BETA HEMOLYTIC STREPTOCOCCAL INFECTIONS: MOSTLY GROUP A WITH A LITTLE C, G

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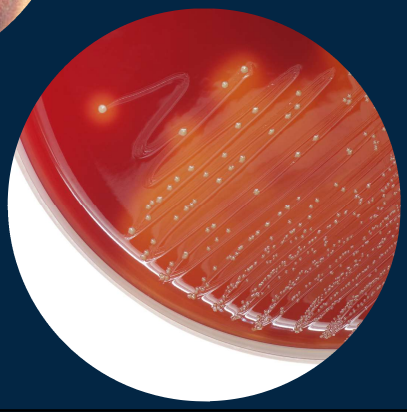

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OBJECTIVES

1. Review diagnosis and management of Strep throat
2. Review the other beta hemolytic Streptococci associated with pharyngitis
3. Discuss invasive group A Streptococcal infections

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7 YEAR OLD MALE WITH ACUTE ONSET SORE THROAT THEN FEVER PRESENTING FOR SICK VISIT

On exam oropharyngeal erythema with small amount exudate on right tonsil
Anterior cervical nodes less than 1 cm in size and tender
No runny nose or cough
He typically can swallow pills, no allergies

CAUSES OF ACUTE PHARYNGITIS?

Bacterial (10-15%)
– Group A Streptococcus (GAS)
– Group C and G Streptococcus
– Arcanobacterium haemolyticum
– Fusobacterium nucleatum
– Corynebacterium diptheriae
– Neisseria gonorrhea
– Others

Viral (60%)
– Rhinovirus
– Adenovirus
– Coronavirus
– Epstein-Barr virus
– Enterovirus
– Others

Unknown

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SINCE VIRAL ETIOLOGY MORE COMMON HOW TO DIAGNOSE?

Clinical judgement and diagnostic testing

Suggestive of GAS
– Sudden onset sore throat
– Pain on swallowing
– Fever
– Scarlet fever rash
– Headache
– Nausea, vomiting, abdominal pain
– Tonsillopharyngeal erythema
– Tonsillopharyngeal exudates
– Soft palate petechiae
– Beefy, red, swollen uvula
– Tender, enlarged anterior cervical nodes
– Patient 5 to 15 years of age
– Season (winter, early spring temperate)
– Exposure

Viral
– Conjunctivitis
– Coryza (infants can have purulent nasal discharge, excoriated nares)
– Hoarseness
– Cough
– Diarrhea
– Characteristic rash (exanthem)
– Characteristic oral lesions (enanthem)

Clinical differentiation can be difficult
– Rapid antigen detection test (RADT)
– Throat culture
~15% school-age children asymptomatic GAS carriers

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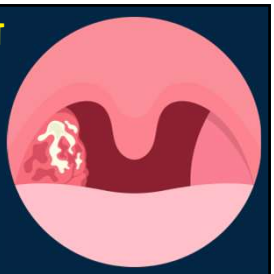
7 YEAR OLD MALE WITH ACUTE ONSET SORE THROAT THEN FEVER PRESENTING FOR SICK VISIT

On exam oropharyngeal erythema with small amount exudate on right tonsil
Anterior cervical nodes less than 1 cm in size and tender
No runny nose or cough
RADT negative, throat culture sent



SENSITIVITY OF DIAGNOSTIC TESTS?

- •RADT
  - –55-85% sensitive
- •Throat Culture
  - –95% sensitive
- •Lower sensitivity of RADT indicates false negative results are not uncommon
- •Reflexive culture specimens with negative RADT results is recommended for diagnosing GAS
- •Since RADT highly specific for GAS, specimens with positive results do not need to be cultured

SHOULD YOU START TREATING BEFORE CULTURE RESULTS?

