PEDIATRIC ACQUIRED HEART DISEASES

- **KAWASAKI DISEASE (MUCOCUTANEOUS LYMPH NODE SYNDROME)**
  - 10-15 per 100,000 children < 5 years in USA
  - 150 per 100,000 children of Japanese descent
- **ACUTE RHEUMATIC FEVER / RHEUMATIC HEART DISEASE**
  - 0.5-3 per 100,000 population in developed countries
  - 200-300 per 100,000 in developing countries
- **MYOCARDITIS / PERICARDITIS**
- **BACTERIAL ENDOCARDITIS**
- **CARDIOMYOPATHY**
- **CARDIAC TUMOR**
Kawasaki Disease

• What is it?
  – Also known as Mucocutaneous lymph node syndrome
  – #1 cause of acquired heart disease in U.S. kids
  – Systemic inflammatory process (vasculitis) with no known etiology
  – May be infectious etiology: cycles q 3 yrs; usually winter and spring; usually younger ages (most < 4 yrs old)
1. Skin Rashes
2. Conjunctivitis
3. Stomatitis
4. Hand & Feet Changes
5. Cervical LNs

Nonpurulent Conjunctivitis

Erythematous Induration $\geq 1.5$ cm
• How to diagnose:
  – Fever ≥ 5 days
  – At least 4 of the following:
    • Changes in the extremities
      – Erythema and edema of hands and feet
      – Subsequent peeling of distal ends of digits
    • Polymorphous rash
    • Nonpurulent bilateral conjunctivitis
    • Mucosal changes
      – Strawberry tongue; red, cracked lips
    • Cervical lymph node (1.5cm in diameter)
SKIN RASHES
DESQUAMATION
Second to fourth weeks
<table>
<thead>
<tr>
<th>TABLE 61.2</th>
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<tbody>
<tr>
<td><strong>KAWASAKI DISEASE: ASSOCIATED FEATURES</strong></td>
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<table>
<thead>
<tr>
<th>Clinical findings</th>
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<tbody>
<tr>
<td>Myocarditis</td>
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<tr>
<td>Pericarditis</td>
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<tr>
<td>Aseptic meningitis</td>
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<tr>
<td>Diarrhea</td>
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<td>Gallbladder hydrops</td>
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<tr>
<td>Obstructive jaundice</td>
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<td>Uveitis</td>
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<td>Urethritis</td>
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<thead>
<tr>
<th>Laboratory findings</th>
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<tbody>
<tr>
<td>Elevated acute phase reactants: C-reactive protein, sedimentation rate, α-1 antitrypsin</td>
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<td>Thrombocytosis (usually in the 2nd and 3rd weeks of illness)</td>
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<tr>
<td>Sterile pyuria and proteinuria</td>
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<td>Elevation of liver enzymes</td>
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<tr>
<td>Decreased serum protein and albumin</td>
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<tr>
<td>Anemia (normochromic, normocytic and self-limited)</td>
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<tr>
<td>Negative or low antistreptolysin O titer</td>
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**TABLE 2.** Differential Diagnosis of Kawasaki Disease: Diseases and Disorders With Similar Clinical Findings

<table>
<thead>
<tr>
<th>Condition</th>
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<tbody>
<tr>
<td>Viral infections (eg, measles, adenovirus, enterovirus, Epstein-Barr virus)</td>
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<tr>
<td>Scarlet fever</td>
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<tr>
<td>Staphylococcal scalded skin syndrome</td>
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<tr>
<td>Toxic shock syndrome</td>
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<tr>
<td>Bacterial cervical lymphadenitis</td>
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<tr>
<td>Drug hypersensitivity reactions</td>
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<tr>
<td>Stevens-Johnson syndrome</td>
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<tr>
<td>Juvenile rheumatoid arthritis</td>
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<tr>
<td>Rocky Mountain spotted fever</td>
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<tr>
<td>Leptospirosis</td>
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<tr>
<td>Mercury hypersensitivity reaction (acrodynia)</td>
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<td>Stage 1 (0–9 days)</td>
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<tr>
<td>Microvascular angitis</td>
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<tr>
<td>Acute endoarteritis and perivasculitis of major coronary arteries</td>
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<tr>
<td>Pericarditis, valvulitis, and endocarditis</td>
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<tr>
<td>Myocarditis including atrioventricular conduction system</td>
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</table>

