

Fever and Hematuria in a Pediatric Patient with an Artificial Heart Valve

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Disclosures

- I have no financial or non-financial disclosures.

Case PCP Visit

Test Name	In Range	Out Of Range
URINALYSIS, COMPLETE		
COLOR	YELLOW	
APPEARANCE		TURBID
SPECIFIC GRAVITY	1.014	
PH	< OR = 5.0	
GLUCOSE	NEGATIVE	
BILIRUBIN	NEGATIVE	
KETONES	NEGATIVE	
OCCULT BLOOD		3+
PROTEIN		3+
NITRITE	NEGATIVE	
LEUKOCYTE ESTERASE		TRACE
WBC		20-40
RBC		> OR = 60
SQUAMOUS EPITHELIAL CELLS	NONE SEEN	
BACTERIA		MODERATE
URIC ACID CRYSTALS	FEW	
HYALINE CAST	NONE SEEN	

PCP refers to nephrology

11 yo M with history of truncus arteriosus with artificial pulmonary valve presenting with prolonged fevers and dark urine. Patient also with weight loss, headaches, fatigue and anorexia.

History of tooth extraction several months prior with antibiotic prophylaxis and parainfluenza diagnosis at onset of fevers.

Three family members with SLE, mother and maternal grandparents all on hemodialysis for CKD secondary to DM and hypertension.

Initial PCP workup: UA

Case: Outpatient Nephrology

CBC

~~7.6
6.1 122
24.2~~

CMP

137	104	19	92
4.5	20	2.9	

**Direct admission to nephrology
service for AKI**

Two weeks later presents with continued fevers (100.6), dark urine, fatigue and malaise.

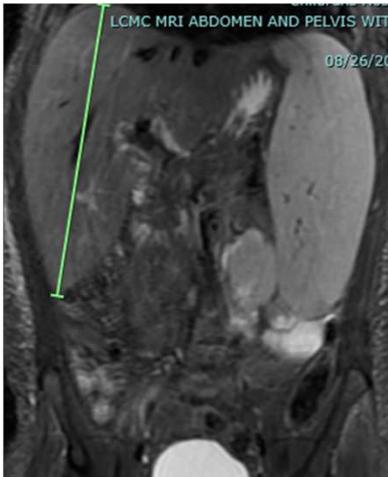
Physical exam only notable for previously present heart murmur.

Lab workup:

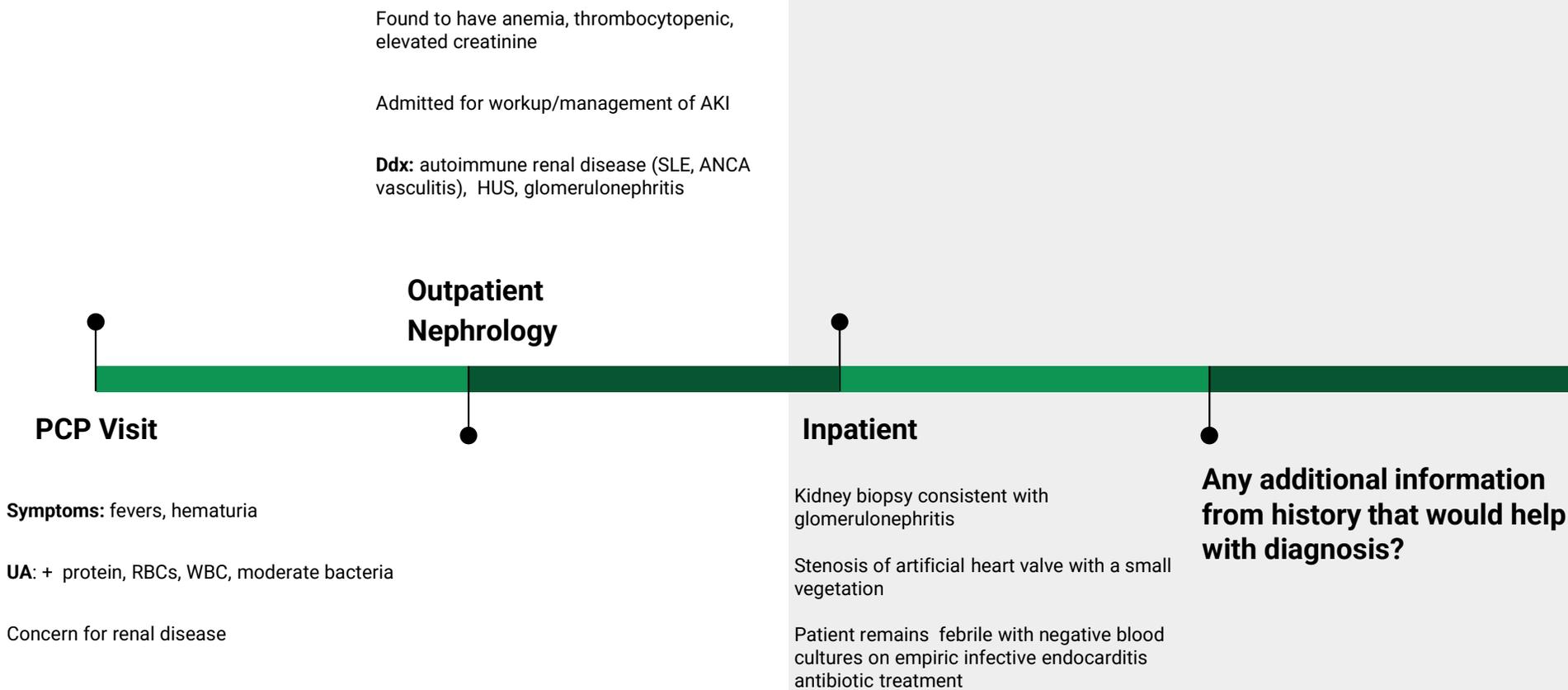
- Urine culture (normal)
- ANA, C3, C4, TSH (normal)
- Urine protein creatinine ratio (confirmed proteinuria)
- Renal ultrasound consistent with medical renal disease and enlarged spleen
- CBC, CMP

Case

Inpatient course



- Started on ceftriaxone at admit
- Kidney biopsy consistent with glomerulonephritis
- TTE with poor visualization of PA conduit, signs of stenosis
- TEE shows small vegetation
- Blood, urine cultures no growth



Case

Inpatient course

Diagnosis of Bartonella henselae

Serology Results*

	Initial (D0)	Mid- treatment (D23)
IgM	negative	1:32
IgG	>1:1024	>1:1024

Additional evidence of *B. henselae* infection:

~ Karius positive for *Bartonella henselae*

~ PCR of valve tissue positive for *Bartonella henselae*

- *Bartonella henselae* serology ordered
- Melody valve removed, replaced with homograft
- All other cultures no growth

Treatment

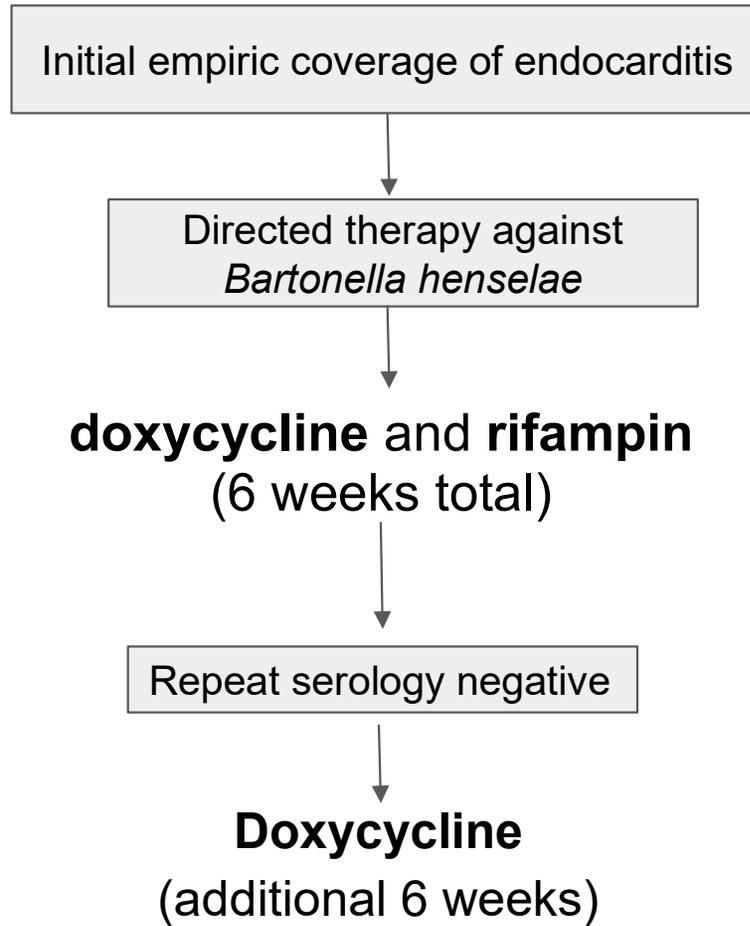
Initial empiric coverage of endocarditis