If appears nontoxic, no concern for scarlet fever can wait for culture results
Up to 9 days to start from the onset of symptoms for the prevention of rheumatic heart disease

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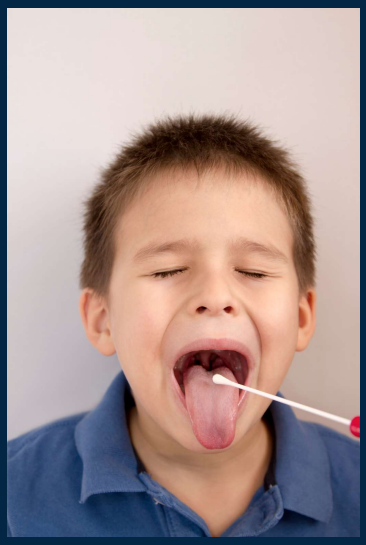

Swab in area of tonsils

Gram positive cocci in chains
Catalase negative
Bacitracin susceptible

Lancefield grouping

Carbohydrate antigen in cell wall
– Group A: S. pyogenes
– Group B: S. agalactiae
– Group C: S. equisimilis
– Group D: Enterococcus
– Group G: S. canis
– Group H: S. sanguis

Rebecca Lancefield
serological method for classifying
Streptococci into one of 20 groups

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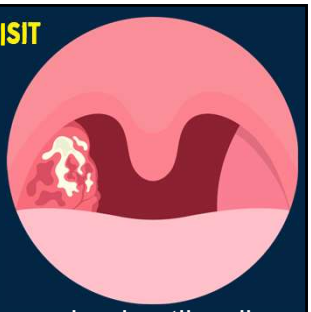

On exam oropharyngeal erythema with small amount exudate on right tonsil
Anterior cervical nodes less than 1 cm in size and tender
RADT negative, throat culture group A beta hemolytic Streptococcus
He can swallow pills so you prescribe penicillin

WHEN CAN HE RETURN TO SCHOOL?

Children with GAS pharyngitis or skin infection should not return to childcare or school until well appearing and at least 12 hours since starting antibiotics

SHOULD HOUSEHOLD MEMBERS BE TESTED OR TREATED?

Only if symptomatic
Caveat someone in household with rheumatic heart disease, known outbreak with nephritis, ARF

WHAT IF HAD INVASIVE GAS SUCH AS TOXIC SHOCK OR BACTEREMIA?

Household members at increased risk of developing invasive GAS
Risk not high enough for routine testing and treatment of colonization
No clearly effective prophylaxis though if over 65 yo or HIV or diabetes some may offer
Not recommended for school or child care facilities

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TRANSMISSION AND EPIDEMIOLOGY OF GAS

Pharyngitis	Impetigo, pyoderma
Almost exclusively in humans Age 5-15 years Peak incidence early school years Spread by close personal contact (less fomites) Colonization, acute infection, asymptomatic carrier Acute symptomatic phase: a few days, untreated can persist for weeks after symptoms resolve Asymptomatic carrier phase: decrease anterior nares and persists in lower number in throat Incubation pharyngitis 2 to 5 days Abrupt sore throat, headache, fever Children vomiting, abdominal pain Symptoms resolve 3-5 days if no suppurative complications	Age 2-5 years Climate Hygiene Skin trauma, insect bite, eczema Skin colonization often 10 days prior to impetigo

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TREATMENT

Pharyngitis	Penicillin V (oral)	Children <27 kg: 250 mg 2 or 3 times daily children ≥27 kg adolescents, adults: 250 mg 4 times daily or 500 mg 2 times daily	10 days
	Amoxicillin (oral)	50 mg/kg once daily	10 days
	Benzathine penicillin G (intramuscular)	<27 kg: 600,000 U; ≥27 kg: 1,200,000 U	1 dose
	Cephalexin (oral)	40 mg/kg per day divided 2 times daily (max = 500 mg/dose)	10 days
	Azithromycin (oral)	12 mg/kg once daily (max = 500 mg)	5 days
	Clarithromycin (oral)	15 mg/kg per day divided 2 times daily (max = 250 mg/dose)	10 days
	Clindamycin (oral)	20 mg/kg per day divided 3 times daily (max = 300 mg/dose)	10 days

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WHAT ARE THE COMPLICATIONS OF GROUP A STREPTOCOCCAL PHARYNGITIS?