<table>
<thead>
<tr>
<th>Initial anti-inflammatory treatment: intravenous immunoglobulin (IVIG) plus high-dose aspirin&lt;sup&gt;a&lt;/sup&gt;</th>
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<tbody>
<tr>
<td>IVIG dosage: 2 g/kg as single infusion over 8–12 h</td>
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<tr>
<td>Aspirin dosage: 80–100 mg/kg per day orally in four divided doses given every 6 h until the patient is afebrile for 48 hrs</td>
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<tr>
<td>In case of persistent or recrudescent fever:</td>
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<tr>
<td>Repeat dose of IVIG 2 g/kg as single infusion; consider IV methylprednisolone 30 mg/kg once a day; may be repeated as necessary up to a total of three doses</td>
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<tr>
<td>Subsequent antiplatelet treatment:</td>
</tr>
<tr>
<td>Aspirin 3–5 mg/kg orally once daily</td>
</tr>
<tr>
<td>Duration of treatment: 6–8 weeks from onset or until sedimentation rate and platelet count return to normal; aspirin is discontinued at this point, if no coronary artery abnormalities are observed on echocardiogram</td>
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<tr>
<td>Continued indefinitely if coronary abnormalities are observed</td>
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<tr>
<td>If large aneurysms are noted with or without thrombus:</td>
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<tr>
<td>Start IV heparin or subcutaneous low-molecular-weight heparin</td>
</tr>
<tr>
<td>Start warfarin and titrate dose (target international normalized ratio 2–2.5); continue low-dose aspirin at the same time</td>
</tr>
<tr>
<td>Following IVIG administration, immunization of the patient with live virus vaccine such as measles, mumps, and rubella (MMR) should be delayed by 11 months or until the antibody titer has returned to a very low level.</td>
</tr>
</tbody>
</table>
Fig 2. 2D echocardiogram

Fig 4. Coronary angiogram demonstrating giant aneurysm of the LAD with obstruction and giant aneurysm of the RCA with area of severe narrowing in a 6-year-old boy.

