities: (Initial stage): Reddening of palms and soles, indurative edema (Convalescent stage): Membranous desquamation from fingertips
6. Acute nonpurulent cervical lymphadenopathy

At least five items of 1-6 should be satisfied for diagnosis of Kawasaki disease. However, patients with four items of the principal symptoms can be diagnosed as Kawasaki disease when coronary aneurysm or dilatation is recognized by two-dimensional echocardiography or coronary angiography.

B. OTHER SIGNIFICANT SYMPTOMS OR FINDINGS

The following symptoms and findings should be considered in the clinical evaluation of suspected patients.

1. Cardiovascular: Auscultation (heart murmur, gallop rhythm, distant heart sounds), ECG changes (prolonged PR/QT intervals, abnormal Q wave, low-voltage, ST-T changes, arrhythmias), chest X-ray findings (cardiomegaly), 2-D echo findings (pericardial effusion, coronary aneurysms), aneurysm of peripheral arteries other than coronary (axillary etc.), angina pectoris or myocardial infarction
2. GI tract: Diarrhea, vomiting, abdominal pain, hydrops of gall bladder, paralytic ileus, mild jaundice, slight increase of serum transaminase
3. Blood: Leukocytosis with shift to the left, thrombocytosis, increased ESR, positive CRP, hypalbuminemia, increased α_2 -globulin, slight decrease in erythrocyte and hemoglobin levels
4. Urine: Proteinuria, increase of leukocytes in urine sediment
5. Skin: Redness and crust at the site of BCG inoculation, small pustules, transverse furrows of the finger nails
6. Respiratory: Cough, rhinorrhea, abnormal shadow on chest X-ray
7. Joint: Pain, Swelling
8. Neurological: CSF pleocytosis, Convulsion, Unconsciousness, Facial palsy, Paralysis of the extremities

REMARKS

1. For item 5 under principal symptoms, the convalescent stage is considered important.
2. Non-purulent cervical lymphadenopathy is less frequently encountered (approximately 65%) than other principal symptoms during the acute phase.
3. Male: Female ratio: 1.3-1.5; 1, patients under 5 years of age: 80-85%, fatality rate: 0.1%
4. Recurrence rate: 2-3%, proportion of siblings cases: 1-2%
5. Approximately 10 percent of the total cases do not fulfill five of the six principal symptoms, in which other diseases can be excluded and Kawasaki disease is suspected. In some of these patients coronary artery aneurysms (including so-called coronary artery ectasia) have been confirmed.

Material(3-1)

Dr. Kawasaki and Japan Kawasaki Disease Research Center Founded in 1999



Activities of Japan Kawasaki Disease Research Center

- It was founded by the late Dr. Tomisaku Kawasaki, who discovered Kawasaki disease (KD) , with the main purpose of investigation into the cause of KD.
- It provides research support by inviting universities and research institutes across Japan to conduct research on the etiology and onset mechanisms.
- It conducts a nationwide survey once every two years to contribute to clarifying the actual situation of KD.

Continued

- It also carries out consultation projects, education, and awareness activities on KD.
- Furthermore, it supports the holding of study groups and academic conferences including the Japan KD Society, International Symposium on KD and also holds its own study sessions.
- It will continue its efforts to investigate the cause of KD.
- The center is run with the cooperation of 165 members, including 10 directors, 2 auditors, 3 advisors, and 4 staff members.

Dr. Tomisaku Kawasaki
The founder of the center



Dr. Yoshio Imada
The present chairman



Staff members of the center



Snap shots of late Dr. Kawasaki

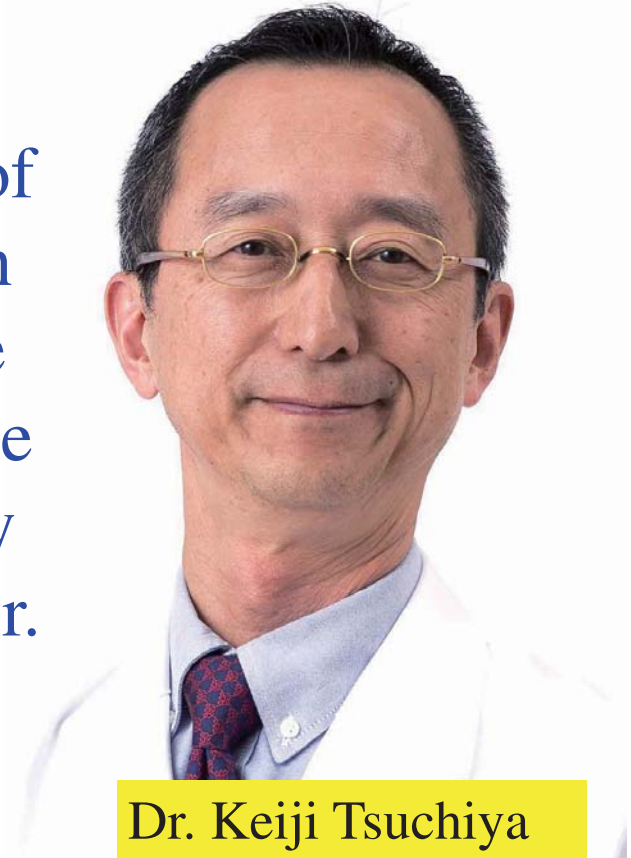


Two persons of importance in Japan KD Research Center



Dr. Yoshio Imada

Both doctors serve on the board of directors of the Japan KD Research Center and they are the driving force behind the center's activities. They were both trained by Dr. Kawasaki in the JRCS Central Hospital.