Suppurative (pus)
– Peritonsillar or retropharyngeal abscess
– Lymphadenitis
– Sinusitis
– Otitis media
– Mastoiditis
– Invasive infections (e.g. toxic shock syndrome, necrotizing fasciitis)

Non-Suppurative
– Acute rheumatic fever
latent period ~ 18 days
– Acute glomerulonephritis
latent period ~10 days
after skin infection ~30 days

other pyogenic Streptococci not associated



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OTOGENIC CEREBRAL VENOUS SINUS THROMBOSIS

GAS otitis media one study accounted for less than 10% culture positive cases
Older age (>2 yo)
Higher local aggressiveness
Lower fever
Tympanic membrane perforation
Mastoiditis

Organisms such as Strep pneumoniae, Haemophilus influenzae, Staph aureus, Fusobacterium necrophorum, Pseudomonas, Proteus have also been reported with ocvst

COMMUNITY ACQUIRED PNEUMONIA

Para pneumonic effusion and pleural empyema in one study of 106 children with positive blood or pleural fluid cultures 19% due to GAS (66% Strep pneumo)
Compared to pneumococcal infection more likely to have moderate-to-large pleural effusions, to need mechanical ventilation, and have a longer hospital stay

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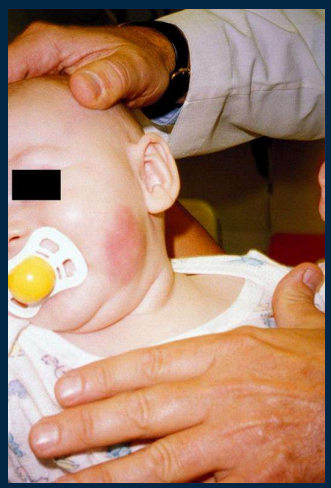
CUTANEOUS MANIFESTATIONS



Next slides toxin mediated changes: erythrogenic, exfoliative

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Impetigo	Mupirocin (topical)	Apply 2 times daily	5 days
	Retapumulin (topical)	Apply 2 times daily	5 days
	Cephalexin (oral)	25–50 mg/kg/day divided 3–4 times daily (max = 250 mg/dose)	7 days
	Clindamycin (oral) (if MRSA also suspected)	20–30 mg/kg per day divided 3 times daily (max = 300 mg/dose)	7 days
Erysipelas: mild, nonpurulent	Amoxicillin (oral)	40–90 mg/kg per day divided 2 or 3 times daily	5 days
Cellulitis: mild, nonpurulent	Cephalexin (oral)	50 mg/kg per day divided 4 times daily (max = 500 mg/dose)	5 days
	Clindamycin (oral)	25–30 mg/kg per day divided 3 times daily (max = 1,800 mg daily)	5 days
Vulvovaginitis and perianal cellulitis	Amoxicillin (oral)	50 mg/kg per day divided 3 times daily (max = 500 mg/dose)	10 days
	Clarithromycin (oral)	15 mg/kg divided 2 times daily (max = 1,000 mg daily)	7–10

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WHAT IS THIS SKIN FINDING CONCERNING FOR IN SETTING OF FUO?

