



RhAPP

RHEUMATOLOGY ADVANCED
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If the walls could talk:

Pediatric Vasculitides

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WAYNE
PEDIATRICS



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Faculty Disclosures

- Azurity Pharmaceuticals: Consultant

Objectives

The learner will be able to:

- Form differential diagnoses of pediatric vasculitides
- Order appropriate laboratory studies for the appropriate suspected vasculitide and be able to correctly interpret them
- Recognize the most common pediatric vasculitides, understand pathophysiology of the disease and knowledgeable of current treatment options
- Identify complications of common pediatric vasculitides, further testing required and management
- Determine multispecialty team needed for management of pediatric vasculitides

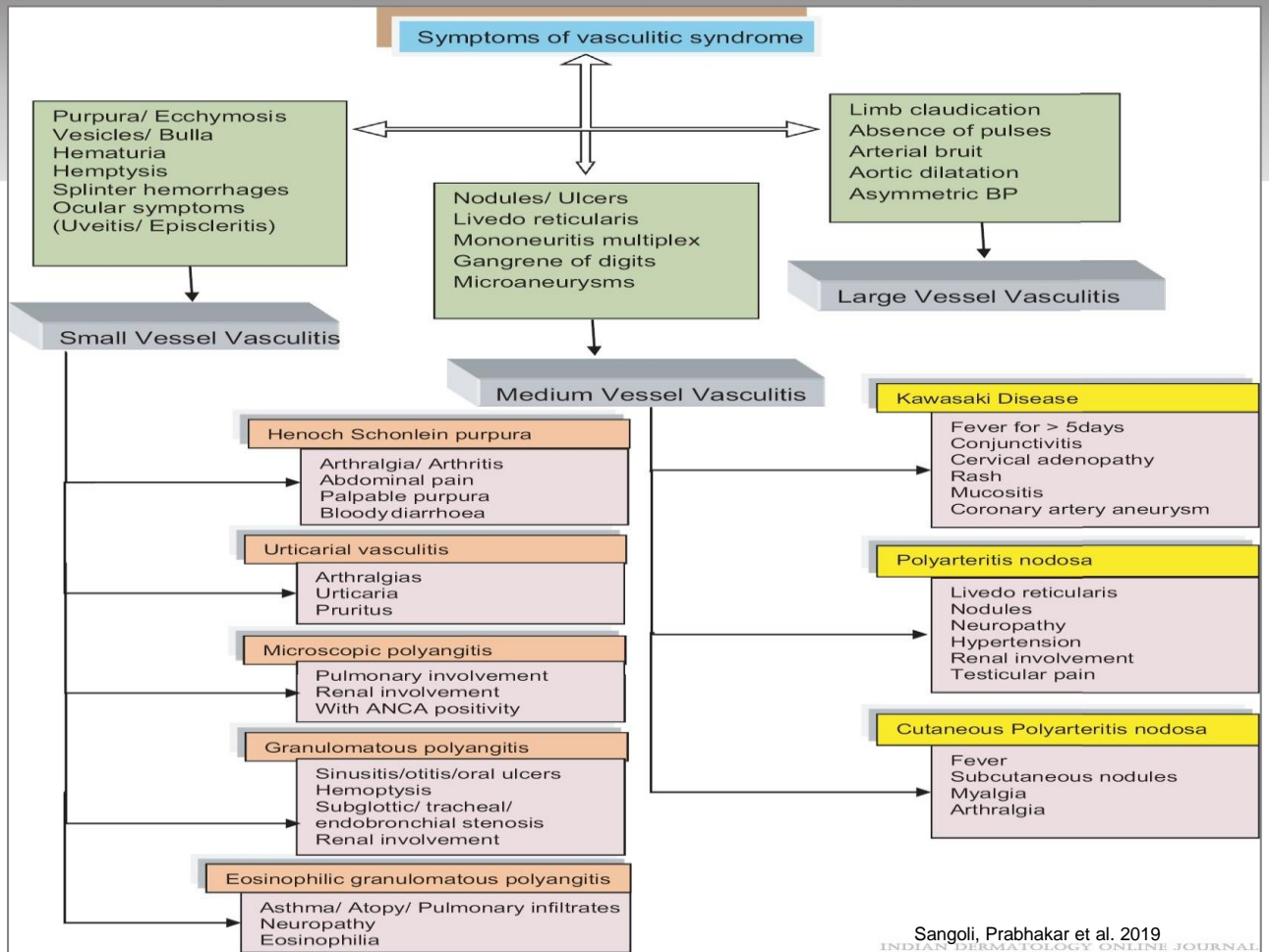


Defensive
Player

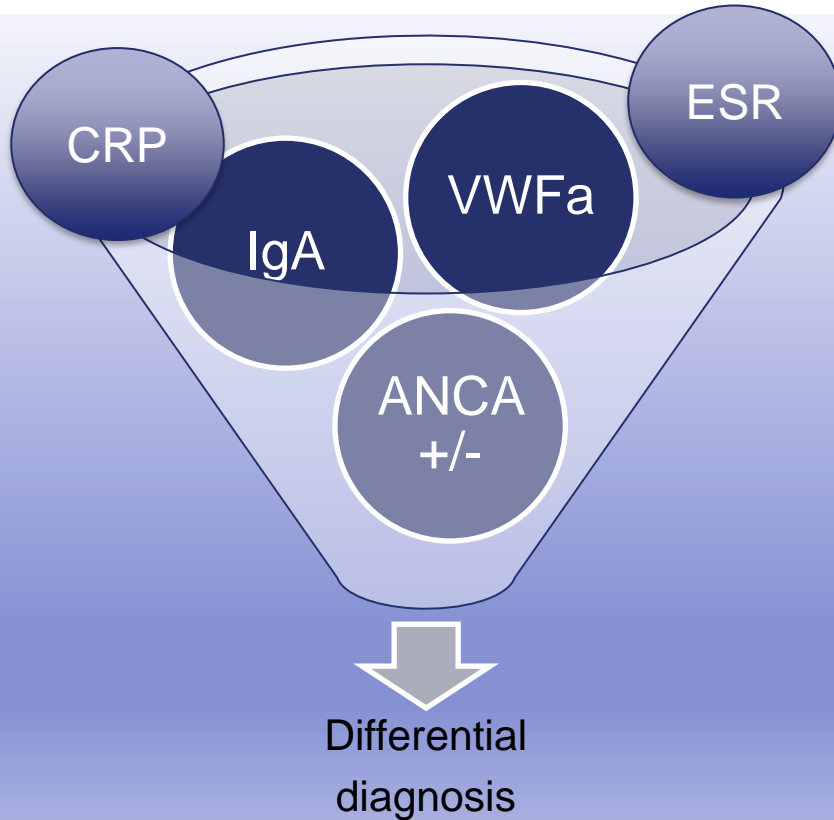


Pathophysiology of Pediatric Vasculitis:

- Theoretical at best
- Different pathophysiology in many vasculitides
- Genome-wide association studies(GWAS):
Polygenic for predisposition and unclear triggers(TA, Kawasaki, BD and AAV)
- Mast cells may increase vessel permeability, fibrosis and targeting cell killing in vessel wall
- Antibodies against endothelial cells, B cells