Dr. Keiji Tsuchiya



Dr. Kawasaki's daughter (Madoka-san) and son (Michiru-san)

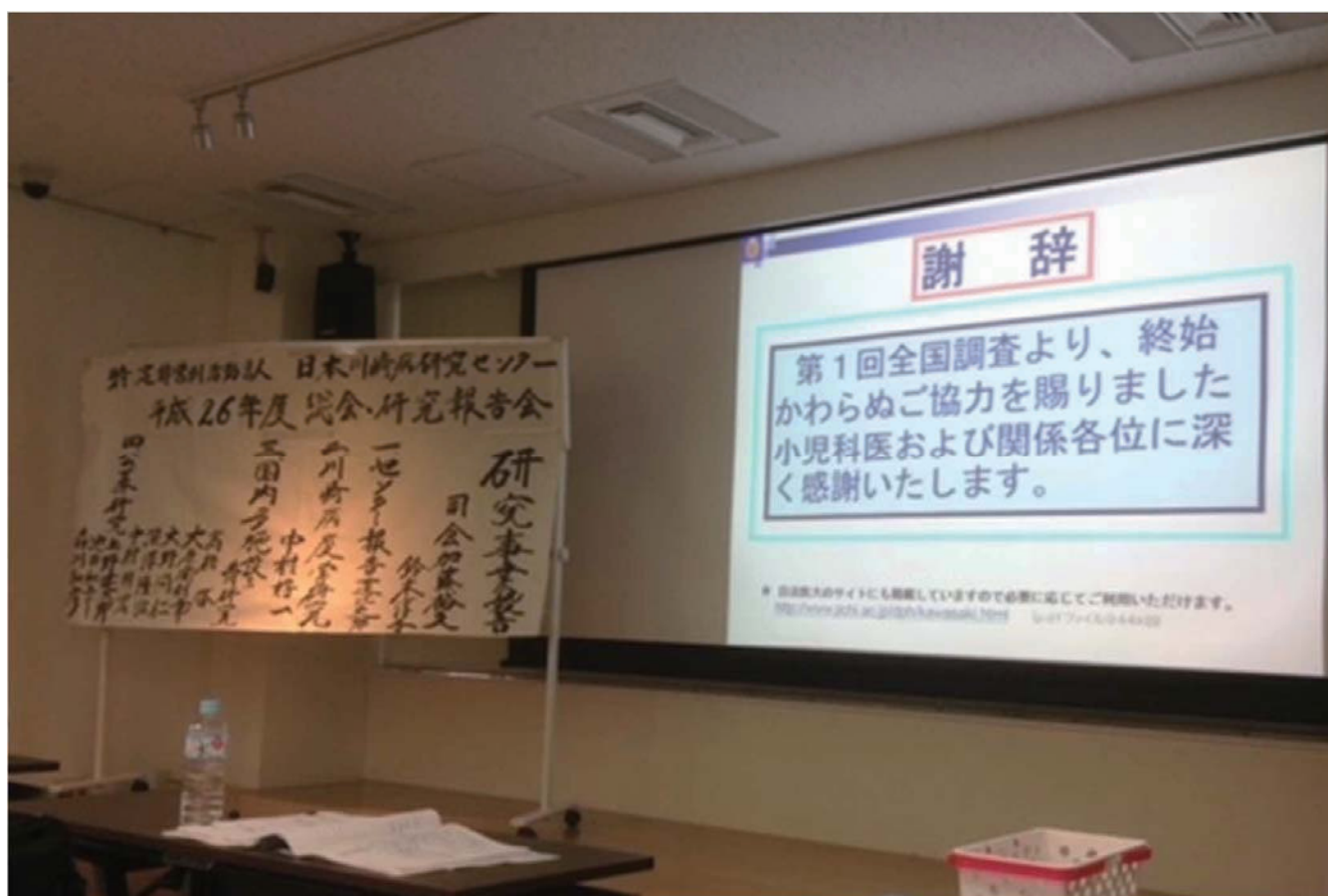


Dr. Imada and staff members



Dr. Kawasaki responds to telephone consultations and interviews at the office





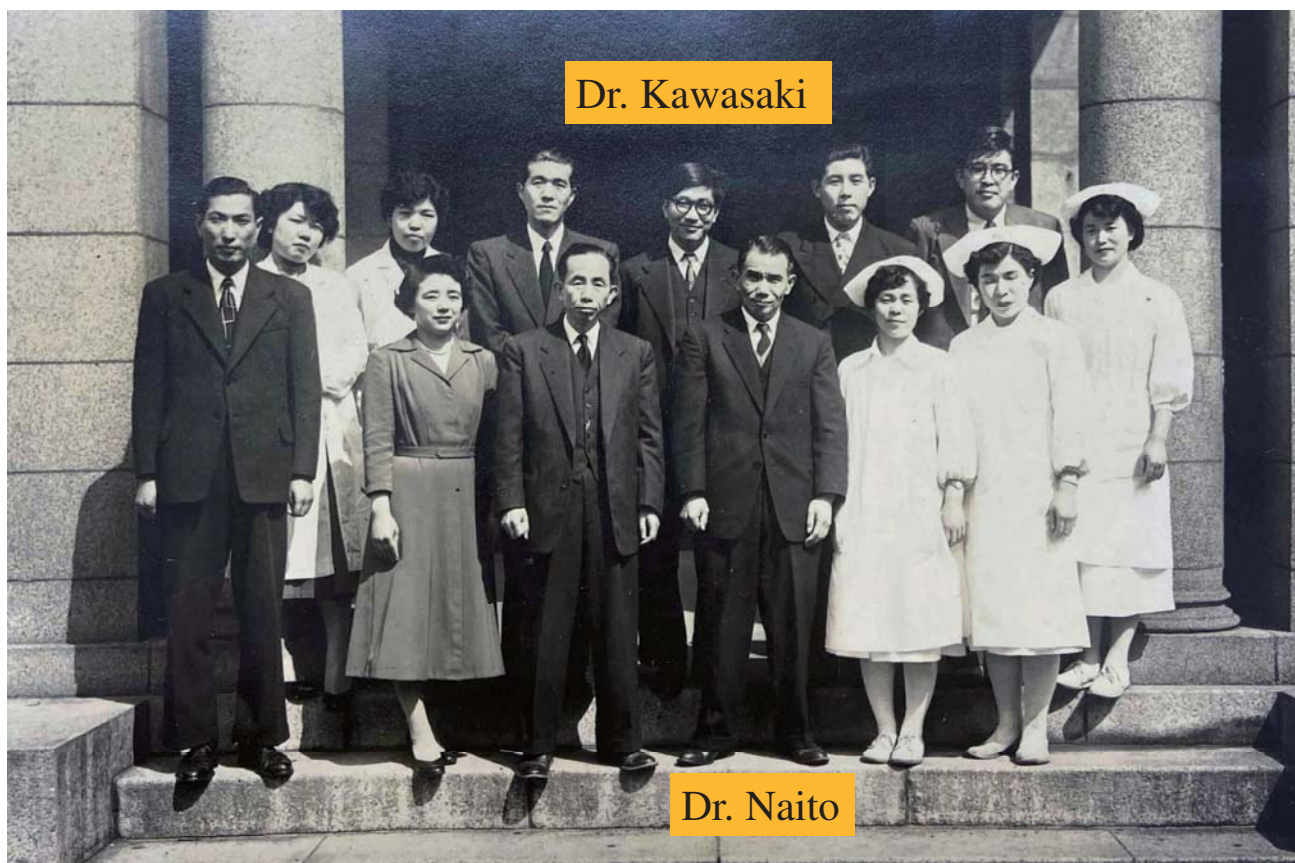
A scene from a research presentation



Dr. Kawasaki creates a poster for a research presentation in his office

Dr. Kawasaki and his colleagues at Pediatrician's Office, Japan Red Cross Central Hospital





At the entrance of Japan Red Cross Central Hospital 1956



Young Kawasaki Sensei



Japan Pediatric Society Award Commemorative Meeting



Year end party at Roppongi hills 2006

Commemorating the Health Culture Award to the Association of Parents of KD children



Dr. Shigematsu



Mr. & Mrs. Asai, Chairman of the Association of Parents of KD children





Drs. Zhang and Du visited the center, May 2016



With Dr. and Mrs. Shigematsu

Visit China for KD education and epidemiological surveys



Chengdu, Nov. 2002



Chongqing, Nov. 2002



Rushun, May 2001



Beijing, Dec. 2004



Kunming, Apr. 2002



Ulaanbaatar, Sep. 2008

Annual Meeting of Japanese Society of KD



14th 1994



16th 1996



19th 1999
With Dr. Hinuma



20th 2000



22nd 2002



24th 2004



28th 2008



36th 2006

Material(3-2)

Kawasaki disease History of academic research



January 1961 (a 10-year career as a pediatrician at the JRCS Central Hospital)

