

Kawasaki Disease

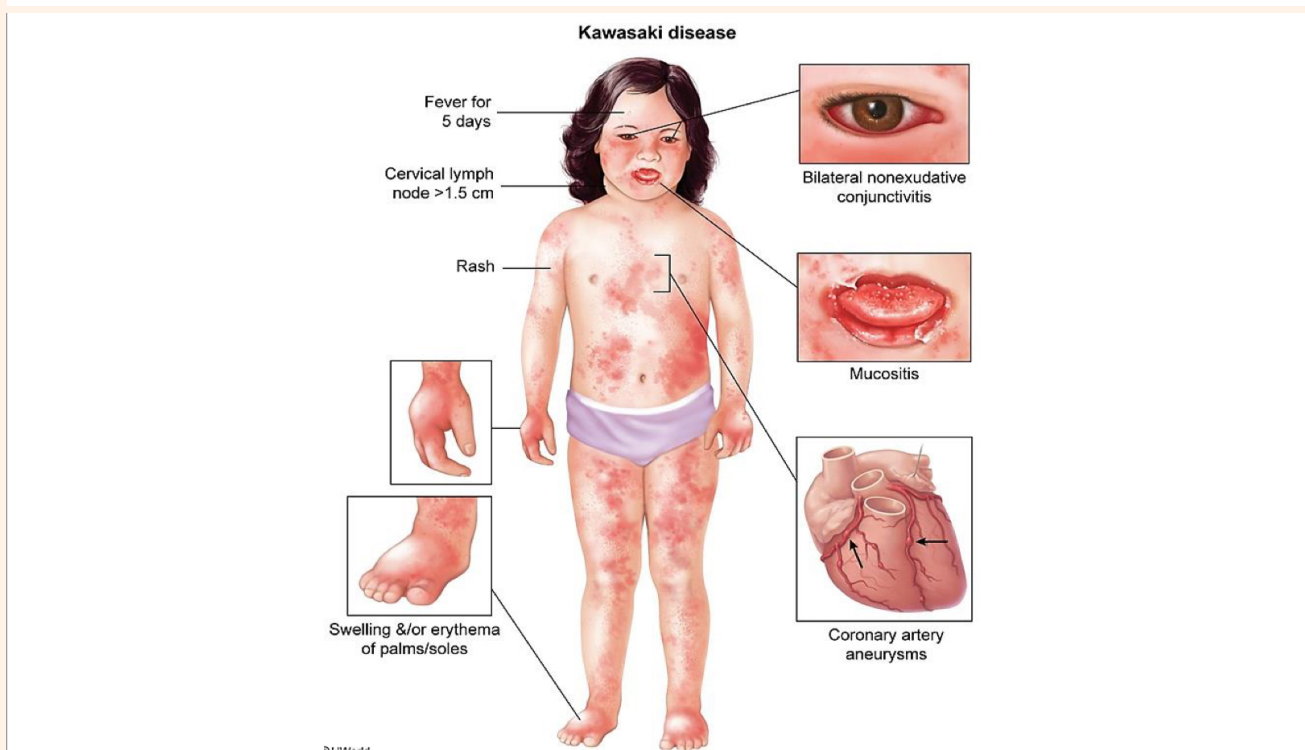
Summary

Kawasaki disease (KD) is an **acute, necrotizing vasculitis of unknown etiology**. The condition primarily affects children **under the age of five** and is more common among those of Asian descent. KD is characterized by **high fever, desquamative rash, conjunctivitis, mucositis** (e.g., **strawberry tongue**), **cervical lymphadenopathy**, as well as **erythema and edema of the distal extremities**. The **most concerning manifestation is coronary artery aneurysms**, which can lead to **myocardial infarction or arrhythmias**. KD is a clinical diagnosis that is supported by findings such as elevated ESR or evidence of cardiac involvement on **echocardiography**. Treatment with **intravenous immunoglobulins (IVIG)** and **aspirin** is **essential** and should be initiated as soon as possible after diagnosis.