Laboratory studies & interpretation



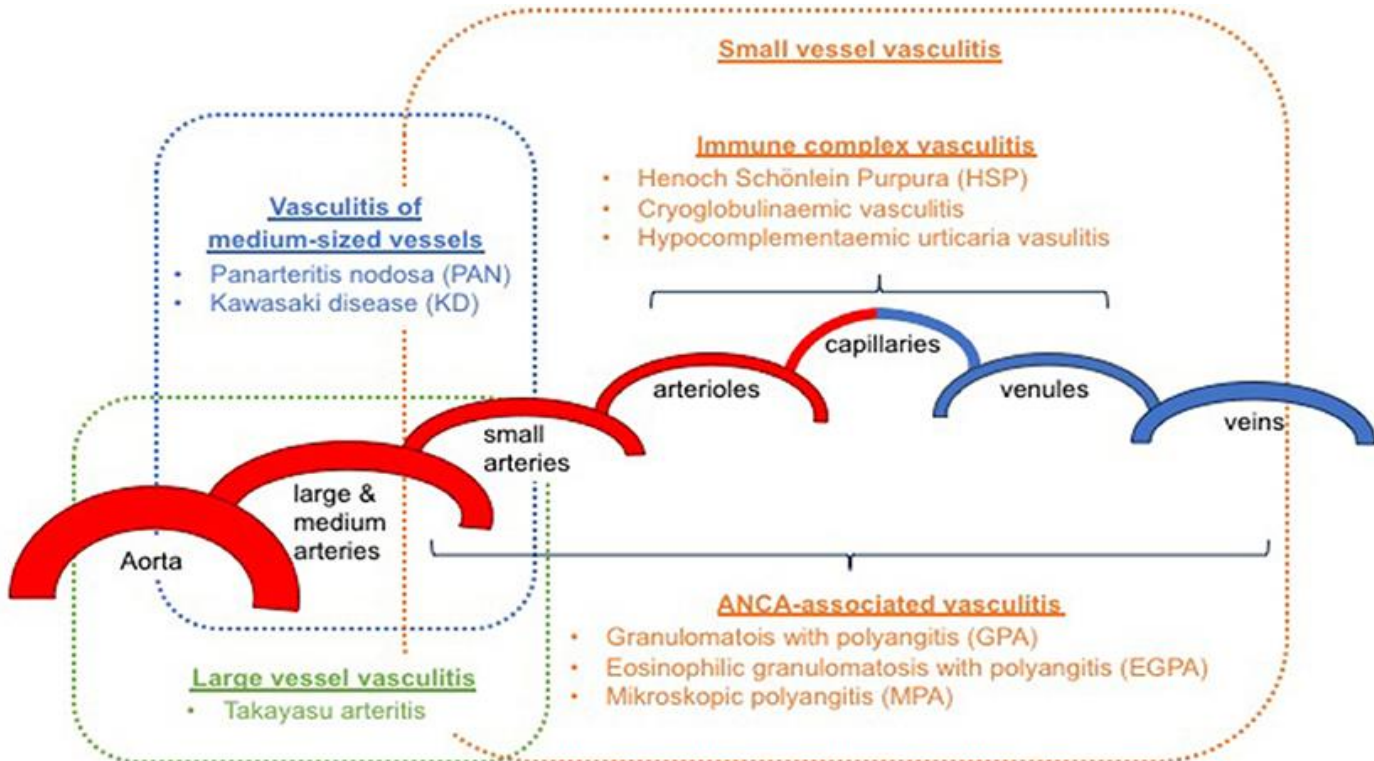
Differential Diagnosis



Primary

Secondary

Pediatric Vasculitides

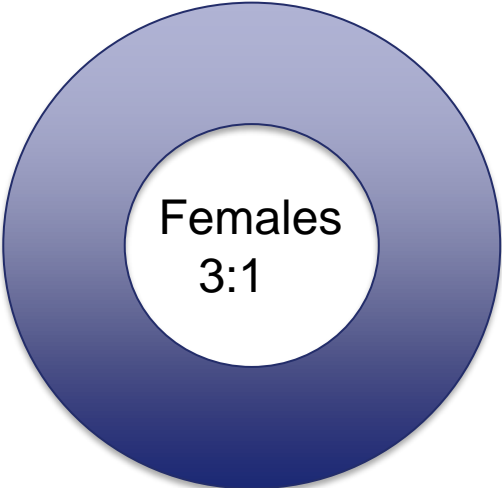


A New kid on the block: COVID-19

Small Vessel	Medium Vessel	Large Vessel
JDM	Kawasaki	Takayasu's Arteritis
HSP	PAN	
Cryoglobulinaemic		
Hypocomplementemic urticarial		
Behcet's	Behcet's	Behcet's
Cogan's Syndrome	Cogan's Syndrome	Cogan's Syndrome
COVID-19 Vasculitis	COVID-19 vasculitis	COVID-19 vasculitis