RISK SCORES FOR CORONARY ANEURYSM

• HARADA SCORE

1. WBC > 12,000
2. Platelet < 350,000
3. CRP > 3+
4. Hct < 35
5. Albumin < 3.5
6. Age <= 12 months
7. Male sex

BEISER ET AL
Baseline WBC, Hb, Platelet Temperature post IVIG within 1 day
<table>
<thead>
<tr>
<th>Risk Level</th>
<th>Pharmacological Therapy</th>
<th>Physical Activity</th>
<th>Follow-Up and Diagnostic Testing</th>
<th>Invasive Testing</th>
</tr>
</thead>
<tbody>
<tr>
<td>I (no coronary artery changes at any stage of illness)</td>
<td>None beyond 1st 6–8 weeks</td>
<td>No restrictions beyond 1st 6–8 weeks</td>
<td>Cardiovascular risk assessment, counseling at 5-y intervals</td>
<td>None recommended</td>
</tr>
<tr>
<td>II (transient coronary artery ectasia disappears within 1st 6–8 weeks)</td>
<td>None beyond 1st 6–8 weeks</td>
<td>No restrictions beyond 1st 6–8 weeks</td>
<td>Cardiovascular risk assessment, counseling at 3- to 5-y intervals</td>
<td>None recommended</td>
</tr>
<tr>
<td>III (1 small-medium coronary artery aneurysm/major coronary artery)</td>
<td>Low-dose aspirin (3–5 mg/kg aspirin per day), at least until aneurysm regression documented</td>
<td>For patients &lt;11 y old, no restriction beyond 1st 6–8 weeks; patients 11–20 y old, physical activity guided by biennial stress test, evaluation of myocardial perfusion scan; contact or high-impact sports discouraged for patients taking antiplatelet agents</td>
<td>Annual cardiology follow-up with echocardiogram + ECG, combined with cardiovascular risk assessment, counseling; biennial stress test/evaluation of myocardial perfusion scan</td>
<td>Angiography, if noninvasive test suggests ischemia</td>
</tr>
<tr>
<td>IV (≥1 large or giant coronary artery aneurysm, or multiple or complex aneurysms in same coronary artery, without obstruction)</td>
<td>Long-term antiplatelet therapy and warfarin (target INR 2.0–2.5) or low-molecular-weight heparin (target: antifactor Xa level 0.5–1.0 U/mL) should be combined in giant aneurysms</td>
<td>Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations guided by stress test/evaluation of myocardial perfusion scan outcome</td>
<td>Biannual follow-up with echocardiogram + ECG; annual stress test/evaluation of myocardial perfusion scan</td>
<td>1st angiography at 6–12 mo or sooner if clinically indicated; repeated angiography if noninvasive test, clinical, or laboratory findings suggest ischemia; elective repeat angiography under some circumstances</td>
</tr>
<tr>
<td>V (coronary artery obstruction)</td>
<td>Long-term low-dose aspirin; warfarin or low-molecular-weight heparin if giant aneurysm persists; consider use of β-blockers to reduce myocardial ( \text{O}_2 ) consumption</td>
<td>Contact or high-impact sports should be avoided because of risk of bleeding; other physical activity recommendations guided by stress test/myocardial perfusion scan outcome</td>
<td>Biannual follow-up with echocardiogram and ECG; annual stress test/evaluation of myocardial perfusion scan</td>
<td>Angiography recommended to address therapeutic options</td>
</tr>
</tbody>
</table>
Kawasaki cont’d

- Prognosis
  - 1/2 to 2/3 of aneurysms will “resolve” by 1-2 yrs post disease onset
    - Positive factors for regression:
      - Small (giant aneurysms (>8mm in diameter) have worst prognosis)
      - Fusiform (saccular and “beads on a string” have worse prognosis)
      - < 1 yr of age at time of disease onset
      - Aneurysm in a distal coronary segment
  - Myocardial dysfunction resolves post treatment (unless ischemic damage)
    - No correlation between severity of myocarditis and risk for coronary aneurysms
  - Peak mortality: 15-45 days post fever onset
    - Myocardial infarction
  - Recurrence rate: ~3% (Japan)
Acute Rheumatic Fever

• What is it?
  – A pathological immune mediated inflammatory disorder of the heart, brain, joints, and skin after group A Strep throat infection
  – More common in underdeveloped countries
  – How to diagnose:
    • Evidence for group A Strep throat infection and 2 major, or 1 major and 2 minor, criteria
Acute Rheumatic Fever cont’d

- Diagnostic criteria (major)
  - Joints—severe polyarthritis, responds well to ASA
  - O (Heart)—carditis; often MR, MR/AI
  - Nodes—subcutaneous nodules (hard and painless) on extensor surfaces
  - Erythema marginatum—evanescent, comes and goes, on trunk
  - Sydenham’s chorea—neuropsychiatric disorder
Acute Rheumatic Fever cont’d

• Diagnostic criteria (minor)
  – Arthralgia
  – Fever
  – Elevated acute phase reactants (ESR, CRP)
  – Prolonged PR
ERYTHEMA MARGINATUM
SUBCUTANEOUS NODULES
Acute Rheumatic Fever cont’d

• Treatment:
  – Benzathine PCN—knocks out strep
  – ASA—relieves arthritis, helps mild to moderate carditis
  – Prednisone—only for severe carditis
  – Support if CHF
  – ABX prophylaxis
Myocarditis