Erythema marginatum

Acute Rheumatic Fever
Incidence varies globally
Higher in low and middle income countries

1920s in US leading cause of mortality in 5- 20 yo (group A Strep 1930s, 1942 penicillin)
US <2 cases per 100 000 school-aged children compared up to 150 cases per 100 000 worldwide
US, native Hawaiian and Samoan children are at significantly greater risk
Native Americans prevalence 7.6 times greater than the national prevalence
Twins increased risk
Antibody-mediated response triggers a cellular response, leading to cardiac inflammation with eventual scarring and RHD
1-3% with GAS infection will develop

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947 children from 22 hospitals (60 invited)
Median age diagnosis 9
13% had traveled to endemic area
Pacific Islands, Africa
37% Sydenham chorea
27% diagnosed with chronic RHD
35% gave history consistent with acute RHD
Severe disease more common if patient or parent first language not English
Higher than expected children identified as Black or Indigenous

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Revised 2015 Jones criteria for diagnosis of acute rheumatic fever (ARF) based on population-risk

	Low-risk populations	Moderate / high-risk populations
Major criteria	Migratory polyarthritis	Migratory polyarthritis/monoarthritis
	Carditis	Carditis
	Chorea	Chorea
	Erythema marginatum	Erythema marginatum
	Subcutaneous nodules	Subcutaneous nodules
Minor criteria	Polyarthralgia	Monoarthralgia
	Fever ≥38.5°C	Fever ≥38.0°C
	ESR ≥60 mm/hour and/or CRP ≥30 mg/L	ESR ≥30 mm/hour and/or CRP ≥30 mg/L
	Prolonged PR interval on ECG	Prolonged PR interval on ECG

Low-risk population is defined as an ARF incidence ≤2 per 100,000 school-aged children or ≤1 per 1000 population per year. For a diagnosis, two major criteria or one major and two minor criteria must be fulfilled in the presence of a recent group A streptococcus (GAS) infection (positive RADT/culture, rising ASO)

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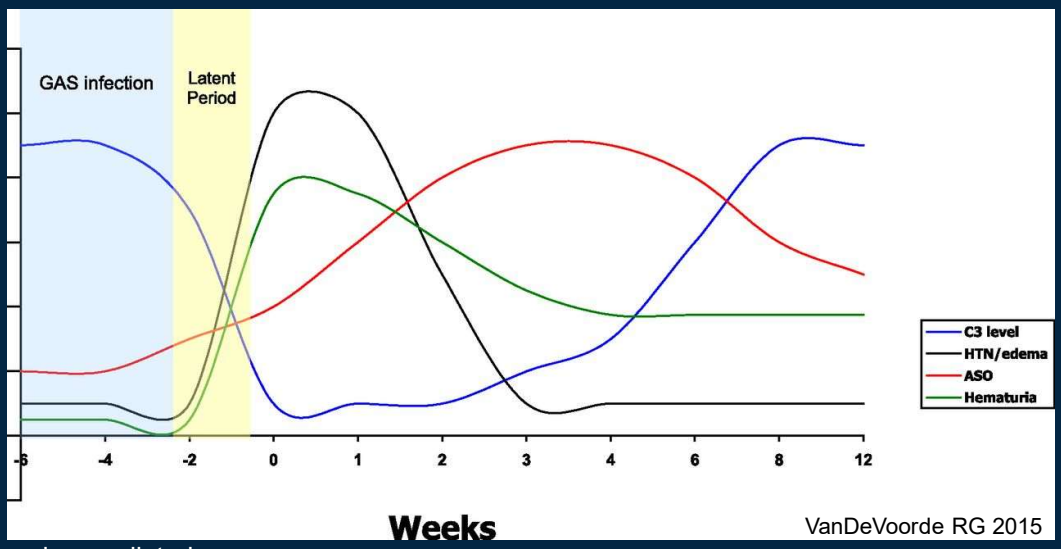
ACUTE POSTSTREPTOCOCCAL GLOMERULONEPHRITIS



Immune complex mediated
Latency period after infection may vary from 1 to 2 weeks after pharyngitis to 3 to 6 weeks after skin infections
ASO titers do not typically rise in GAS skin infections because streptolysin may be bound by lipids in the skin
Elevated anti-DNase B levels may be seen with GAS pharyngitis and pyodermal infections
C3 levels are decreased in more than 90% of all cases of PSGN

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IS THERE CONTROVERSY REGARDING TREATMENT OF STREP THROAT?