Directed therapy against
Bartonella henselae

doxycycline and **rifampin**
(6 weeks total)

Repeat serology negative

Doxycycline
(additional 6 weeks)



Bartonella henselae

1) When to consider *B henselae* on the differential?

1) Challenges in the diagnosis of *B henselae* infections

Immunocompetent Host:

- Asymptomatic
- Cat scratch disease
- Parinaud oculoglandular syndrome
- Hepatosplenomegaly
- Prolonged fevers
- Complications of:
 - CNS
 - Skin
 - Lungs
 - Bones
 - Blood cells

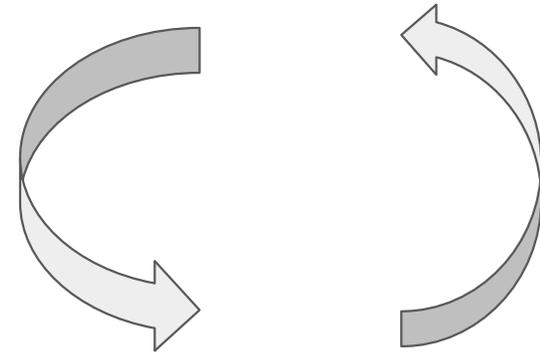


Abnormal cardiac valve

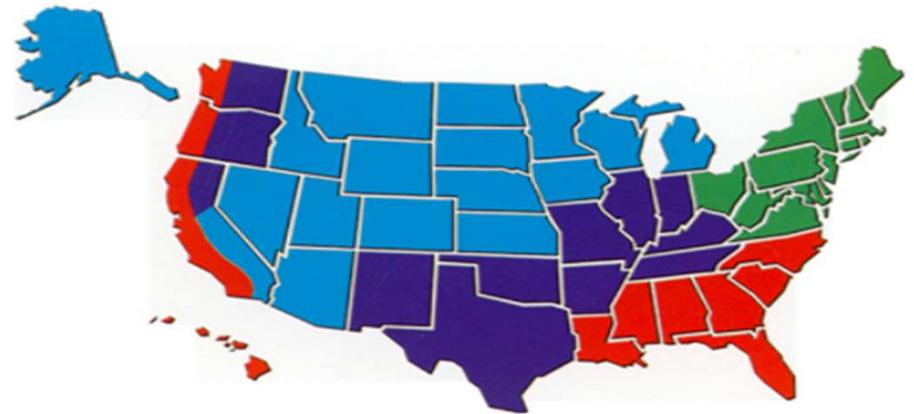
- Endocarditis

Immunocompromised host

- Vascular proliferation:
 - Bacillary angiomatosis
 - Bacillary peliosis



- Most cases of CSD and related infections occur in the pediatric population
- Most *B. henselae* infections requiring hospitalization occur in southern states
- Cats in warmer climates have higher rates of bacteremia with *Bartonella henselae*



Incidence of *Bartonella* infection in cats increases in hot and humid climates because fleas flourish in these conditions.