Large Vessel

Takayasu's Arteritis



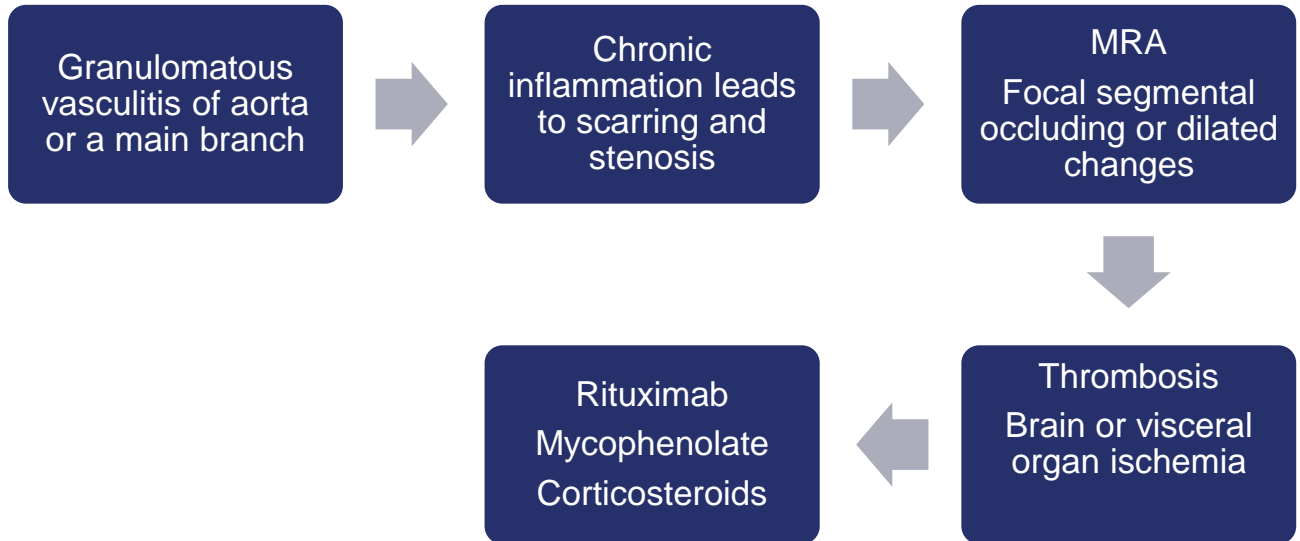
Females
3:1



TO



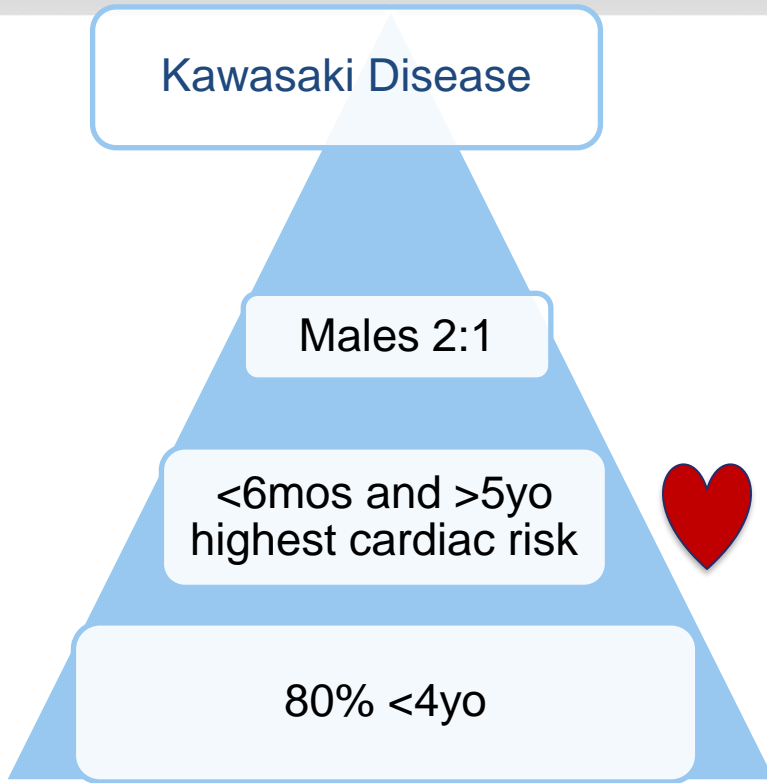
TA disease, progression and treatment



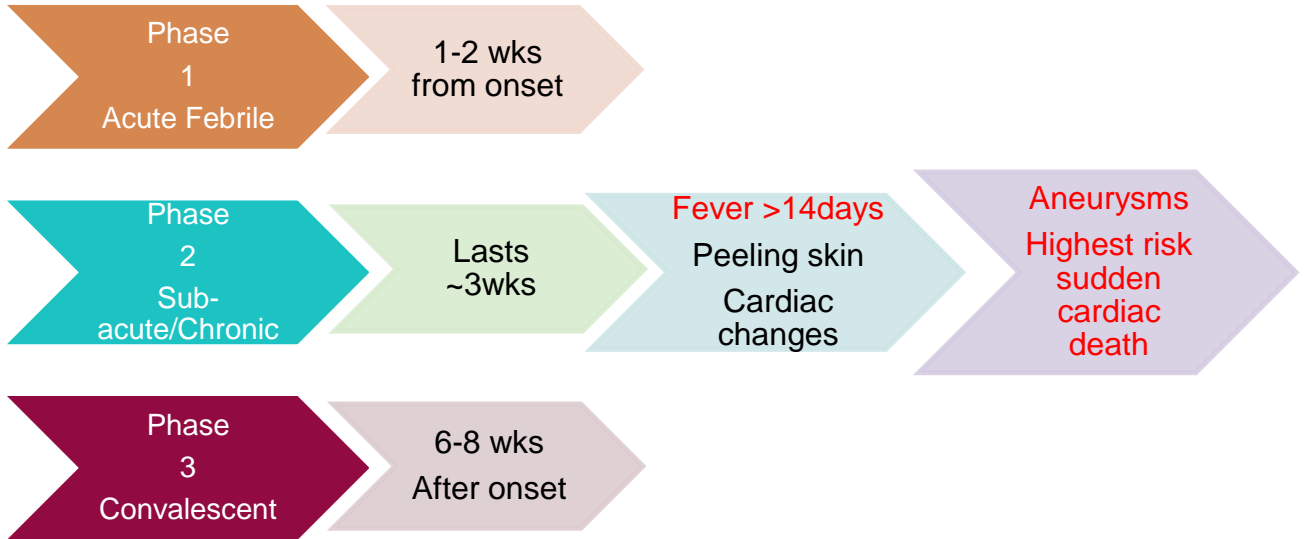
Takayasu's Arteritis

Often characterized by these Signs and Symptoms:	Dx Criteria	Treatment
<p>Markedly elevated ESR & CRP Fevers, night sweats, malaise, myalgia and arthralgia</p> <p>Headaches and other neurological symptoms</p> <p>Abdominal pain and GI symptoms</p> <p>Pulselessness or weak pulses or murmur</p> <p>Hypertension and/or asymmetrical BPs</p> <p>Bruits: carotid, abdominal</p> <p>Claudication</p> <p>Arterial hypertension</p>	<p>PRINTO</p> <p>MRI/MRA</p> <p>Whole body F-FDG MRI/PET</p>	<p>Corticosteroids</p> <p>MTX or Mycophenolate</p> <p>anti-TNF inhibitor (etanercept, adalimumab, infliximab)</p> <p>IL-6 inhibitor (tocilizumab)</p> <p>B-cell depleting agent (rituximab)</p> <p>Cyclophosphamide reserved for life threatening refractory cases</p>

Medium Vessel



KD 3 phases of disease



