CARDIAC SEQUELAE OF KAWASAKI DISEASE AND MANAGEMENT

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I DEFINITION AND THREE-PROCESS CORONARY ARTERIOPATHY (AHA 2017 & 2024 UPDATE)

- **Definition:** Kawasaki Disease (KD; mucocutaneous lymph node syndrome) is an acute, self-limited systemic vasculitis of **medium-sized extraparenchymal muscular arteries** occurring predominantly in infants and young children (**80 percent under 5 years of age**), with a specific predilection for the **epicardial coronary arteries**—making it the leading cause of acquired heart disease in children in developed nations and an increasingly recognized cause of premature adult CAD in India.
- **Three Linked Pathological Processes of Kawasaki Arteriopathy (Orenstein / AHA Model):**
  - **Acute Necrotizing Arteritis (Days 1 to 14 — Self-Limited):** Synchronized **neutrophilic infiltration** starting from the luminal endothelium and progressing outward across the wall destroys the **tunica media and internal and external elastic laminae** via matrix metalloproteinases (MMP-9) and elastases, causing loss of structural integrity and **saccular or fusiform Coronary Artery Aneurysms (CAAs)** (and rare acute fatal **coronary rupture** within the first 2 to 3 weeks).
  - **Subacute and Chronic Vasculitis (Weeks to Months/Years):** Asynchronous infiltration of **CD8+ cytotoxic T-lymphocytes, IgA plasma cells, eosinophils, and macrophages** beginning in the adventitia/vasa vasorum and progressing inward.
  - **Luminal Myofibroblastic Proliferation (LMP — Months to Decades):** Smooth-muscle-derived **myofibroblasts** (stimulated by TGF-beta and PDGF) proliferate concentrically within the intima, accompanied by **layered mural thrombosis** and **heavy dystrophic "eggshell" calcification**—progressively narrowing the lumen (especially at the **proximal entrance and distal exit of giant aneurysms**) and causing late **occlusive coronary stenosis and myocardial infarction** in adolescence or young adulthood.

II CARDIAC SEQUELAE: VASCULAR, MYOCARDIAL, VALVULAR AND ELECTRICAL

- **Coronary Artery Aneurysms (CAAs — AHA Body Surface Area-Adjusted Z-Score Classification):** Develop in **20 to 25 percent of untreated children** (reduced to **~3 to 5 percent** with timely IVIG therapy). Anatomic predilection sites: **Proximal LAD > Proximal RCA > Left Main Coronary Artery (LMCA) > LCx > Distal RCA**. Because absolute millimeter cut-offs (historical Japanese Ministry of Health criteria) systematically underdiagnosed aneurysms in infants, the **AHA Z-Score Classification** (standard deviations from normal BSA-adjusted mean) is mandatory:

AHA Z-Score Classification (McCrindle 2017 / Jone 2024)	Coronary Internal Lumen Z-Score / Absolute Size	Natural History & Remodeling Trajectory	Chronic Antithrombotic Regimen (AHA 2017 / 2024 Update)
No Involvement	**Always Z < 2.0**	Normal coronary architecture	Low-dose **Aspirin (3–5 mg/kg/d) for 4–6 weeks**, then discontinue
Dilation Only	**Z 2.0 to < 2.5** (or decrease in Z >=1.0 during follow-up)	Resolves completely within 4–8 weeks in >95%	Low-dose **Aspirin (3–5 mg/kg/d) for 6–8 weeks** until lumina normalize
Small Aneurysm	**Z >= 2.5 to < 5.0**	80–90% regress to normal luminal diameter within 1–2 years	**Low-dose Aspirin (3–5 mg/kg/d)** until regression documented
Medium Aneurysm	**Z >= 5.0 to < 10.0**, AND absolute dimension **< 8 mm**	~50% luminal "regression" (via intimal myofibroblastic filling; vessel wall remains stiff/calcified with impaired vasoreactivity)	**Low-dose Aspirin + Second Antiplatelet (Clopidogrel 0.2–1.0 mg/kg/d) (DAPT)** while persistent
Large or Giant Aneurysm	**Z >= 10.0**, OR absolute dimension **>= 8 mm**	**Never truly regress**; sluggish turbulent flow (low shear stress) causes **high risk of occlusive thrombosis, distal stenosis, and MI**	**Low-Dose Aspirin PLUS Therapeutic Anticoagulation: Warfarin (INR 2.0–3.0), LMWH (Anti-Xa 0.5–1.0 U/mL)**, or **DOAC (Rivaroxaban/Apixaban per AHA 2024 Update)** (+ consider **Triple Therapy** [+ Clopidogrel] and **Statin** in highest-risk giant aneurysms)