- States with the highest incidence of infection
- States with moderately high incidence of infection
- States with moderate incidence of infection
- States with low incidence of infection

Typical Presentation of *Bartonella henselae* infection: Cat-Scratch Disease

90-95% of cases of *Bartonella henselae* infection present as:

- No fever or low grade fever
- Mild systemic non-specific symptoms (malaise, fatigue)
- Primary lesion followed by local lymphadenopathy
- Spontaneous resolution over weeks
- Does not require treatment; course of azithromycin may hasten resolution of lymphadenopathy

Primary Lesion of CSD

- Papule, pustule or nodule, usually 1cm or less in size
- Incubation period of days to a month after inoculation by cat bite/scratch
- Lesion may ulcerate
- Lesion may last for days to months, self-resolving



Lymphadenopathy of CSD

- Timing: weeks to months after initial inoculation
- Location: proximal to area of inoculation, usually upper body, occasionally generalized
- May be tender to the touch, ~20% may develop suppuration
- Self-resolving over months (up to 4)

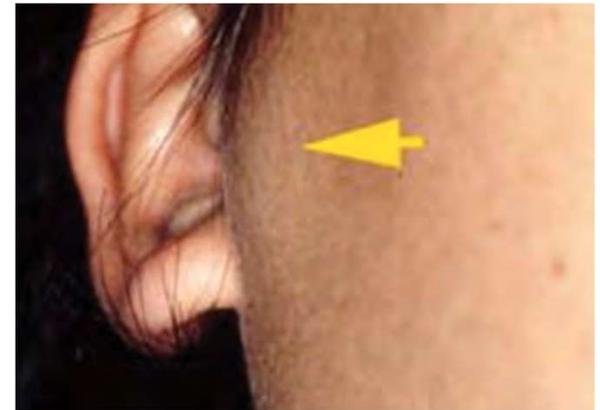
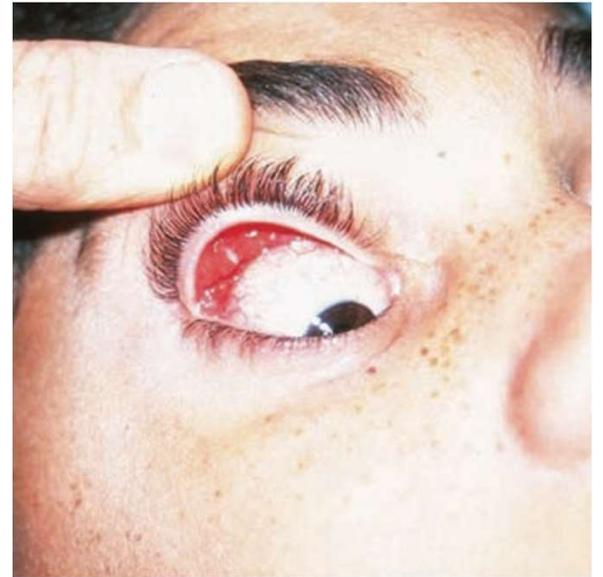


Atypical Presentations of *Bartonella henselae* infection

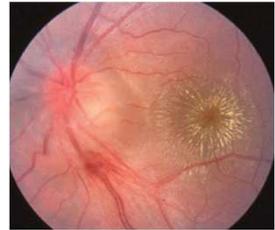
- Occur in 5-10% of cases
- Likely secondary to bloodstream dissemination of *Bartonella* throughout the host

Parinaud oculoglandular syndrome

- **Most common atypical presentation**
- Occurs when site of inoculation is conjunctiva or eyelid, conjunctival granuloma forms
- Features:
 - Painful palpebral conjunctivitis without drainage
 - Preauricular lymphadenopathy



Neurologic symptoms



2-5% of cases of CSD may also have neurologic manifestations; up to 10% with ocular findings

Neuroretinitis

- Single most common infectious cause of neuroretinitis
- Painless unilateral vision loss, usually preceded by flu-like symptoms or CSD symptoms
- Good prognosis

Encephalopathy

- Occurs 1-6 weeks after lymphadenopathy
- Seizures, altered behavior, coma, focal neurologic signs
- Self-resolving over months up to a year
- No CT findings; CSF may have mild pleocytosis or mildly elevated proteins

