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ABSTRACTS FROM THE SEVENTH INTERNATIONAL KAWASAKI DISEASE SYMPOSIUM

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KAWASAKI DISEASE, THE FIRST 130 YEARS

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Some 34 years ago Dr. Tomisaku Kawasaki published his landmark paper reporting 50 children from 1960-1967 with the distinctive syndrome that now carries his name. This historic report marked the beginning of the continuing effort to uncover the mysteries associated with this fascinating illness. Individual reports of fatal coronary arteritis in children, often labeled Infantile Periarteritis Nodosa, can be found in the pediatric and pathology literature in the decades prior to Kawasaki's astute recognition of the clinical features. Clinical summaries of these cases are generally recognizable now as Kawasaki Disease. Probably the earliest such case was reported by Dr. Samuel Jones Gee of St. Bartholomew's, London, in 1870, 131 years ago. At least 28 convincing pre-1967 cases can be found in the Western literature, in addition to at least 11 cases now recognized in Japan that date back at least to 1945.Much progress has been made regarding pathogenesis, diagnosis, treatment and prognosis of Kawasaki Disease over the past 34 years. The issues that must be resolved before we fully understand the disorder and its implications include the following: 1) What is the etiology of Kawasaki Disease? 2) What are the key pathogenetic mechanisms? 3) Do all patients with Kawasaki Disease have cardiac involvement and/or diffuse arterial involvement? 4) What are the long-term implications of Kawasaki Disease? 5)What is the optimal therapy for Kawasaki Disease? and 6) What is the mechanism of action of IVIG in Kawasaki Disease?In 2001, 131 years after Gee, and 34 years after Tomi Kawasaki's recognition of Kawasaki Disease as a clinical illness, we work in the era of molecular biology, molecular immunology and with knowledge of the human genome. Our challenge is to solve the riddles of Kawasaki Disease using these molecular tools and techniques, and to recruit outstanding young scientists to this effort.

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THE RELATIONSHIP OF KAWASAKI DISEASE TO OTHER SYSTEMIC VASCULITIDES

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The vasculitis of Kawasaki disease shares some pathologic attributes with other forms of systemic vasculitis, however, it has a number of distinctive characteristics, including a 1) unique association with mucocutaneous lymph node syndrome although MCLNS may not be completely expressed in all patients, 2) strong predilection for coronary arteries although other arteries may be involved, and 3) pattern of inflammation that shares features with other forms of arteritis but has distinctive characteristics. The three major categories of systemic vasculitis are large vessel vasculitis (chronic granulomatous arteritis), medium-sized vessel vasculitis (necrotizing arteritis), and small vessel vasculitis (necrotizing polyangiitis). Kawasaki disease arteritis and polyarteritis nodosa belong to the medium-sized vessel vasculitis category. There is no problem distinguishing acute Kawasaki disease arteritis from the two major large vessel vasculitides (Takayasu arteritis and giant cell arteritis). Necrotizing arteritis that resembles Kawasaki disease arteritis occurs in polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome. Although these vasculitides share some pathologic features with Kawasaki disease arteritis, the overall clinical manifestations and some aspects of the pathologic lesions, allow confident differentiation of Kawasaki disease from these systemic vasculitides. For example, the small vessel vasculitides (e.g., microscopic polyangiitis, Wegener's granulomatosis, and Churg-Strauss syndrome) often have clinical and pathologic evidence for involvement of capillaries (e.g., glomerulonephritis and pulmonary capillaritis) and venules (e.g., dermal leukocytoclastic venulitis) that does not occur with Kawasaki disease. Polyarteritis nodosa has the greatest pathologic similarity to Kawasaki disease arteritis, however, compared to polyarteritis nodosa, the acute arteritic lesions of Kawasaki disease have less neutrophil infiltration, more mononuclear leukocyte infiltration, more edema of the muscularis, and less fibrinoid necrosis. The term infantile polyarteritis nodosa should be abandoned because most patients given this diagnosis actually have Kawasaki disease. In summary, Kawasaki disease and the arteritis of Kawasaki disease are distinct from other forms of systemic vasculitis.

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RECENT ADVANCES IN PERCUTANEOUS CORONARY INTERVENTION FOR ISCHEMIC HEART DISEASE

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Catheter-based percutaneous coronary intervention (PCI) for atherosclerotic coronary artery disease in adult patients has been introduced into clinical practice since 1977, which has dramatically changed therapeutic strategy both in acute and chronic ischemic disease. Initial balloon angioplasty showed lots of limitations. Many efforts to overcome these limitations resulted in development of various types of new device in 1990s. Coronary stents increased success rate, decreased acute complications, expanded PCI indications and decreased restenosis. Atherectomy devices provided different approaches to treat coronary obstruction. Especially rotablator is the only effective device to treat severely calcified lesions. Currently nearly two million cases of PCI are estimated to be performed in the world. Overall mortality rate of recent PCI is less than 0.5% and major acute complications 2-3% despite of expanded indications, however, reintervention is still required in 10-20% of patients because of restenosis, which has been the Achilles heel since the beginning of PCI. Recent clinical trials of drug eluting stent reported no in-stent restenosis in drug-coated stent groups. It hopefully means that restenosis-free coronary intervention has come to reality. Coronary artery involvement is one of the most serious complications in Kawasaki disease (KD), about 4% of which is reported to develop ischemic events. KD in childhood is also supposed to be an increasing cause of coronary artery disease in adults, especially in young adults under 40 years of age. PCI has been successfully applied to manage coronary obstruction in KD children. Especially rotational atherectomy (rotablator) is effective for severely calcified lesions in KD children as well as in adult coronary intervention. Possible limitations and benefits of interventional treatment for ischemic events in KD children and in adult survivors of KD will be discussed, including the influence of recent advances in adult interventional cardiology.

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THIRTY-YEAR-OBSERVATION OF THE INCIDENCE RATE OF KAWASAKI DISEASE IN JAPAN

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Background . Since 1970, 16 nationwide epidemiologic incidence surveys of Kawasaki disease have been carried out successively in every two year-period with equivalent criteria in Japan. The diagnostic criteria of KD in this series was either the patients with at least 5 items of 6 principal symptoms or with at least 4 items when coronary aneurysm is recognized by two dimensional echo cardiography or coronary angiography. **Objective** . The purpose of this study is to describe epidemiologic pictures of patients reported through the surveys, especially yearly trend of the incidence rates in Japan over 30 years since 1970. **Methods** . Sixteen nationwide epidemiological surveys have been conducted to all the pediatric departments of the hospitals with more than 100 beds throughout Japan in every two-year period. **Results** . Total number of patients occurred by the end of December 2000 were 168,394 (Males: 97,700, Females: 70,694, Male/female ratio=1.38). The number of cases increased straightly year by year with three outbreaks in 1979, 1982 and 1986. The incidence rates were higher in males and in younger age groups of one year or less. The fatality rates decreased from 1% in 1974 to 0.05% in 2000. The incidence rates per 100,000 children of $<$ 5 years old were 113.5 in 1999 and 134.2 in 2000. [Preliminary tabulation as of June 30, 2001] **Conclusions** . The incidence rate is steadily increasing year by year in Japan. The patterns of descriptive epidemiology, such as seasonal variation and cyclic changes of the occurrence supported the infectious agent as an etiology.