No
– American Academy of Pediatrics
– American Heart Association
– Infectious Diseases Society of America

Yes
– Downeast Emergency Medicine vimeo.com/231456202
– rebelem.com/patients-strep-throat-need-treated-antibiotics/
– European Society for Clinical Microbiology and Infectious Diseases established the Sore Throat Guideline Group

Adult epidemiology is different, risk of rheumatic fever less
Centor criteria scoring (0-4; exudate, tender nodes, fever, no cough) not applicable to children
RADT alone, without confirmation of negative RADT results by a negative throat culture considered in adults

www.mdcalc.com/calc/104/centor-score-modified-mcisaac-strep-pharyngitis
www.mdcalc.com/calc/3316/feverpain-score-strep-pharyngitis

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WHAT ABOUT GROUP C AND GROUP G?

Streptococcus dysgalactiae subsp equisimilis
S. anginosus or S. milleri group can also react with C or G typing sera
Can colonize skin, oropharynx, gastrointestinal, vagina
Rare cause of infection
If cultured from sterile site typically infection-bacteremia, endocarditis, septic arthritis
Nonsterile site possible colonization-there are reports of epidemic pharyngitis, impetigo
Animals and humans
Similar to GAS, GCS and GGS are susceptible to beta-lactam antibiotics such as penicillin

IF YOU DECIDE TO TREAT, HOW LONG?

Tailor to clinical response for noninvasive infection
Pharyngitis 5 days penicillin since not known to trigger acute rheumatic fever
(fever, tonsillar exudate, tender cervical nodes, absence cough or runny nose)

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CAN YOU EVALUATE CHILD FOR MIS-C WHO IS BEING ADMITTED TO ICU?

-1 day prior to admission (PTA) reported right shoulder pain but was able to participate in after school activity
-Overnight vomiting 4-5 times
-"pink eye" in morning
-Temp 104.5 presented to urgent care at which time tachycardia, tachypnea, fever, hypotension
Appeared toxic, right shoulder edematous-ambulance called to transport, bolus started
-Labs, more boluses, bedside US did not show fluid in right shoulder joint
BNP, lactate, WBC, creatinine elevated: ceftriaxone, vancomycin, clindamycin started

IS THE RESOLVED SORE THROAT A WEEK PRIOR PERTINENT?

-Took ibuprofen few days week prior for sore throat, no runny nose or fever (was able to eat)

Throat, blood, right shoulder fluid between deltoid and humerus group A beta hemolytic Strep
Continued ceftriaxone, clindamycin.....why clindamycin?

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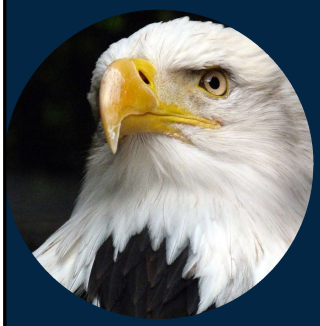
WHY IS CLINDAMYCIN ADDED AS ADJUNT TO BETA LACTAM ANTIBIOTIC WITH SEVERE GAS INFECTIONS?



The Eagle Effect

- Large inoculum affect on penicillin noted by Harry Eagle in 1948
- Clindamycin thought to be less affected by inoculum size
- Clindamycin has a longer postantimicrobial effect
- Inhibition of bacterial protein synthesis-suppression of toxins
- Mice with GAS myositis have better survival with clindamycin than penicillin
- Observational studies invasive GAS with lower mortality adjunct clindamycin
- Clindamycin should not be used alone due to potential for resistance
  - In 2017 22% invasive GAS isolates CDC Active Bacterial Surveillance were resistant to clindamycin
- Once adequate source control, clinical improvement can discontinue after a few days

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CONCERN FOR SHOULDER TYPE II ACUTE NECROTIZING FASCIITIS (ANF)