- I was given the opportunity to take care of a 4y3m old boy with Kawasaki disease (KD), typical case in retrospect.
- The encounter with this case was decisive for my fate after that.
- A year later, I encountered a 2nd case, which convinced me of the uniqueness of the disease, and subsequently experienced a series of similar cases.
- Fascinated by its uniqueness, I became immersed in clinical research on KD, and I was addicted to it, and finally **I couldn't get out of its abyss.**

Continued

- 6 years up to the submission of the original article to “Allergy” in 1967 were the most concentrated periods of my life on a single purpose, both physically and mentally.
- There was a controversy about whether this disease was Stevens-Johnson syndrome or not, and the uniqueness of KD was temporarily denied, but then a series of case reports followed.
- **Dr. Fumio Kosaki** (then Director of the Department of Pediatrics) ordered me to apply for a research grant from the Ministry of Health and Welfare (MHW).
- ⇒ **Failed (1969) and Reapplied(1970)**
- I caught the attention of **Dr. Shunichi Kakurai**, then Scientific Counselor in the Minister's Secretariat of MHW.
- He advised me to consult with **Dr. Itsuzo Shigematsu** (then Director of the Department of Epidemiology(DE) of the National Institute of Public Health(NIPH)) .

52 years after the fateful meeting with Dr. Kawasaki

February 1970 **Dr. Kawasaki** visited **Dr. Shigematsu** at NIPH, and talked passionately about the clinical picture of KD.