Diagnostic Criteria for Kawasaki Disease

Diagnosis requires ≥ 5 days of fever plus ≥ 4 of following 5 criteria:



Bilateral bulbar conjunctival injection



Oral mucous membrane changes, including injected or fissured lips, injected pharynx, or strawberry tongue

Peripheral extremity changes, including erythema of palms and soles, edema of hands and feet (acute phase), and peritongual



Polymorphous rash

Cervical lymphadenopathy (≥ 1 lymph node >1.5 cm in diameter)



all images
© Kawasaki Disease Foundation

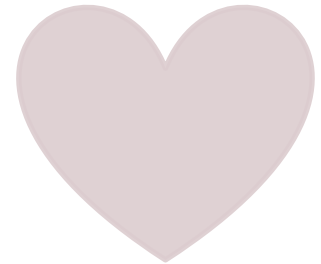
KD Cardiac manifestations

Cardiac changes

- Arrhythmias
- Prolonged QT/or ST
- ST-T changes
- Low voltage

CXR

- Cardiomegaly



Medium Vessel: Kawasaki (IgA mediated)

Laboratory Findings	Treatment	Complications
ESR >40 CRP >40 AST >50 Thrombocytosis Leukocytosis Hypoproteinemia Anemia	ASA Prednisone IVIg Anti-TNF Infliximab (IL-1 has been implicated) AHA rec's for f/u	Infants increased severity of coronary disease 15-20% develop aortic dilatation due to delayed tx Unresolved aortic arch dilatation