Rapidly progressing deep tissue infection

Mortality in adults ~20%, less in children

Initially can be mild swelling but pain often out of proportion to exam

In 24-72 hours rapidly more pronounced inflammation then purple with overlying bullae

In next few days necrosis, needs surgery to halt progression of necrosis

Adult study with no benefit of IVIG

CONCERN FOR STREPTOCOCCAL TOXIC SHOCK

Streptococcal toxic shock syndrome: hypotension, multiorgan dysfunction (often associated with skin and soft tissue infection) also considered invasive
Superantigen toxins trigger massive T-cell proliferation and a subsequent “cytokine storm'

CDC case definition: Hypotension less than 5th percentile for kids under 16
Multiorgan involvement: 2 or more of the following
-Renal impairment, twice upper limit of normal for age creatinine
-Coagulopathy, platelets less than 100,000 or DIC
-Liver involvement, ALT, AST, t bili twice upper limit normal for age
-Acute respiratory distress syndrome, hypoxemia with diffuse infiltrates
-Generalized erythematous rash
-Soft tissue necrosis

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	Kawasaki disease	Scarlet fever	Toxic shock	MIS-C
Age (years)	<5	2-8	Any age, <2	8-11
Fever	Persistent	Variable, <10d	<10 days	Persistent
Eyes	Nonexudative, limbic sparing	Normal	Conjunctivitis	Variable 32-83%
Oral mucosa	Diffuse red Strawberry tongue	Pharyngitis, Strawberry tongue	Red	Variable 37-49%
Extremities	Red palms/soles periungal desquamation	Flaky desquamation	Swelling hands/feet	Variable 8-52%
Rash	Red, polymorphous	Sandpaper rash Pastia Circumoral pallor	Erythroderma	Variable 50-70%
Cervical adenopathy	1.5 cm	Painful swelling	Normal	Variable
Labs	ESR, CRP, anemia, transaminitis, thrombocytosis 7 days	Throat culture	Thrombocytopenia AKI	ESR, CRP, lymphopenia, thrombocytopenia
Other	Arthritis	Throat culture GAS	Mental status, shock, coagulopathy	Myocardial dysfunction, shock, GI symptoms

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INCREASE IN PEDIATRIC INVASIVE GROUP A STREPTOCOCCAL INFECTIONS-CDC HAN 12/22/2022

Strep infection rates remain high in the U.S., even relative to pre-pandemic levels

Rates of strep throat diagnoses in February were nearly 30% higher than during the previous peak in February 2017, one report found.

~1000 deaths per year in US

Infection in typically sterile site: blood, CSF, joint fluid

Can occur at any age but in children peak incidence < 2 yo, adults over 50

Factors that may increase risk iGAS: chickenpox, influenza, trauma/burns, immunocompromise, younger than 1 year, emm type (M-type) GAS strain

Increase in Pediatric Invasive Group A *Streptococcus* Infections — Colorado and Minnesota, October–December 2022