• What is it?
  – Inflammed myocardium

• Etiology?
  – Viral
    • Enteroviruses, esp. Coxsackie B
    • Adenoviruses
    • Others: Flu, HSV, Parvo, CMV, HCV, EBV, Mumps, Rubella, Varicella, HIV, RSV…
  – Bacterial, Rickettsial, Fungal, Parasitic
  – Other Noninfectious Inflammatory Diseases
    • SLE, Kawasaki, Rheumatic Fever…
Myocarditis cont’d

• Presentation:
  – Clinically, symptoms and signs similar to dilated cardiomyopathy (CHF)
  – ECG: low voltages, arrhythmias (any type), ST and T wave changes, ± wide Q waves
  – CXR: cardiomegaly, pulmonary edema
  – Echo: dilated and poorly functioning ventricles; often occurs with pericardial effusion
Myocarditis cont’d

ECG of myocarditis; Pediatric ECG Interpretation, Deal et al, 2004
Myocarditis cont’d

- **Treatment**
  - Support to relieve CHF and to maintain good cardiac output
    - Don’t aggressively load Digoxin in acute inflammatory stage (hypersensitivity)
  - Treat arrhythmias
    - Lidocaine or amiodarone for ventricular arrhythmias (may require cardioversion if unstable)
    - Complete heart block: pace
  - Treat etiology, if known
  - No proven benefit of immunosuppressives
  - If irreversible damage to myocardium, may need surgical intervention
Dilated cardiomyopathy

- Large, thin-walled chamber
- Poor systolic function
- Etiologies:
  - Idiopathic (50%)
  - Infectious (viral, esp. HIV)
  - Drugs (anthracyclines)
  - Ischemic
  - Poor nutrition (low carnitine, selenium, thiamine)

Braunwald, 2001
Dilated cardiomyopathy cont’d

- What’s the big deal with DCMP?
  - Some types are reversible (improve w/ time and/or Rx), but most are progressive
  - 5 yr survival as low as 20-80%
  - Death due to intractable CHF, ventricular arrhythmias
Dilated cardiomyopathy cont’d

• Common medical therapies
  – Goal: improve ventricular function/efficacy and reduce pulmonary venous congestion
  – **Digoxin**: inotrope, improves systolic function and helps reduce end-diastolic pressure
  – **Enalapril**: ACE-I, reduces afterload
  – **Lasix &/or Aldactone**: diuretic, relieves pulmonary congestion
  – **Carvedilol**: beta-blocker, alpha-blocker, antioxidant, improves survival
  – **Warfarin**: anticoagulant, prevents thromboemboli

• Invasive therapies
  – **ICD**: defibrillator, useful w/ ventricular arrhythmias
  – **Transplant**: last option
Etiologies of pericarditis

• **Purulent**
  – #1 Staph aureus
  – #2 H flu B
  – Others: Neisseria, Pseudomonas, Salmonella, Listeria, Pasteurella, E. coli, Brucella, Yersinia, Legionella, Campylobacter
  – ABX and drain (surgical)
  – 25-75% mortality

• **Viral**
  – Coxsackie, ECHO, Adeno, Flu, Mumps, Varicella, EBV, HIV
  – Many WBC’s in fluid
  – Supportive care and antiinflammatories
  – Up to 15% relapse
Etiologies of pericarditis cont’d

- Drug induced
  - Lupus-like syndrome
    - Hydralazine
    - Isoniazid
    - Procainamide
  - 33% of those who develop +ANA will develop lupus-like syndrome
  - Treat w/ antiinflammatories and stop drug

- Postpericardiotomy syndrome
  - Unclear mechanism
  - Less likely in kids <2y/o
  - Typically:
    - Fever, irritability, chest pain, malaise, poor appetite
    - Presents 1 wk post surgery (can be many months)
  - Treat w/ ASA (or other antiinflammatory)
Etiologies of pericarditis cont’d

• **TB**
  - Usually secondary to direct spread or hematogenous spread
  - Fluid shows mostly Lymphocytes
  - Cx takes up to 6 wks
  - 15-42% show acid-fast bacilli in fluid
  - Fluid adenosine deaminase level >50 U/L
  - Treat w/ INH, Pyrazinamide, Rifampin, Streptomycin +/- steroids initially
  - 35% may develop constrictive pericarditis

• **Connective tissue diseases**
  - Up to 50% of kids w/ JRA
  - Treat with NSAIDS
  - Up to 50% of kids w/ SLE
  - Fluid may show low complement levels, +ANA, or +Rheumatoid factor
Clinical presentation

- Dull chest pain, increases with lying supine
- + rub
- Muffled heart sounds
- Pulsus paradoxus if tamponade
- ECG: low voltages, may have ST changes
- CXR: cardiomegaly, often no pulm congestion
- ECHO: pericardial effusion
What is pulsus paradoxus?