Medium Vessel: Polyarteritis Nodosu(PAN)


Characteristics at Presentation	Diagnostic Criteria	Treatment	Complications
<p>Fever, malaise, weight loss, non-specific abd pain</p> <p>Organ related: arthralgia/arthritis Myalgia/myositis Pulmonary Cardiology w/wo coronary arteritis Neurological Renal vascular hypertension</p>	<p>Labs consistent w/inflammation</p> <p>MRI/MRA</p> <p>Bx: necrotizing arteritis w/segmental vascular and nodular involvement w/aneurysm</p>	<p>HD steroids</p> <p>Biologics more recently: TNFi Anti-CD-20(Ritux) OR IV Cytoxan monthly</p> <p>Maintenance: MTX mycophenolate Azathioprine IVIG</p>	<p>Cutaneous PAN can progress to systemic PAN or relapse as systemic PAN</p> <p>Aneurysms and rupture</p>

Did you know.....

What disease was once called Infantile
Polyarteritis Nodosa?

Kawasaki disease

Common Small Vessel Vasculitides



Eosinophilic
GPA (Churg
Strauss)


HSP

Hypocomplementemic
urticarial
vasculitis

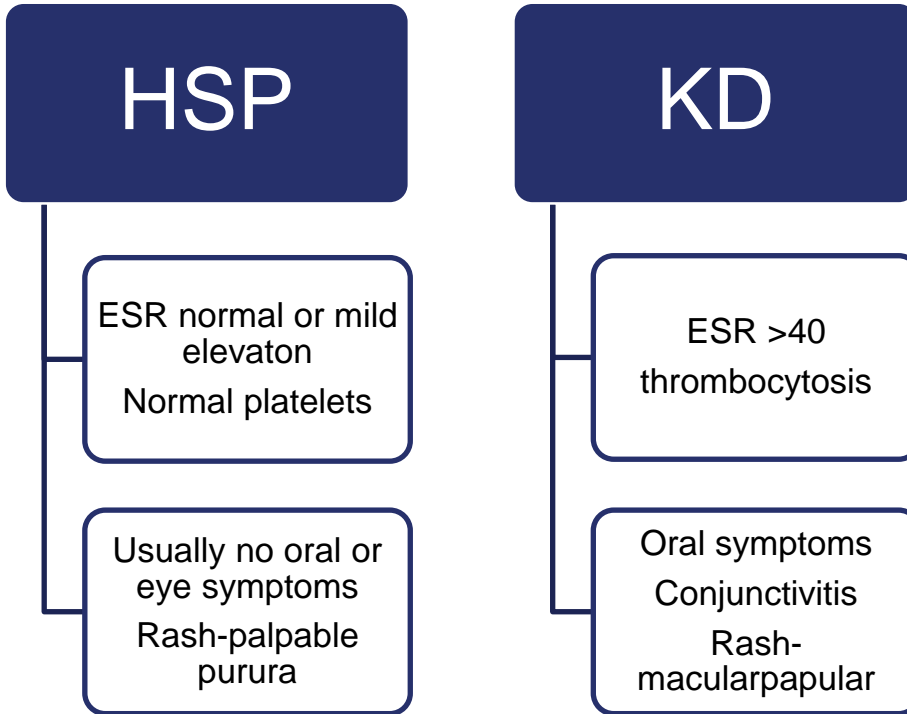


GPA
(Wegener's)

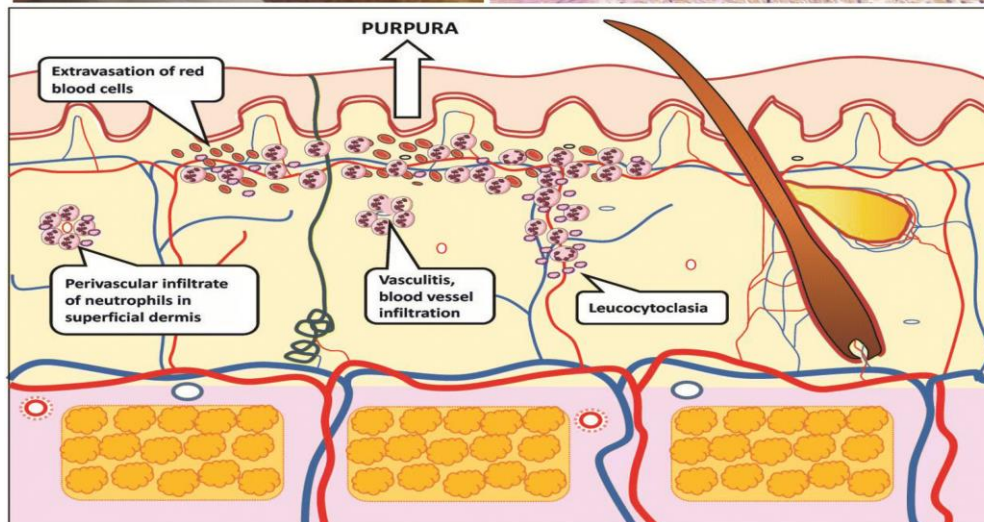
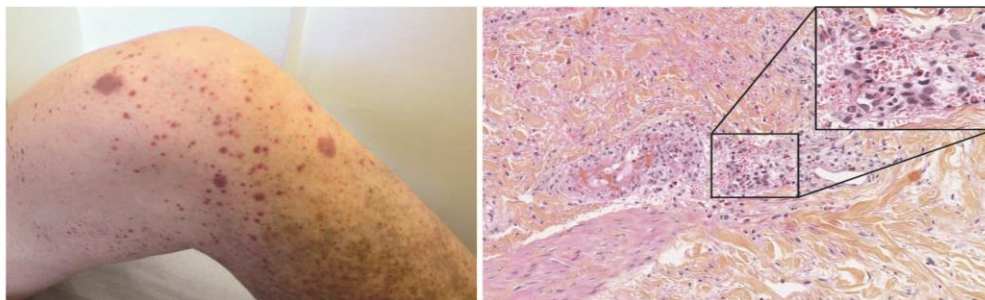
Henoch-Scholen Purpura(HSP)