Fever of Unknown Origin (FUO)

- Key cause of FUO in children (5% of cases overall)
- Malaise, fatigue, myalgias, arthralgias, weight loss
- Abdominal pain may be a prominent feature
- **Half of these cases do not present with lymphadenopathy**

Splenic or Liver Lesions

- Hepatic and splenic filling defects on ultrasound,
- Half of the time with generalized enlargement

Endocarditis

- Significant contributor to culture-negative endocarditis
- Main risk factors: abnormal valves, exposures to cat
- Frequent association with glomerulonephritis
- Prolonged illness frequently requires valvular surgery

Other atypical presentations

Glomerulonephritis or kidney microabscesses

Osteomyelitis

Myositis

Arthritis

Skin findings: erythema nodosum, maculopapular rash, erythema multiforme, thrombocytic purpura or petechiae

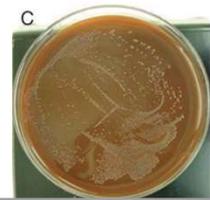
Blood disorders: thrombocytopenia, non-immune hemolytic anemia

Lung findings

Diagnosis

Culture

- Usually does not grow on culture
- Can increase probability of positive culture by holding plates for up to 21 days, special growth techniques



Serology

- Common diagnostic tool
- Positive IgM not required for diagnosis of active infection
- IgG may remain elevated for up to a year after acute infection

PCR

- Increasingly used
- PCR on blood typically negative
- PCR most helpful if done on affected valve, primary lesion, pus drawn from lymph node

Challenges in Interpreting Serology

Limitations of a negative test

- Variable sensitivity (usually ~ 80%)
 - negative serology does not rule out diagnosis
 - consider repeat serology (late seroconversion)
- IgM may be absent in acute infection

Limitations of a positive test (IgG > 1:256)

- Cross-reactivity with other organisms (*Chlamydia pneumoniae*, *Rickettsia* spp., *Coxiella burnetti*, *Bartonella quintana*)
- IgG may remain positive for a year or more and asymptomatic infections occur
 - Can assess for rising titers for sign of active infection

Take Away Points

B. henselae is an important cause of pathology in children, especially in hot and humid regions of the US

Atypical *B. henselae* can mimic many disease processes

Consider *B. henselae* in the differential for:

- Lymphadenopathy
- Prolonged fevers of unclear cause
- Splenic or liver lesions
- New onset seizures in school-aged children
- Encephalopathy
- Painless vision changes
- Patients with artificial or damaged heart valves

Take Away Points

Diagnosis

- Negative IgM does not rule out current active infection
- Consider repeat titers if diagnosis is unclear

Treatment

- Quality studies on treatment of *B henselae* infection have been limited to azithromycin for CSD
- Other treatment options are based on limited data, but general include prolonged courses of macrolides, tetracyclines, aminoglycosides or rifampin combinations
- Any atypical *Bartonella henselae* case could benefit from ID consult

References

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References (pictures)

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Cherry, James D. et al. *Feigin and Cherry's Textbook of Pediatric Infectious Diseases*. Eighth edition. Philadelphia, PA: Elsevier, 2019. (black/white primary lesions with axillary lymphadenopathy)

Fischer, Marc, Sarah S. Long, and Charles G. Prober. *Principles and Practice of Pediatric Infectious Diseases "Bartonella Species"*. Sixth edition. Philadelphia, PA: Elsevier, 2023. 160, 901-905.e1