Dr. Shigematsu said "It's interesting, let's start!"
(The first encounter between pediatrician and epidemiologist in KD research)

Research Group on “Infantile **Muco-Cutaneous Lymph-node Syndrome (MCLS)**” funded by the MHW started in 1970.

(Later MCLS was named **Kawasaki Disease**) .

“**Diagnostic guideline**“ was created through collaboration between pediatrician and epidemiologist.



Dr. Kawasaki and Dr. Shigematsu

Continued

The first nationwide survey of KD was conducted January 1971.

(**Yanagawa** was ordered to be in charge of the survey)

27 surveys for 52 years with two-year intervals by 2022

Persons responsible for the survey



Shigematsu (NIPH)



Yanagawa (NIPH, JMU*)



Nakamura(JMU*)

*Jichi Medical University

Calendar on KD studies

Jan 1961	Encountered the first KD case (Dr. Kawasaki)
Oct 1962	Presentation of 7 cases (61st Annual Meeting of the Japan Pediatric Society in Chiba)
Mar 1967	Original paper published with 50 cases (Allergy 1967; 16:178-222)
Apr 1970	Research Group on KD (MHW) Representative (Dr. Kosaki)
Jan 1971	1st Nationwide Epidemiological Survey Leader (Dr. Shigematsu)
Sep 1974	First publication in an international journal (Pediatrics 1974; 54:271-276)
Sep 1980	First International Symposium on KD (16th International Congress of Pediatrics, Barcelona)

First publication in an international journal (Pediatrics 1974; 54:271-276)



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NUMBER 3

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AMERICAN ACADEMY OF PEDIATRICS
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Pediatrics

THE AMERICAN ACADEMY OF PEDIATRICS

ARTICLES

A New Infantile Acute Febrile Mucocutaneous Lymph Node Syndrome (MLNS) Prevailing in Japan

Tomisaku Kawasaki, M.D., Fumio Kosaki, M.D., Sumio Okawa, M.D.,
Itsuzo Shigematsu, M.D., and Hiroshi Yanagawa, M.D.

From the Department of Pediatrics, Japan Red Cross Medical Center, and the Department of Epidemiology, Institute of Public Health, Tokyo

ABSTRACT. What may be a new disease has been afflicting infants and young children in Japan since 1960. It is an acute, febrile, mucocutaneous condition accompanied by swelling of cervical lymph nodes (tentatively called mucocutaneous lymph node syndrome [MLNS]). It may be misdiagnosed as scarlet fever, the Stevens-Johnson syndrome, or infantile periarthritis nodosa. The disease is now known to be widely occurring all over Japan with an increasing incidence each year. More than 6,000 cases have been reported as of 1973. One to two percent of the patients reported have died suddenly of cardiac failure. All the autopsies showed infantile periarthritis nodosa-like arteritis accompanied by coronary thrombosis and aneurysm. Some of the surviving cases have been shown to have similar changes. These findings lead us to believe that this clinical picture is a new clinical entity. Recently, rickettsia-like bodies were found by electron microscopy in biopsy specimens from the skin and lymph nodes of the patients. The bodies were isolated by yolk sac culture and their pathogenicity is now under investigation. *Pediatrics*, 54:271, 1974. MUCOCUTANEOUS LYMPH NODE SYNDROME, PERIARTERITIS NODOSA, INFANTILE PERIARTERITIS NODOSA.

What may be a new disease has been afflicting infants and young children in Japan since around 1960. It is an acute, febrile, mucocutaneous condition accompanied by swelling of cervical lymph nodes (tentatively called mucocutaneous lymph node syndrome [MLNS]). It may be misdiagnosed as scarlet fever, the Stevens-Johnson syndrome, or infantile periarthritis nodosa.

The first report on MLNS was made by one of us (T. K.) in 1967 based on his experience of 30 cases with this condition.¹ Since then similar cases have been successively reported throughout Japan. Four thousand cases have been reported up to the present time.

In 1970 the Research Committee of MLNS,

supported by the Ministry of Health and Welfare of the Japanese Government, was organized under the chairmanship of Dr. Fumio Kosaki to elucidate the clinical, pathologic, epidemiologic and etiologic features of the disease.

This paper mainly deals with the clinical and epidemiologic aspects of MLNS.

CLINICAL ASPECTS OF MLNS

Since the first case was seen by one of us (T. K.) in January 1961, 168 cases of MLNS have been observed in the Department of Pediatrics, Japan Red Cross Medical Center by the end of December 1973. During that period four sudden deaths occurred in infants with MLNS. Autopsy was performed on three of these infants and showed infantile periarthritis nodosa-like arteritis of the coronary artery accompanied by thrombosis and aneurysm.

The major symptoms of MLNS are depicted in Table I which was prepared by the Committee in 1970 and based on the original report of Dr. Kawasaki in 1967.¹

The principal symptom is a fever ranging from 101 to 104 F, which lasts from one to two weeks and does not subside after treatment with antibiotics. This is accompanied by bilateral congestion of the ocular conjunctivae (color Fig. 1, B), a redness of the lips and oral cavity, protuberance of

(Received October 19, 1973; revision accepted for publication January 3, 1974.)

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ARTICLES

A New Infantile Acute Febrile Mucocutaneous Lymph Node Syndrome (MLNS) Prevailing in Japan

Tomisaku Kawasaki, M.D., Fumio Kosaki, M.D., Sumio Okawa, M.D.,
Itsuzo Shigematsu, M.D., and Hiroshi Yanagawa, M.D.