- SBP drop >10 mmHg with inspiration
- Mechanism in tamponade:
  - Inspiration increases venous return to RA/RV
  - Delayed venous return to LV and leftward displacement of IVS decreases LV filling (preload)
  - Diminished SV
  - SBP drops
- Neurohormonal compensation for lower CO:
  - Increased sympathetic tone and catechol release
  - Elevated HR, increased contractility, vasoconstriction

Pericarditis: typical ECG

ECG of pericarditis; Pediatric ECG Interpretation, Deal et al, 2004
ECG of large pericardial effusion

Radiography

• Cardiac silhouette
  – May be normal if acute
  – Enlarged, “water-bottle”, triangular

• Usually no pulm. vasc. congestion/edema

Yale, 2004 (http://info.med.yale.edu/intmed/cardio/imaging/cases/pericardial_effusion/)
Echocardiography

- Presence and relative size of effusion
- Chamber dimensions and wall dynamics (compression)
  - Early diastole: RV free wall compression
  - Late diastole: RA compression
  - LA compression—very specific for tamponade
  - Swinging heart—large effusion
- May be limited by quality of imaging windows and location of fluid (if loculated)

Spodick, NEJM 2003
Assessing hemodynamic significance

- **Insignificant pericardial effusion**
  - No JVD (JVP <7mmHg)
  - Nml VS’s and good perfusion
  - No compression on echo

- **Significant, but compensated**
  - JVD/elevated JVP (8-12mmHg)
  - Nml HR and BP, good perfusion
  - Mild pulsus paradoxus (<20 mmHg)

- **Severe with maximum compensation**
  - JVD/elevated JVP (>15mmHg)
  - Elevated HR, poor perfusion (vasoconstriction)
  - Nml BP
  - Significant pulsus paradoxus (>20 mmHg)
  - Significant chamber collapse

- **Severe and decompensated**
  - JVD/elevated JVP (>20mmHg)
  - Elevated HR, RR
  - Poor perfusion
  - Low BP, palpable pulsus paradoxus
  - Chamber collapse/swinging heart

Modified from Goldstein, Current Prob Cardio, 2004; 29(9)
Pericarditis cont’d

• Treatment
  – Treat underlying disorder (uremia, etc.)
  – If idiopathic or viral, ASA
  – If tamponade, pericardiocentesis
  – If purulent, surgical drainage/Antibiotics
Infective Endocarditis

• What is it?
  – Seeding of bacteria and inflammatory response within the endocardial layer of the heart
  – Occurs when
    • 1) pt is bacteremic and
    • 2) pt has intracardiac structural abnormality

• Clinical findings:
  – MURMUR
  – Fever
  – Emboli (skin, eye, nails, lungs, brain, kidney, etc.)
Infective Endocarditis cont’d

Splinter hemorrhage, Dermatlas, 2001-04

Janeway lesion, AllRefer.com, 2004

Osler nodes, Dermatlas, 2001-04
Infective Endocarditis cont’d

• Bugs:
  – **Strep viridans** (bad teeth)
  – **Staph aureus** (post-operative cardiac pts)
  – **Enterococci** (GU/GI procedures)
  – **HACEK** (neonates, immunocompromised pts): Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella)
  – **Fungal**
    – *(Pseudomonas or serratia (IV drug users))*

• Treatments:
  – PCN
  – Oxacillin or Vanc
  – Amp/PCN and Gent
  – CTX
  – Ampho B