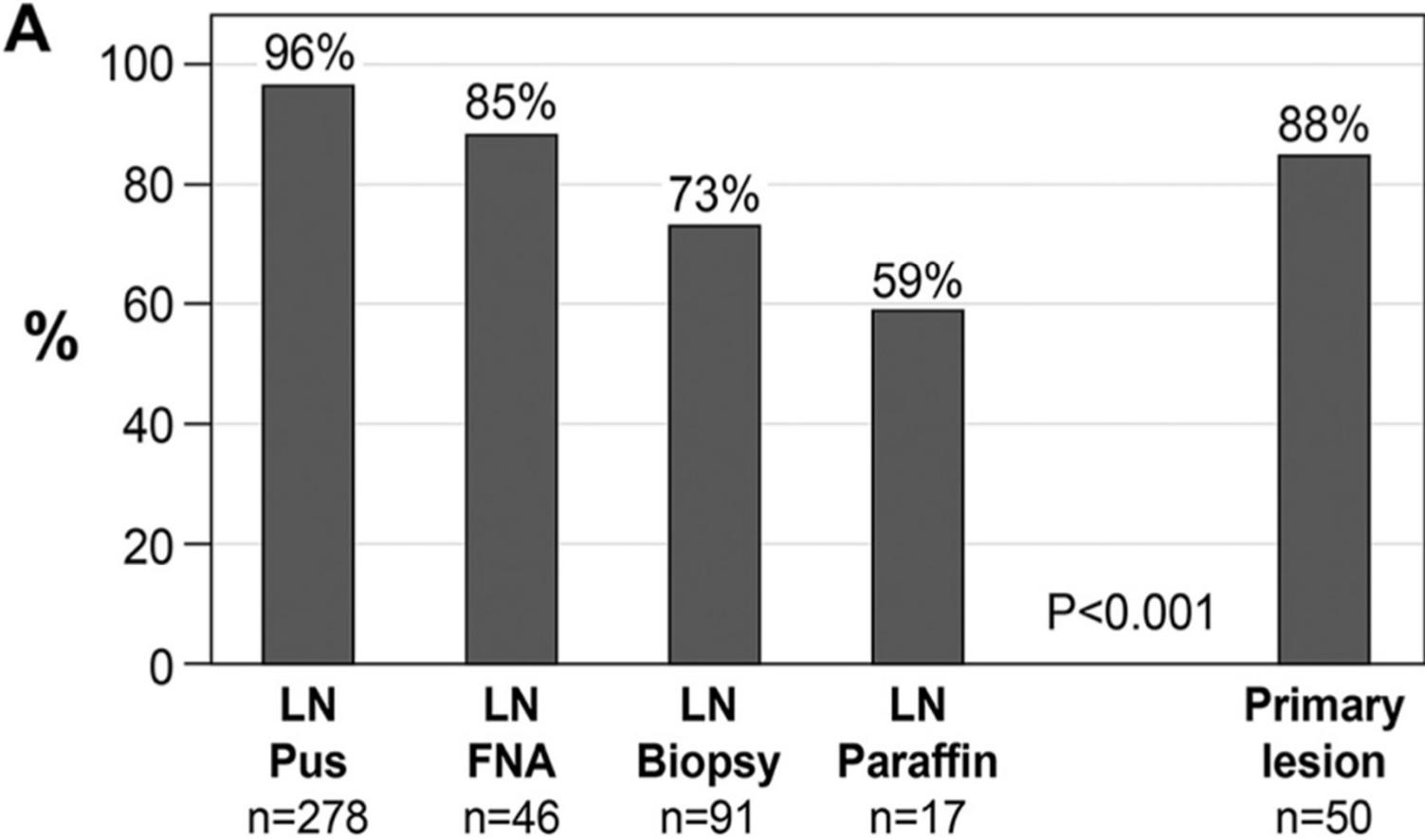
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EXTRA SLIDES

Sensitivity of PCR Assay on different specimens



Goaz S, et al. M. Molecular Diagnosis of Cat Scratch Disease: a 25-Year Retrospective Comparative Analysis of Various Clinical Specimens and Different PCR Assays. Microbiol Spectr. 2022 Apr 27;10(2):e0259621.

Red Book (2021-2024)

Page 228:

“No antibiotic regimen has been shown to be beneficial in improving the clinical cure rate, and in most cases, antibiotic therapy is not indicated.”

Treatment

Per CDC, suggested dose if treated given:

- Children <45.5kg 10mg/kg day 1, followed by 5mg/kg for 4 days
- Adults and children >45.5kg 500mg on day 1, followed by 25mg for 4 days