- A. **Definition.** An **acute febrile vasculitis of childhood**; this disease involves **multiple organ systems, including the heart, skin, mucous membranes, GI tract, central nervous system (CNS), joints, and peripheral vascular bed.**
- B. **Epidemiology**
1. KD is the **most common cause of acquired heart disease** in children in the United States.
 2. **Males** are slightly more commonly affected than females.
 3. Most common in **children of Asian ethnicity** but can occur in any ethnicity.
 4. The **mean age** at presentation is **18–24 months** (80–90% of cases occur in children younger than 5 years). It is uncommon in children younger than 6 months.

ETIOLOGY

- KD is a vasculitis of unknown etiology that is **characterized by multisystem involvement and inflammation of small to medium-sized arteries**(predominantly) with resulting **aneurysm formation.**
- strongly supported to **be an infectious origin**
- Kawasaki disease has recurred in **families** when previously affected parents have children who develop the disease.



CLINICAL MANIFESTATIONS

- **Aneurysmal involvement of the coronary arteries is the most important manifestation of KD.**
- The clinical course of KD can be divided into three phases

ACUTE PHASE

- The acute phase of KD lasts 1 to 2 weeks.
- marked by sudden onset of a **high, hectic fever** ($\geq 40^{\circ}\text{C}$) without an apparent source.
- ✓ The duration of fever without treatment is generally 1-2 wk, but it may persist for 3-4 wk.
- ✓ Prolonged fever is prognostic for the development of coronary artery disease.
- followed by **conjunctival erythema** -The conjunctivitis is bilateral and nonsuppurative; mucosal changes, including dry, **cracked lips** and a **strawberry tongue**.
- **Cervical lymphadenopathy** is found in 70% of children and should be greater than 1.5 cm in diameter for the purposes of diagnosis.
- **swelling of the hands and feet**.
- **A rash**, vary in appearance, occurs in 80% of children with KD, particularly in the inguinal area and on the chest. (maculopapular, erythema multiforme, or scarlatiniform)
- **Perineal desquamation** is common in the acute phase.
- Extreme **irritability** is prominent, especially in infants.
- **arthritis**, particularly of medium-sized to large joints, can arise.
- **Abdominal pain, hydrops of the gallbladder** and **CSF pleocytosis**.
- **Carditis** in the acute phase manifested by **tachycardia, SOB**, or overt **CHF**.
- **Giant coronary artery aneurysms**, rare, can appear during this phase. most commonly in very young children.

SUBACUTE PHASE

- lasts until the fourth week
- characterized by **gradual resolution of fever** (if untreated) and other symptoms.
- **Periungual desquamation** of the fingers and toes begins 1-3 wk after the onset of illness and may progress to involve the **entire hand and foot**
- **The platelet count**, previously normal or slightly elevated, increases to a significant degree (often >1 million/ mm^3).
- **This phase heralds the onset of coronary artery aneurysms**, which appear in the subacute and convalescent phases, and pose the highest risk of sudden death.
- Risk factors for development of coronary artery aneurysms include:

1. prolonged fever,
 2. prolonged elevation of inflammatory parameters such as the ESR,
 3. age younger than 1 year,
 4. male gender.
 5. laboratory values at presentation
- ✓ low hemoglobin or platelet levels
 - ✓ high neutrophil and band counts
 - ✓ Hyponatremia
 - ✓ low albumin and age-adjusted serum IgG levels.

CONVALESCENT PHASE

- begins with the disappearance of clinical symptoms and continues until the ESR returns to normal
- usually 6 to 8 weeks after the onset of illness.
- **Beau lines** of the fingernails may appear during this phase

NOTE:

Beau lines are **deep grooved lines** that **run from side-side on fingernail**.

Causes: infection, trauma, coronary occlusion, hypocalcaemia, skin disease, diabetes, chemotherapy malnutrition.



LABORATORY AND IMAGING STUDIES

- In the acute phase, inflammatory parameters are elevated, including :
 - WBC count (with neutrophilia and immature forms)
 - platelet count
 - the ESR (often >80 mm/hr).
- Hypoalbuminemia, Hyponatremia, Elevated serum transaminases, Leukocytosis in synovial fluid
- It is particularly important to exclude other causes of fever, notably infection.
 - blood culture.
 - urine culture.
 - chest x-ray.
 - A lumbar puncture (may show pleocytosis)
- Tests of hepatobiliary function may be abnormal.
- Greatly elevated platelet counts develop during the subacute phase.
- two-dimensional echocardiograms identify The development of coronary artery aneurysms (acute phase, at 2 to 3 weeks, and at 6 to 8 weeks).