Diagnostic Criteria	Laboratory Studies	Treatment	Complications
<ul style="list-style-type: none"> ✓ Palpable purpura w/normal platelets ✓ Arthritis ✓ Colicky abd pain often w/bleeding ✓ Age <21 	<p>*Not all pts have elevated IgA</p> <p>*VWFa elevated</p> <p>*ESR normal or slight </p> <p>*Bx: granulocytes in arterioles or venules</p>	<p>NSAIDs</p> <p>Oral corticosteriods if abdominal pain or hematuria</p> <p>May have intermittent less severe flares for 7+months</p>	<p>Elevated BP</p> <p>Hematuria</p>

HSP or Kawasaki differential diagnosis

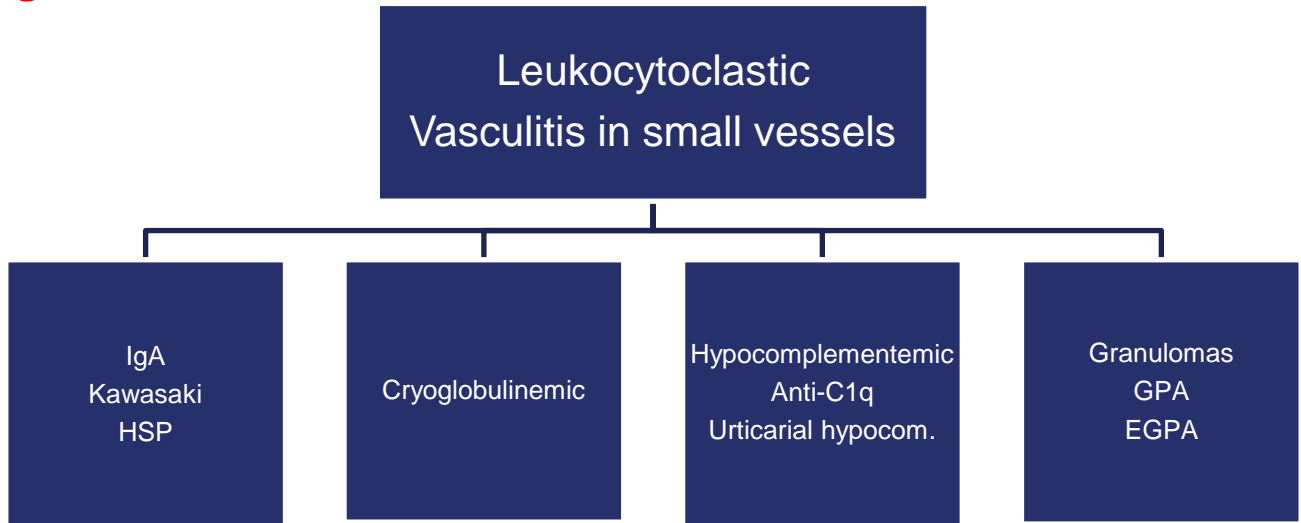


Understanding palpable purpura as a small vessel vasculitis

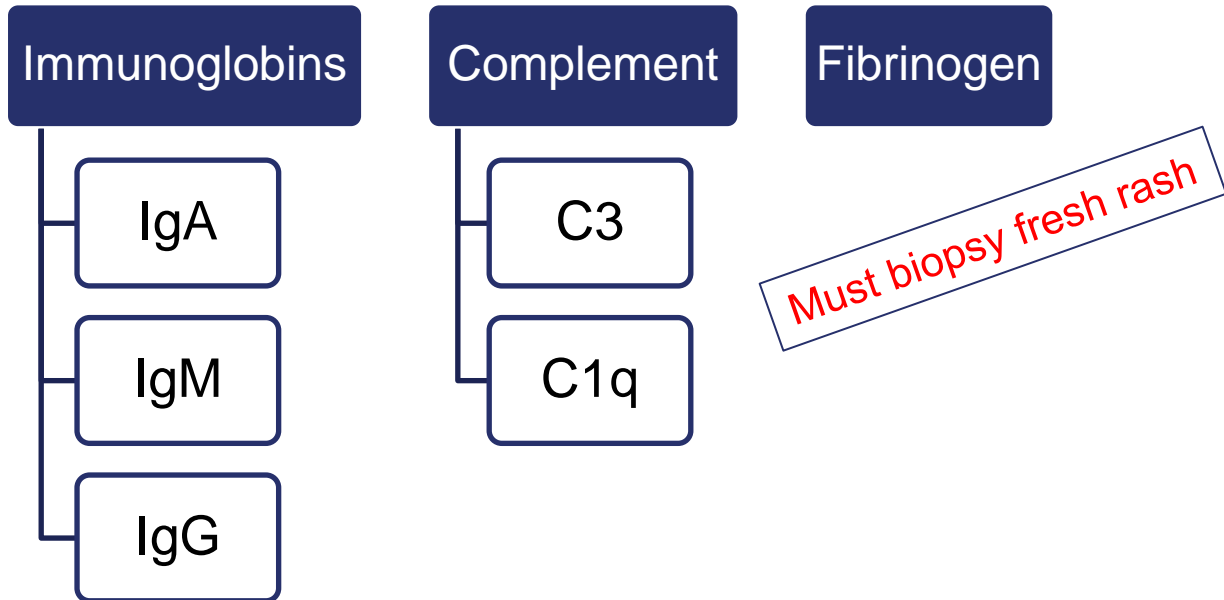


When neutrophils breakdown and release debris in small vessels this is what you get...

Skin findings in your vasculitides



All leukocytoclastic vasculitis are the consequence of immune complex deposits into the vessel wall, and therefore with positive direct immunofluorescence on skin biopsy



Small vessel


ANCA Associated Vasculitides(AAV)

Signs & Symptoms	Diagnostic Criteria	Treatment	Complications
Granulomatous w/polyangitis/GPA (Wegener's)	Usually ANCA + Biopsy-predominance of macrophages with or without giant cells	Rituximab OR Cytoxan Maintenance with DMARD Azothioprine	
Microscopic polyangiitis/MPA (Anti-C1q vasculitis)			
Eosinophilic GPA (Churg-Strauss)			

Hypocomplementemic urticarial vasculitis AKA anti-C1q vasculitis