From the Department of Pediatrics, Japan Red Cross Medical Center, and the Department of Epidemiology, Institute of Public Health, Tokyo

The English translation was forcibly
changed from A to B by the journal editors

A: Original name by authors:

Muco-Cutaneous-Lymphnode Syndrome → MCLS

B: Editors correction:

Mucocutaneous Lymph Node Syndrome → MLNS

First International Symposium on KD

16th International Congress of Pediatrics

Barcelona, September 8-13, 1980



After the symposium, many participants gathered for Dr. Kawasaki's autograph



Nationwide epidemiological survey 1971-2022 (27 surveys)

Once every 2 years

Total No. of patients reported

445,618 cases

Fatal cases

459 (Fatality rate 0.11%)

Two key persons of the surveys

Dr. Nakamura (Prof. Emeritus, JMU)

Ms. Yashiro (Former Chief Technician, JMU)



Two key persons

Most important persons for the
nationwide surveys of KD in Japan



Drs. Shegematsu and Kawasaki

*Both leaders love conversation
With happy drinking!*

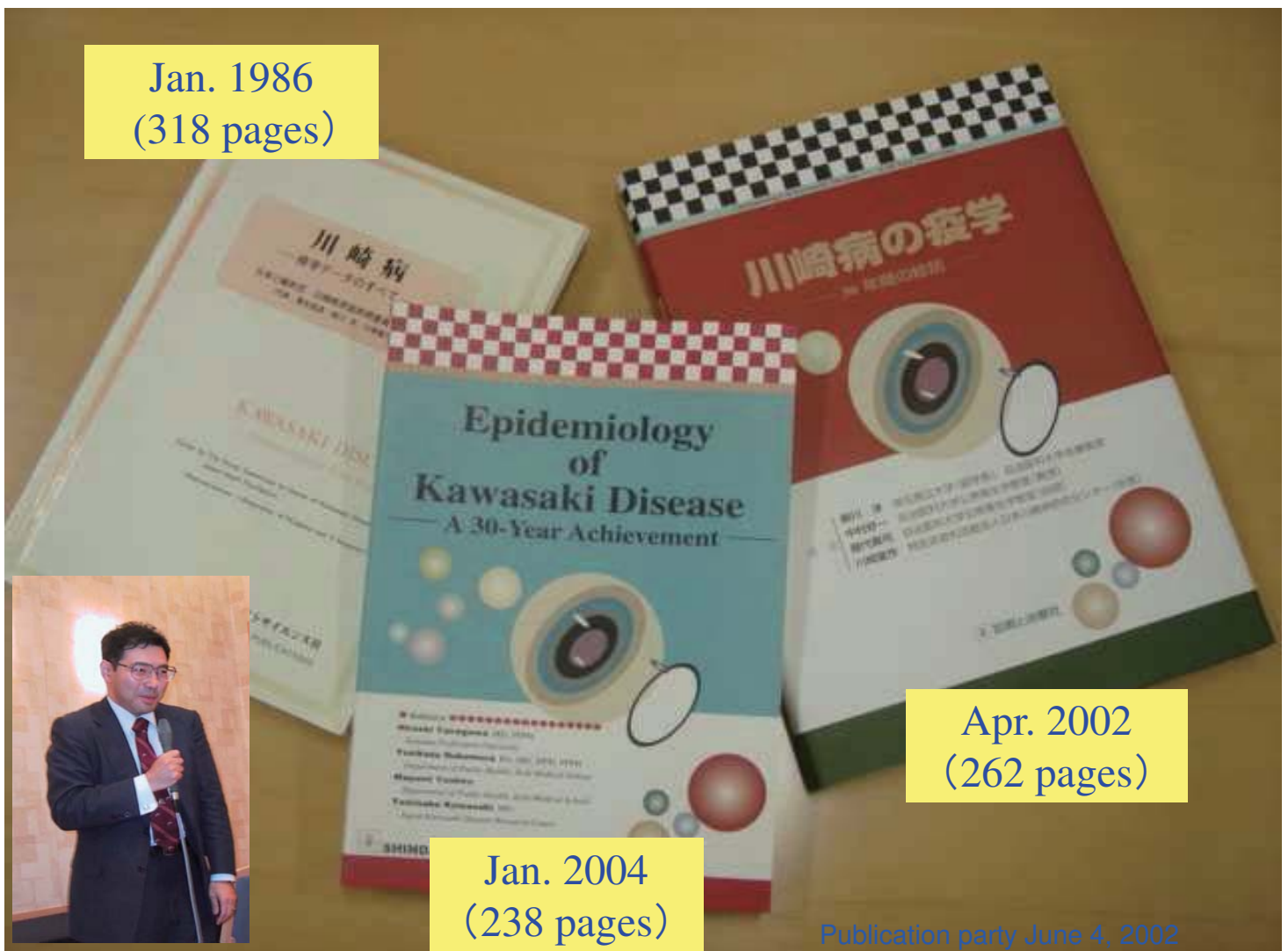


At a British Pub “Scatto” in Utsunomiya

A compilation of 30 years of epidemiological research on KD



Jan. 1986
(318 pages)



Apr. 2002
(262 pages)

Jan. 2004
(238 pages)

Publication party June 4, 2002

KD in Asia

1. KOREA (1984)

Nationwide survey with the cooperation of 144 hospitals in Korea under the collaboration of Professor Du Bong Lee, Department of Pediatrics, Catholic University of Medical Science in Seoul.