NOTE:

The is no specific lab test for KD diagnosis

Table 16-2

Clinical Manifestations, Laboratory Findings, and Treatment of Kawasaki Disease

	Phase I	Phase II	Phase III
	Acute Phase	Subacute Phase	Convalescent Phase
Time Course	1–2 Weeks	Weeks to Months	Weeks to Years
Clinical manifestations	Fever	Defervescence and decreased inflammation	Gradual resolution of aneurysms
	Conjunctivitis		
	Oropharyngeal changes	Peeling from nail beds or distal extremities	
	Cervical adenopathy		
	Rash	Coronary artery aneurysms	
	Swollen hands		
Laboratory findings	(↑) ESR and CRP	ESR and CRP decreasing from acute phase(↑) Platelet count	Normalization of all laboratory findings
	(↑) WBC count		
	(↓) Hemoglobin		
	(↑) AST/ALT		
	(↓) Albumin		
	Sterile CSF pleocytosis		
	Sterile pyuria		
Treatment	High-dose IVIG	Low-dose aspirin	Continue low-dose aspirin only if aneurysms remain
	High-dose aspirin		

ESR = erythrocyte sedimentation rate; CRP = C-reactive protein; WBC = White blood cell count; AST = aspartate aminotransferase; ALT = alanine aminotransferase; IVIG = intravenous immune globulin; CSF = cerebrospinal fluid.

Diagnostic criteria (Table 16-1)

- Temperature > 38.9°C (102°F) lasting ≥5 days**—most consistent manifestation of KD
- The patient must also have **four of the following five clinical manifestations**:
 - Bilateral conjunctivitis**: bulbar injection with limbic sparing and **without exudate**
 - Mucous membrane changes**: pharyngitis; strawberry tongue; or *most commonly*, **red, cracked, swollen lips**
 - Cervical adenopathy**: a **unilateral nonsuppurative cervical lymph node ≥1.5 cm** in diameter. This is the least consistent feature of KD.
 - Rash**: primarily on the trunk. The rash may assume many forms (“**polymorphous**”), including **erythematous**, **maculopapular**, **morbilliform**, or **scarlatiniform**. It often begins as perineal erythema and desquamation.
 - Changes in distal extremities**
 - Early** (first 7–10 days of illness): swelling and induration of the hands and feet with erythematous palms and soles
 - Later** (7–10 days after the start of fever): peeling around the nail beds of the distal extremities
 - It is important that **the illness must not be explainable by any other disease process**. Known infectious conditions (including bacterial, viral, and rickettsial infections), rheumatologic conditions (including systemic juvenile idiopathic arthritis), and drug reactions must be excluded to make the diagnosis of KD.

DIFFERENTIAL DIAGNOSIS

- The diagnosis of KD is based on the presence of fever for more than 5 days without an identifiable source and the presence of 4/5 of other clinical criteria.

Criteria for Diagnosis of Kawasaki Disease

FEVER OF ≥ 5 DAYS' DURATION ASSOCIATED WITH AT LEAST 4* OF THE FOLLOWING 5 CHANGES

- ✓ **Bilateral nonsuppurative conjunctivitis** (injection without exudates)
- ✓ One of more **of mucous membranes changes** in upper respiratory tract
 - including diffuse injection of oral and pharyngeal mucosa
 - dry fissured lips
 - injected lips
 - "strawberry" tongue
- ✓ One or more **changes of the extremities**:
 - including peripheral erythema, peripheral edema (acute phase)
 - periungual desquamation, and generalized desquamation (subacute phase)
- ✓ **Polymorphous rash**, primarily truncal
- ✓ **Cervical lymphadenopathy** >1.5 cm in diameter, usually unilateral.

- ATYPICAL KD**: if only three clinical criteria + coronary artery aneurysms.

H. Incomplete or atypical KD

- A subset of patients suspected of having KD **may not fulfill all of the clinical diagnostic criteria**. These patients have "incomplete" or "atypical" KD.
- Patients **must still have at least 5 days of fever but otherwise have only have 2–3 clinical features** from **Table 16-1** and **no alternative explanation for symptoms**.
- Laboratory and echocardiographic studies are used to make the diagnosis** in these children.
- Treatment is the same as for typical KD.