- **Acute Non-Coronary Sequelae (Pancarditis):**
  - **Acute Kawasaki Myocarditis and Kawasaki Disease Shock Syndrome (KDSS):** Subclinical myocarditis (interstitial edema and inflammatory infiltrate without myocyte necrosis) occurs in **50 to 70 percent** of patients during the first week (manifesting as **gallop rhythm, sinus tachycardia out of proportion to fever, mild troponin/NT-proBNP elevation, and depressed LV strain/EF**), while **5 percent** present with severe **Kawasaki Disease Shock Syndrome (KDSS)** (hypotension/cardiogenic shock with higher IVIG resistance and CAA risk, overlapping clinically with pediatric MIS-C). Unlike viral myocarditis, KD myocarditis recovers rapidly within 24 to 48 hours of **IVIG administration**.
  - **Valvulitis (10 to 25 Percent):** Acute transient **Mitral Regurgitation** (from papillary muscle dysfunction or leaflet valvulitis) or mild aortic regurgitation (whereas *late* mitral regurgitation results from ischemic papillary muscle infarction).
  - **Pericarditis (15 to 25 Percent):** Small acute pericardial effusion (rarely tamponade unless a giant CAA ruptures).
  - **Electrical and Arrhythmic Sequelae: Prolonged PR interval (First-degree AV block)**, QT dispersion, and flattened T waves in the acute phase; **Ventricular Tachycardia (VT), Ventricular Fibrillation (VF), and Sudden Cardiac Death** resulting from acute occlusive coronary aneurysm thrombosis or chronic ischemic myocardial scar.

III ACUTE ANTI-INFLAMMATORY MANAGEMENT (EXTINGUISHING CORONARY ARTERITIS)

- **Intravenous Immunoglobulin (IVIG — Class I, Level A): 2 g/kg administered as a single intravenous infusion over 10 to 12 hours**, ideally initiated **within the first 10 days of fever onset** (and as early as diagnosed), or even **after Day 10** if persistent fever, elevated CRP/ESR, or evolving coronary aneurysms are present. Reduces CAA incidence from 25 percent to **<4 to 5 percent**. (Defer live-attenuated viral vaccines [MMR, varicella] for 11 months after IVIG.)

- **Aspirin (Biphasic Dosing):**
  - **Acute Febrile Phase:** Moderate-dose (**30 to 50 mg/kg/day divided every 6 hours**) or high-dose (**80 to 100 mg/kg/day divided every 6 hours**) oral Aspirin until the child is afebrile for 48 to 72 hours (note: Aspirin has **zero** independent effect on lowering CAA incidence compared to IVIG alone, so many centers prefer moderate 30–50 mg/kg/day dosing to reduce GI toxicity).
  - **Subacute Phase:** Transition to **Low-Dose Antiplatelet Aspirin (3 to 5 mg/kg/day once daily)** for 6 to 8 weeks (stopped if 6-to-8-week echocardiogram confirms normal coronaries). (**Crucial Rule:** Avoid concomitant **Ibuprofen**, which competitively blocks Aspirin's irreversible acetylation of platelet COX-1, and ensure annual influenza vaccination to prevent **Reye syndrome**.)
  - **Primary Adjunctive Intensification in High-Risk Acute KD (Baseline Z >=2.5 or Young Infants <6 Months — RAISE Trial / AHA 2024 Update):** In children presenting upfront with **coronary aneurysms (Z >=2.5) on baseline echocardiogram** or at high risk of IVIG resistance, adding **upfront Corticosteroids** (**RAISE Trial** regimen: prednisolone 2 mg/kg/day for 2 to 3 weeks alongside initial IVIG) or **Infliximab / Cyclosporine (*KAICA Trial*)** significantly reduces CAA progression.
  - **Salvage Therapy for IVIG-Resistant Kawasaki Disease (Occurs in 10 to 20 Percent):** Defined as **persistent or recrudescent fever (>=38.0 degrees C) at 36 hours or more after completion of the initial IVIG infusion**:
  - **Infliximab (10 mg/kg single IV infusion over 2 hours — KIDCARE Trial, *Lancet Child Adolesc Health* 2021):** The randomized **KIDCARE Trial** proved that **Infliximab** resulted in **shorter fever duration, shorter hospital stay, less hemolytic anemia, and reduced need for additional therapy** compared with a second dose of IVIG.
  - **Alternative Salvage Options:** A **second infusion of IVIG (2 g/kg)** (with close monitoring for Coombs-positive isoagglutinin hemolytic anemia) or **Corticosteroids** (IV Methylprednisolone 2 mg/kg/day or pulse 30 mg/kg/day for 1–3 days followed by oral prednisone taper).