川崎病 (MCLS) 의 實態調査에 關한 付託의 말씀

부러운 여름철에 先生님과 科內 여러 先生님들 또한 健康하시리라 믿습니다. 病院診療와 研究에 多忙하시중 昨年度도 많은 協助를 하까지 많으셔서 總分에 昨年 서울에서의 아세아 小兒科學會에서 이질 病에 대한 우리나라 實態調査를 發表할 수 있었음을 마음으로 感謝 드리는 바입니다.

지금까지 (1982년 6월까지) 우리나라에서 發生한 川崎病 患兒 數는 1982년 10月號 小兒科誌에 發表한바와 같이 約 321名으로 集計되고 있습니다만 이것은 全國主要 修練病院 43個 病院院을 對象으로 한 것이므로 正確한 發生患兒數라고는 볼 수 없습니다. 또한 最近 여름 철에 접어들면서 本疾患兒가 눈에 띄게 많아졌습니다.

그리므로 今後 日本心臟財團 川崎病原因究明委員會의 協助를 얻어서 1973年以後 現在까지의 正確한 患者發生實態를 把握하고 再次 이 調査에 着手하겠습니다.

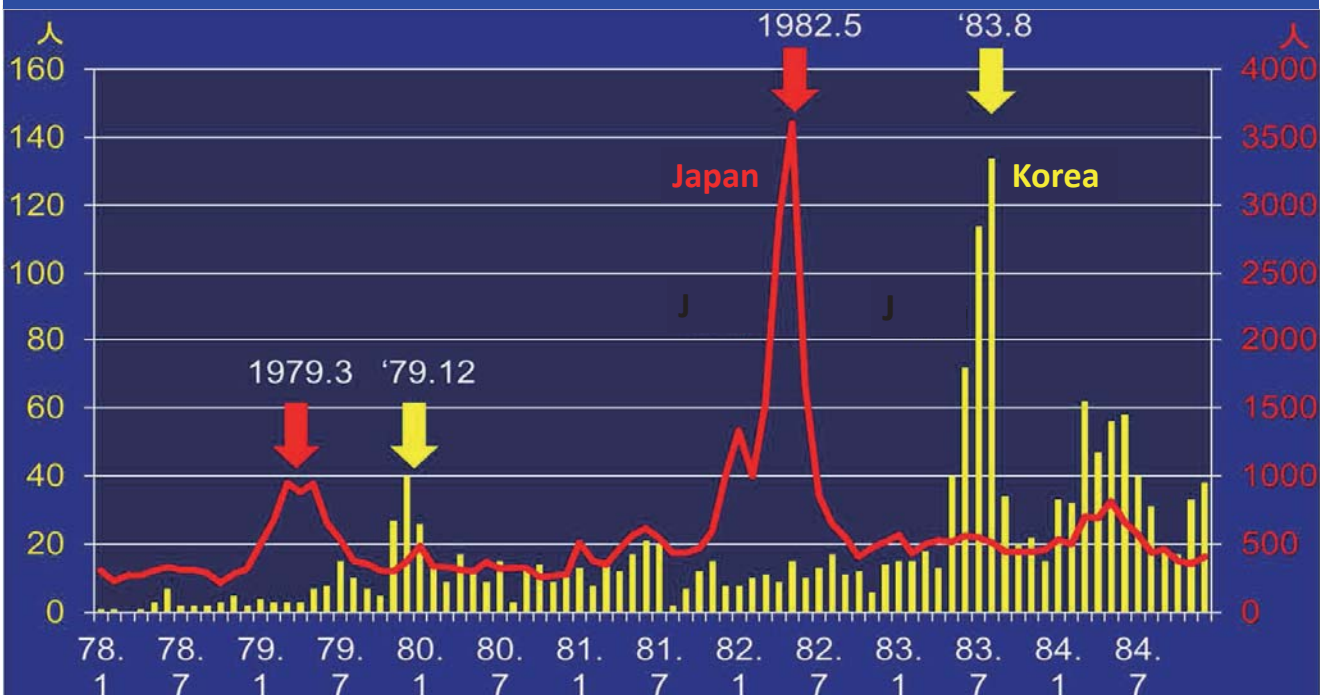
多忙하시 中 번거로우를 끼치서 죄송하옵나만 보내드린 調査表에 現在까지의 經驗例에 대하여 該當事項만을 記入하시어 10月31日까지 返送하여 주시면 感謝하겠습니다.