TREATMENT

- IV immunoglobulin (IVIG)** 2 g/kg over 10–12 hr orally until 14th illness day - is the mainstay of therapy for KD, unknown mechanism of action.
- Aspirin** :
 - ✓ **anti-inflammatory doses** (80 to 100 mg/kg/day divided every 6 hours) in the acute phase.
 - ✓ When the fever has resolved for at least 48 hours, the dose of aspirin is decreased to **antithrombotic doses** (3 to 5 mg/kg/day as a single dose).
 - ✓ This dose is continued through the subacute and convalescent phases until echo. fails to show the presence of coronary artery aneurysms.
- Corticosteroids** are **rarely** used in KD (not like other vasculitis)
 - ✓ acute phase if active carditis is apparent
 - ✓ children with persistent fever after two doses of IVIG.
- ✓ With therapy, the CRP normalizes much more quickly than the ESR, which will often increase immediately after IVIG therapy.

COMPLICATIONS

- There are few long-term complications of KD because most cases resolve without sequelae.
- Sudden cardiac death from coronary artery aneurysm**.
- Myocardial infarction** caused by stenosis of a coronary artery at the site of an aneurysm.

PROGNOSIS

- Other than the risk for persistent coronary artery aneurysms, KD has an **excellent** prognosis
- Coronary artery aneurysms develop in **up to 25% of untreated patients in the 2nd–3rd wk of illness**
- IVIG reduces the prevalence of coronary artery disease from 20% to 25% in children treated with aspirin alone to 2% to 4% in children treated with IVIG and aspirin in the first 10 days of illness.

Complications of Kawasaki Disease

Coronary artery thrombosis
Coronary artery aneurysms
Peripheral artery aneurysm
Peripheral gangrene
Congestive heart failure
Myopericarditis
valvular regurgitation
Irritability
Arthritis
Sterile pyuria (urethritis)
Thombocytosis (late)
Diarrhea
Pancreatitis
Hydrops of gallbladder
Hepatic dysfunction
Aseptic meningitis
Sensorineural hearing loss
Raynaud phenomenon
Anterior uveitis (mild)

To Sum Up:

1. Fever for ≥ 5 days, in addition to ≥ 4 of the following mucocutaneous findings: **"COREL"**

- a. Conjunctivitis
 - i. Bilateral
 - ii. Nonexudative
 - iii. Spares the limbus
- b. Oral mucosal changes
 - i. Erythema
 - ii. Fissured lips
 - iii. Strawberry tongue
- c. Rash
 - i. Blanching maculopapular
- d. Extremity changes
 - i. Erythema
 - ii. Edema
 - iii. Desquamation of hands and feet
- e. Lymphadenopathy
 - i. Cervical
 - ii. >1.5 cm node

2. Irritability is also a common feature

3. Labs:

- a. Leukocytosis
- b. Thrombocytosis
- c. $\uparrow$ ESR
- d. Sterile pyuria

4. Treatment:

- a. IVIG
 - i. Start within 10 days of fever onset to prevent coronary artery aneurysm
- b. Aspirin

5. Assess cardiac complications by echocardiography

6. Risk factors for cardiac complications:

- a. Prolonged fever (>10 days)
- b. Delayed treatment with IVIG
- c. Age <1 year

Disease		Kawasaki
Adenovirus	Purulent conjunctivitis	Nonpurulent conjunctivitis
Scarlet Fever	- Exudative pharyngitis - Sandpaper-textured rash that spares palms and soles	- Nonexudative tonsils - Blanching maculopapular rash

Kawasaki disease	
Epidemiology	90% age <5 - Increased incidence in East Asian ethnicity
Diagnostic criteria	Fever ≥ 5 days plus ≥ 4 of the following findings: - Conjunctivitis: bilateral, nonexudative - Mucositis: injected/fissured lips or pharynx, "strawberry tongue" - Cervical lymphadenopathy: ≥ 1 lymph node >1.5 cm in diameter - Rash: erythematous, polymorphous, generalized; perineal erythema & desquamation; morbilliform (trunk, extremities) - Erythema & edema of hands/feet
Treatment	Aspirin plus intravenous immunoglobulin
Complications	- Coronary artery aneurysms - Myocardial infarction & ischemia