IV CHRONIC MANAGEMENT: THROMBOPROPHYLAXIS, ACUTE THROMBOSIS AND REVASCULARIZATION

- **Emergency Management of Acute Occlusive Giant Aneurysm Thrombosis (STEMI in a Child/Young Adult):**
  - **Challenge:** Unlike adult atherosclerotic plaque rupture (where thrombus forms in a 3 mm vessel), thrombosis inside a **10 to 15 mm Giant Kawasaki Aneurysm** involves a **massive clot burden with stagnant eddy currents**; standard adult primary PCI balloon angioplasty alone often causes distal embolization and no-reflow.
  - **Treatment:** Urgent **Systemic or Intracoronary Thrombolysis (Alteplase [tPA] 0.5 mg/kg/h for 6 hours)** + **IV Unfractionated Heparin** + **Glycoprotein IIb/IIIa Inhibitor (Abciximab)** or mechanical aspiration thrombectomy to dissolve the giant sac thrombus.
  - **Elective Revascularization for Inducible Ischemia (Stress CMR / Stress Echo / PET Positive):**
  - **Coronary Artery Bypass Grafting (CABG) with Bilateral/Pedicled Internal Thoracic Artery (ITA / LIMA & RIMA) Grafts (Preferred in Children — Class I):** Because **pedicled Internal Mammary Artery (ITA) grafts grow somatically in length and diameter along with the growing child** (yielding 20-to-25-year patency rates >85–90%, compared to <50% for saphenous vein grafts in children under 10 years), arterial CABG is preferred for multivessel disease, ostial/LMCA lesions, or long-segment stenoses at the inlet/outlet of giant aneurysms. (Note: Do not bypass a coronary vessel unless the proximal stenosis is critical [>=75–80% / FFR <=0.80], as competitive flow through a patent giant aneurysm causes string-sign graft occlusion.)
  - **Percutaneous Coronary Intervention (PCI):** Reserved for older adolescents/adults with focal single-vessel stenosis without giant aneurysm thrombosis; because chronic KD intimal lesions are **densely fibrotic and heavily calcified**, **Rotational Atherectomy (Rotablator) or Intravascular Lithotripsy (IVL)** with **IVUS/OCT guidance** is usually needed to prevent stent under-expansion or new neo-aneurysm formation (covered stents are used selectively to exclude non-branching aneurysms).

KEY REFERENCES

- **McCrindle BW, Rowley AH, Newburger JW, et al.:** Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association, *Circulation*, 2017.
- **Jone PN, Tremoulet A, Choueiter N, et al.:** Update on Diagnosis and Management of Kawasaki Disease: A Scientific Statement From the American Heart Association, *Circulation*, 2024.
- **Burns JC, Roberts SC, Tremoulet AH, et al. (KIDCARE Investigators):** Infliximab versus second intravenous immunoglobulin for treatment of resistant Kawasaki disease in the USA (KIDCARE): a randomised, multicentre comparative effectiveness trial, *The Lancet Child & Adolescent Health*, 2021.