不 偏

先生任 費下

1983年 7月 20日
가톨릭醫大 小兒科內
川崎病研究班
李 斗 鳳
李 敬 珠
李 西 哲

Comparison of Monthly Patient Numbers (Japan and Korea)



2. CHINA (1983-2005)

Epidemiological surveys at the provincial and special municipal levels



Summary of the procedures of surveys in Japan

[illegible]

厚生省川崎病研究組
日本国第十四次川崎病全国调查结果

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序言

日本从1970年开始进行两年一次的川崎病全国流行病学调查,至今为止已进行了13次,充分掌握了1994年12月底前发病患者的情况。本次调查的对象是1995年1月至1996年12月两年间的发病患者。以下根据本次调查的结果,从报告患者的数、性别别年龄别分布、家族共患病、既往患川崎病、心肺血管症例以及治疗状况等流行病学方面的主要特征作概要报告。

方法

第14次全国流行病学调查期间是自1995年1月1日至1996年12月31日的两年间。调查对象的医疗单位是床位100张以上并设有儿科的医院,以及床位不满100张的儿科医院。调查对象是在满足以上两条件单位条件下的医院中就诊的初诊川崎病患儿。调查对象的名单是根据厚生省健康政策局总务科编纂的《1994年版医院一览》(医学书院出版)做出的。全国共有2,638所符合以上条件的医疗单位。

调查结果

1. 调查的回收率

发出研究协作请求函的2,638所医疗单位中,除外报告已停业的11所医疗单位,共有2,627所医院作为本次调查的对象医疗单位。收回调查表的医疗单位为1,777所,回收率为67.7%。其中,报告有患者的医疗单位为1,059所(占回收医疗单位的59.6%)。表1是各个都道府县对象医疗单位数、回答医疗单位数、有患者的医疗单位数以及报告患者数。

2. 年代变化趋势
本次调查两年间的报告患者数为12,531人,其中1995年6,107人,1996年6,424人。从性别别来看,男性7,239人,女性5,292人。0~4岁儿童发病率24年平均为每千105.3/10万(男118.8,女91.1)。患者数的男女性比为1.37,发病率的男女性比为1.30。男性多于女性,加上本次调查的患者数,共14次调查的报告患者数为140,837人(男181,783人,女59,054人)。从患者数的年代变化趋势来看,如表2和图1所示,男性患者和女性患者自1970年以来都有增加的趋势。

Diagnostic guidelines (Chinese version)

川崎病诊断标准(修订第四版)

日本国川崎病研究课题组

本病主要好发于4岁以下婴幼儿,是一种原因不明疾患。本病的主要特征分为以下主要症状和其它症状。

A、主要症状

- 1、持续发热5天以上
- 2、四肢末梢变化：(急性期)手足硬性肿胀、掌跖及指趾端充血
(恢复期)指趾端甲床皮肤移行处有膜状脱皮
- 3、多形性红斑、皮疹
- 4、双眼结膜充血
- 5、唇和口腔所见：口唇发红、草莓舌、口腔和咽喉粘膜弥漫性充血

6. 急性期出现非脓性颈部淋巴结肿大
以上的6个主要症状中只要出现5个就可以诊断为本病。另外,如果上述的6个症状中只出现4个症状,但通过超声心动检查或血管造影检查证实了冠状动脉瘤(或者动脉扩大),在除外其它疾病的基础上,可确诊为本病。

B、其它症状

临床检查时应当注意的症状和体征:

1. 心血管: 听诊仅(心脏杂音、奔马律、心悸等); 心电图的变化(P、QT间期延长、异常Q波、QRS低电压、ST-T改变); 心律不齐, 胸部X光片心影增大(超声心动图可见改变(心包积液、左房左室增大); 心肌缺血症状、末梢动脉硬化等处)。
2. 消化系统: 腹痛、呕吐、腹泻、胆囊肿大、脾脏性肠梗阻、轻度黄疸、血清转氨酶上升。
3. 血液: 血小板增多, 伴核左移, 血小板增多, 血沉加快、CRP阳性、低白蛋白血症、血2球蛋白增加、轻度贫血。
4. 痰: 痰白、混浊中夹血块增多。
5. 皮肤: BCG接种部位发红结痂、小脓疮、指甲出现横沟。
6. 呼吸系统: 咳嗽、流鼻涕、肺野出现异常阴影。
7. 关节: 疼痛、肿胀。
8. 神经: 脑脊液中单核细胞增多, 惊厥、意识障碍、面神经麻痹、四肢麻痹。

备注:

- 1、主要症状之2以恢复期最为重要。
- 2、本病的男女之比为1.3-1.5:1, 患者以男孩为多见。从年龄分布来看, 4岁以下占80%-85%, 致死率0.3%-0.5%。
- 3、复发病例占2-3%, 有兄弟姐妹发病的比例为1-2%。

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Kubo Building, 1-1-1, Kanda-Sudacho, Chiyoda-ku
Tokyo 101-0041, Japan
Tel: +81-3-5256-1121 Fax: +81-3-5256-1124



Exanthema of Kawasaki disease
(Male 7 mos., 4th day of illness)



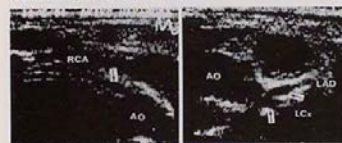
Changes of lips and congestion of ocular conjunctivae
(Female 2 yrs., 4th days of illness)



Reddening and indurative edema of hand
(Female 1.5 yrs., 6th day of illness)

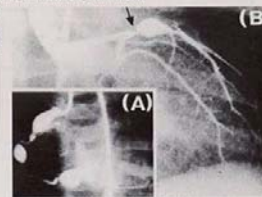


Desquamation at fingertips
(Male 3 yrs., 12th day of illness)



Two dimensional echocardiogram. Arrows indicate aneurysms.
(Male 2 yrs., 12th day of illness)

RCA: right coronary artery
AO: aorta
LAD: left anterior descending artery
LCx: left circumflex artery



Coronary angiogram: (A) Multiple aneurysms of RCA (Male 9 mos., 60th day of illness) (B) Aneurysm and stenotic lesion of LAD (Male 5 yrs., 3 years after the onset, Arrow indicates stenotic lesion).