Signs & Symptoms	Diagnostic Criteria	Treatment	Complications
<p>Urticaria intermittent</p> <p>Angioedema</p> <p>Laryngeal edema</p> <p>Painful skin lesions</p> <p>May be systemic</p> <p>Proteinuria</p> <p>Hematuria</p> <p>Pleural effusion</p>	<p>Low C2, C3 or C4</p> <p>Anti-C1q antibodies</p> <p>May or may not have C1q in serum</p> <p>Urticaria</p> <p>More recent Gene: DNASE1L3 Autosomal recessive</p>	<p>Antihistamines</p> <p>Corticosteroids</p> <p>Epi-pen</p> <p>*Ruled out: coxsacki, mono, hep B/C</p>	<p>Can be secondary to SLE, Sjogren's, monoclonal gammopathy or blood disorders</p> <p>Usually managed by allergy immunology</p>

Variable size vessel:

Disease	Characterized by:	Treatment:
Behcet's HLA-B52	Uveitis Arthritis Oral/genital ulcers Skin findings Vasculitis?vessel size(s)	Treatment of individual systems and vasculitis as separate entities
Cogan's Syndrome	Anemia Aortic regurgitation Eye inflammation Worsening visual acuity Blindness Tinnitus SNHL Vertigo Vasculitis	
COVID-19 vasculitis	+COVID-19 Vasculitis?vessel size(s) and organ affected (ie. Eyes, brain etc)	MTX, TNFi to Cytosan

Genetic testing

A continually advancing tool in our tool box

Highly recommend looking into the following:

Browse their testing panels

Immunodeficiency panel? How many genes? Include our inflammatory disorders?

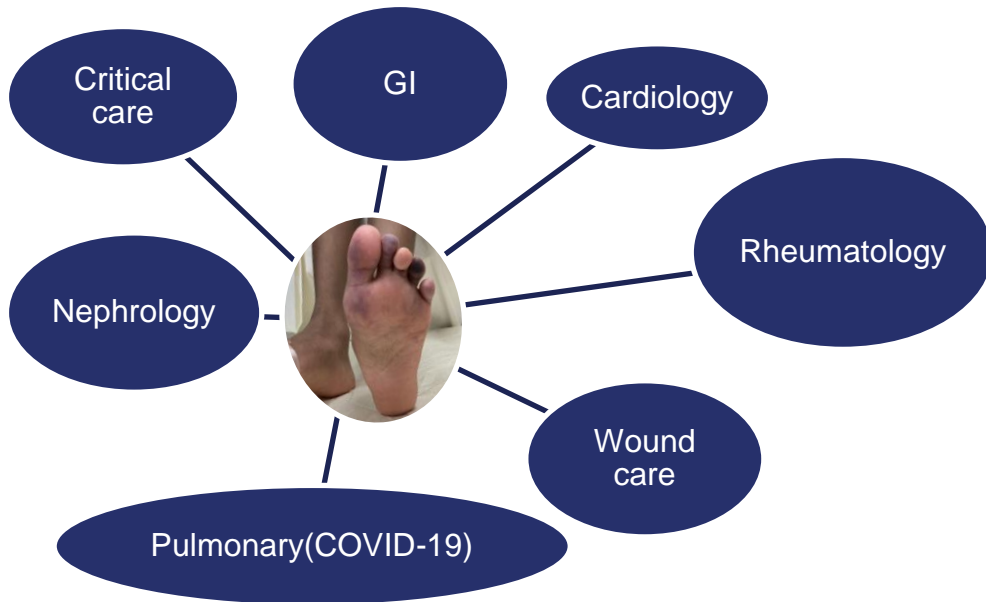
As new tests become available will they automatically run them and send results to provider?