34 cases

Colorado younger 3.1 vs 5.6

35% ICU

2 deaths

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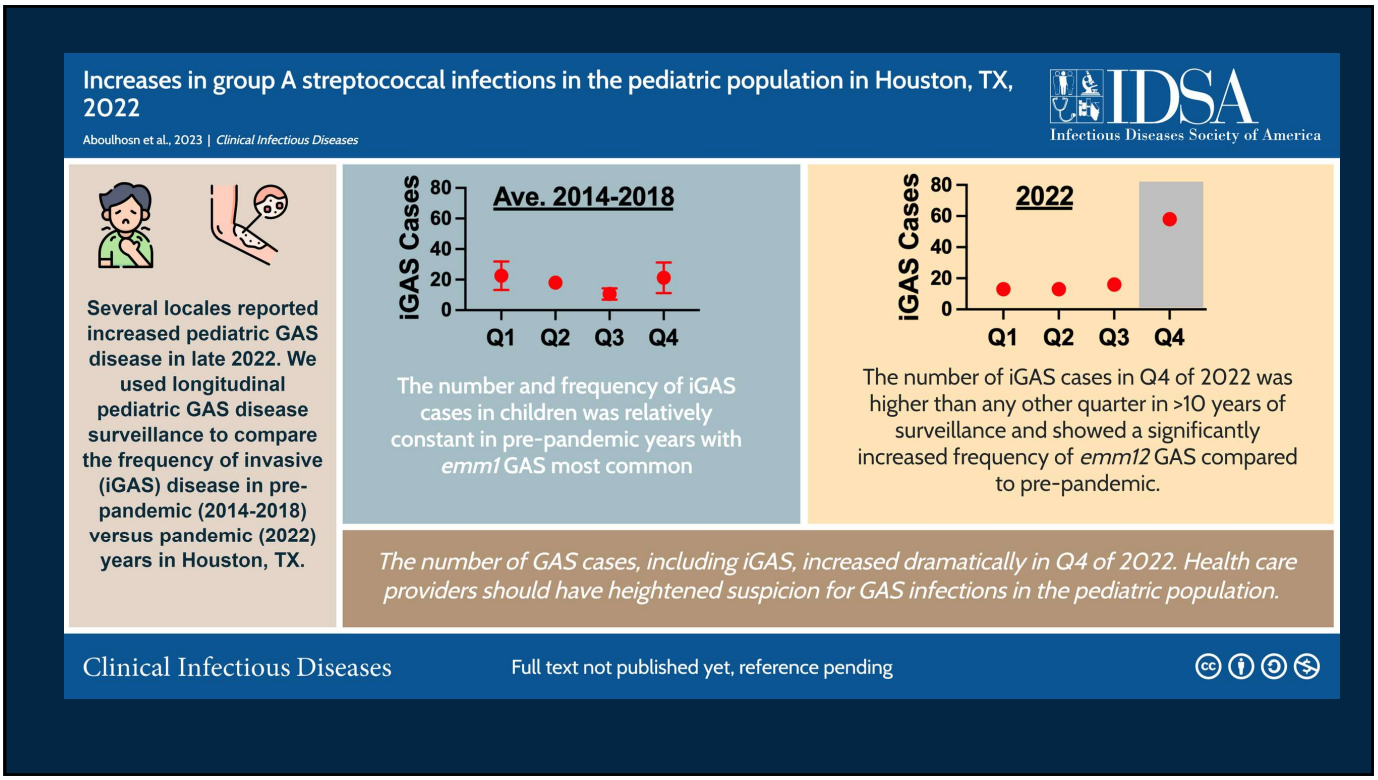

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SAME 7 YEAR OLD RETURNS IN 3 WEEKS WITH SORE THROAT AND FEVER

RADT positive before you enter room

Clear rhinorrhea, throat mild injection, no exudate

DOES HE NEED TO BE TREATED?

Antigen can remain positive for few weeks so should you perform throat culture?

Discuss not treating due to runny nose

Family has flight tomorrow to Florida and would prefer antibiotics

MYCHART MESSAGE SORE THROAT HAS WORSENED WHILE ON ANTIBIOTICS AND NOW HAS MOUTH ULCERS

Strep throat typically improves within 24 hours of penicillin

Repeated pharyngitis within short intervals with repeated positive testing more likely is due to viral infection in someone who is GAS carrier

WHAT HAVE YOU DONE IN PATIENT WITH REPEATED PHARYNGITIS WITH POSTIVE TESTING?

Assess if they are completing prescribed antibiotics, viral symptoms

If non-penicillin antibiotic used ask for susceptibility testing to erythromycin

Test and treat asymptomatic household members

Obtain throat culture, RADT when well to determine if carrier

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Cheers!
questions?

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PHOTOS

Canva
CDC Public Health Image Library (PHIL) website
AAP Pediatrics in Review

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