KD Workshop in Beijing and Shanghai



Nanjing and Xi'an



Nanjing Aug. 1997 and Oct. 1998



Xi'an, Oct. 1998

广东省妇幼保健院

三级甲等妇幼保健院



Hong Kong Nov. 2000



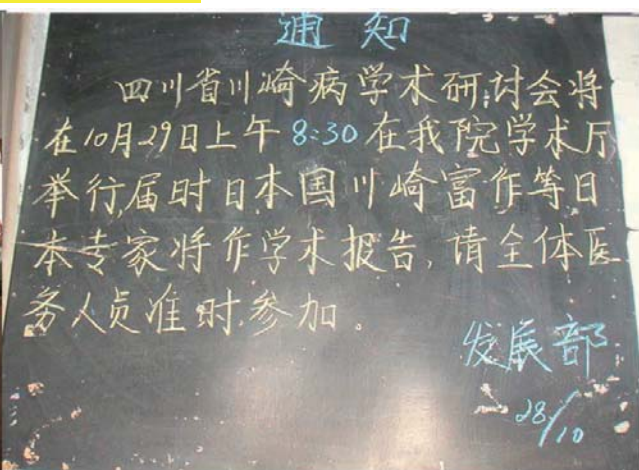
Harbin Apr. 2001



Location of the meeting between Russian General Stessel and General Nogi due to the opening of Rushun in front of the jujube tree in Suishiyang, Jan 1905



Chengdu Oct. 2002



Chongqing Oct. 2002



Shanghai Jun. 2005



Golden snub-nosed monkeys



Beijing Oct. 2004

3. MONGOLIA(2005, 2008, 2017)

Head of Mongolia-Japan Joint Research

Dr. Dambadarjaa Davaalkham
(Japanese nick name “Dava-san”)

Health Science University of Mongolia



Dava-san





KD in Russia 2010



Irkutsk Sep. 2010



KD in Italy 2007

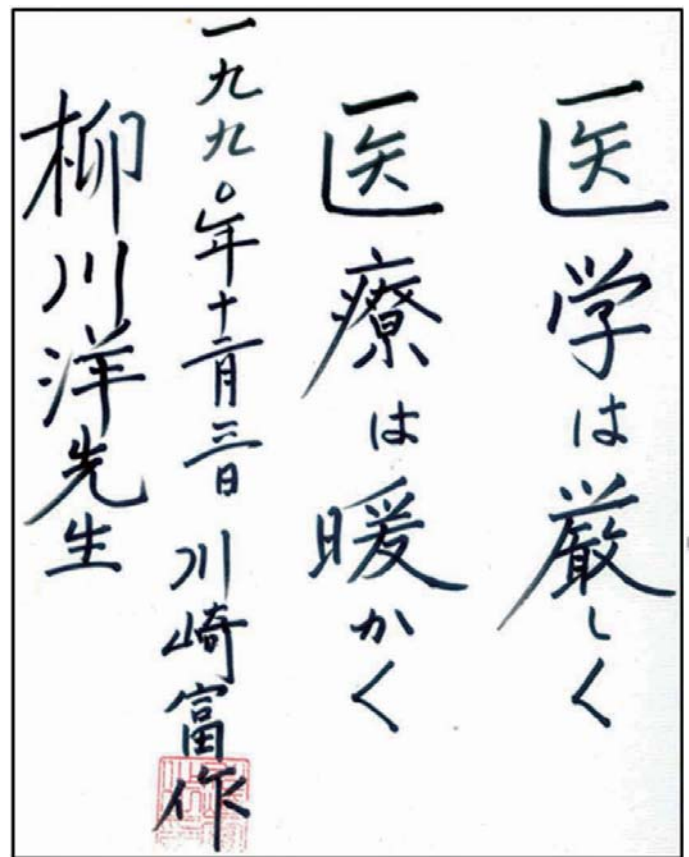


Palermo, Sicily May 2007



Dr. Kawasaki's Beliefs Facing Medicine

Medical science is rigorous,
Medical care is compassionate



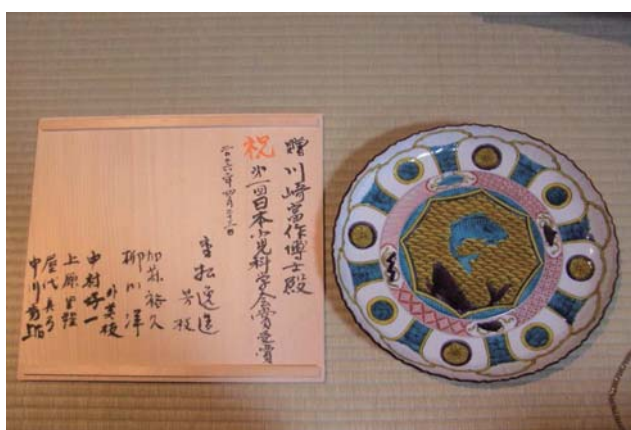


Dr. Tomisaku Kawasaki received
the 1st Japan Academy of Pediatrics Award
April 23, 2006 (Kanazawa)





Grand celebration party held at
Kaga restaurant "Wada"



Rest in peace, Dr. Kawasaki



He passed away on June 5, 2020,
at the age of 95 years