Most insurances will cover but pt responsible for deductibles and co-pays FIRST costing \$\$\$\$

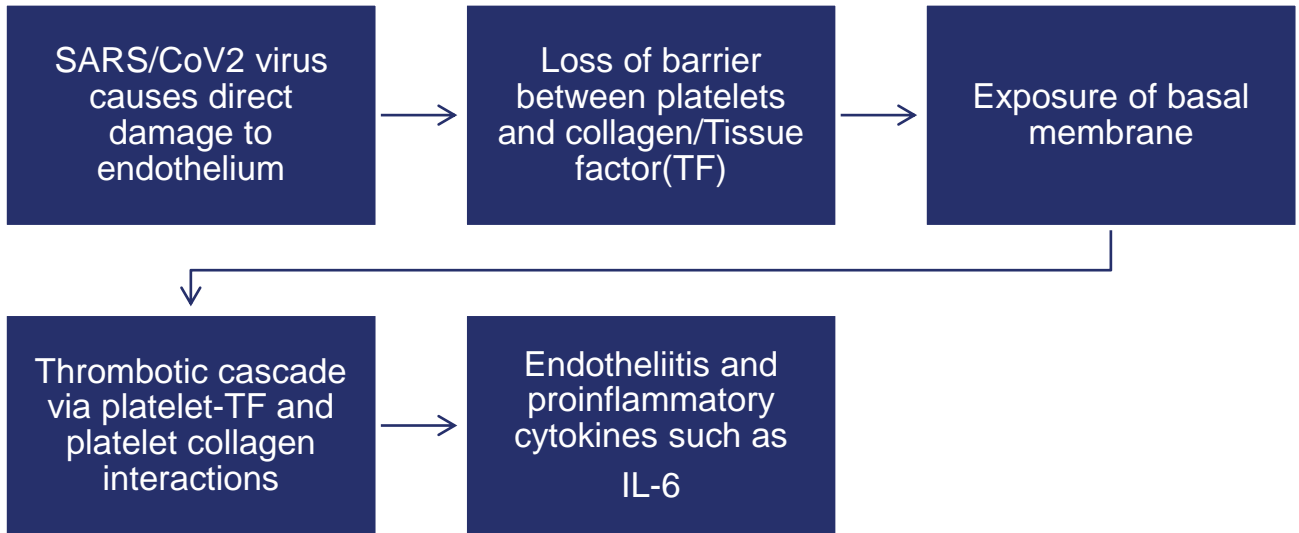
Patient pay an option? Cost?

Check your state M'caid

Management Team for Peds Vasculitides



Pathophysiology SARS/CoV-2 Vasculitis



COVID-19 Related Peds Vasculitis: A review of the literature to date*

- 25 articles
- 36 patients
- 13yo median age
- M/F: 2.3
- Mean time from SARS-CoV-2 exposure 17.5 days n=10 (range of 2-150 days)

*Kawasaki MIS-C cases excluded

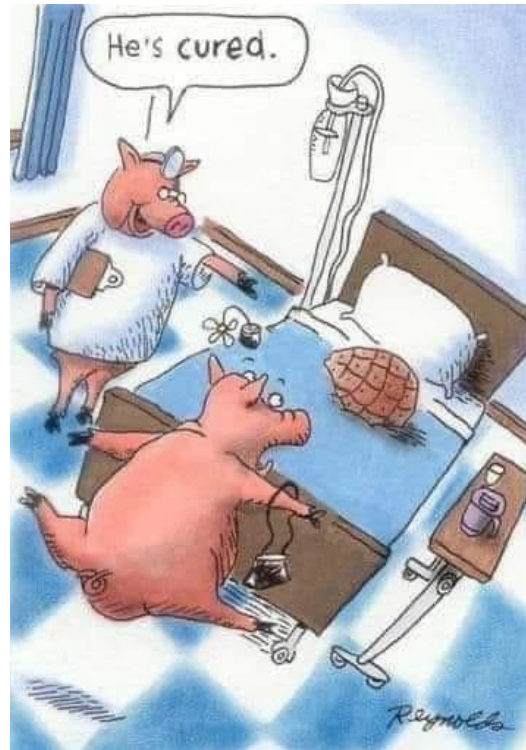
COVID related peds vasculitis

Most frequent phenotype	Most common manifestations	Most common organ affected
HSP/IgA (25%)	Skin 58.3%	Skin 58.3%
Chilblains (19.4%)	Renal 30.5%	Kidney 30.5%
ANCA assoc. (13.8%)		GI 13.8%
Post-viral renal (13.8%)		CNS 13.8%
CNS (11.1%)		Lung 11.1%
Retinal (5.5%)		
Urticarial (5.5%)		
Cutaneous leukocytoclastic (2.7%)		
Acute hemorrhagic edema in infancy AHEI (2.7%)		

COVID-19 peds vasculitis outcomes

Mortality	Remission	Most Common Treatments
5 with CNS vasculitis 1 ANCA + 1 dx post-mortem	23/28 HSP 100%	HSP- NSAIDs Corticosteroids 40% Rituximab 14.2% Cytosan 11.4%

And just like that.....



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