

#### Invasive Group A Streptococcal Infections in Children post COVID-19

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#### Disclosures

• Research grants from NIH and CDC



## **Objectives**

- Review clinical manifestations of invasive GAS (iGAS) infections
- Describe trends in iGAS infections since COVID-19 pandemic
- Describe molecular epidemiology of recent iGAS infections



#### **Clinical case...**

 Previously healthy 14 year old male who presented to an OSH due to changes of color on his skin.



#### HPI

~2 weeks PTA: Family trip to Orlando

#### **7 days PTA** + rhinorrhea

+ cough

+ myalgias

**UC:** +influenza

3-5 days PTA

+ fevers

+ N/V

+ diarrhea

+ right sided chest pain

Day of presentation: Extremities/trunk started to turn red -> OSH ED



#### **OSH emergency department**

- 37.9°C (100.3°F), HR 160, BP 115/<mark>55</mark>, RR 28, SpO2 85%
- PE: toxic appearing with diminished breath sounds on the right inferolateral chest, mildly tachypneic on nasal canula, diffuse erythematous rash over the trunk and extremities
- Lab/imaging highlights:
  - Lactic acid: 12.2; ABG pH: 7.02
  - WBC 8.9 (ANC 6.5), plts 401
  - Na 127, BUN 36, creatinine 3.6, AST 57, ALT 24
  - Rapid GAS antigen test: positive
  - CXR: Lobar consolidation of the RLL with patchy consolidation of the LLL



#### **OSH emergency department**

- Arrested at OSH
- Required 6 minutes of CPR; intubated
- Transferred to a second outside hospital Started on 3 vasopressors
   EMT note: "does not respond to stimuli, has not had sedation since intubation"
- Quickly transferred to VCH for possible need for ECMO



#### **Emergency department**

- 36.2°C (97.2°F), HR 134, BP 84/74, RR 16, SpO2 78%
- Upon arrival to VCH he was emergently cannulated to VA ECMO and had 2 brief arrests during cannulation
- Right sided chest tube placed and pleural fluid cultured
- Labs:









#### In the PICU

#### OSH blood culture... S. pyogenes (GAS)

#### VCH pleural fluid culture... S. pyogenes (GAS)



#### **Hospital course**

- Antibiotics:
  - Ceftriaxone
  - Clindamycin
  - (Stopped vancomycin after confirmation of GAS)
- Required: CRRT, PLEX x5 days, IVIG x3 days
- Decannulated from ECMO
- Weaned off gradually from pressors, mechanical ventilation, and dialysis



#### **Hospital course**

• Had necrosis and worsening ischemia of all limbs

• Underwent 4 extremity amputation





#### Streptococcus pyogenes

- GPC in pairs/chains
- Global disease burden
- Spreads through respiratory droplets
- Most common GAS infections include pharyngitis & SSTIs
- Commonly follow viral infections (ie. varicella, influenza, oth resp viruses)
- No vaccines exist



Steer, et. al., Invasive Group A Streptococcal Disease. Drugs. 2012.

#### What is an invasive Group A Streptococcal (iGAS) infection?

- iGAS is a group of infections caused by Group A Streptococcal (Streptococcus pyogenes)
- "Invasive" meaning:
  - Breach of a normally sterile site (proven)
  - Cause of serious illness (probable)





#### Probable case

A case of probable invasive Strep A infection is defined as a clinically severe illness, such as maternal sepsis, septic shock, STSS, or necrotizing fasciitis, for which no other bacterial etiology has been identified and in which Strep A is isolated or detected from a nonsterile site (eg, throat, sputum, wound, superficial skin abscess, subcutaneous tissue, or placenta)<sup>a</sup>.

#### Confirmed case

A case of confirmed invasive Strep A infection is defined as an illness associated with isolation of Strep A (*Streptococcus pyogenes*) by culture or detection of Strep A by nucleic acid testing from a normally sterile site (eg, blood, cerebrospinal fluid, joint fluid, peritoneal fluid, bone, internal organs).

<sup>a</sup>This is a modification of CDC's ABCs case definition that would categorize STSS and necrotizing fasciitis in association with Strep A cultured from a wound as a confirmed invasive infection.

Miller, et. al., Standardization of Epidemiological Surveillance of Invasive Group A Streptococcal Infections. Open Forum Infect Dis. 2022





Ching, et. al., J Ped Inf Dis Soc. 2017

## **Invasive Group A Streptococcal infections**



Health > Health News

#### KILLER BUG At least 40 children have died from Strep A in the UK as cases of deadly infection grow

Terri-Ann Williams, Senior Health Reporter Published: 11:41 ET, Feb 16 2023 | Updated: 12:38 ET, Feb 16 2023 FORBES > INNOVATION > HEALTHCARE

New CDC Warning: Invasive Group A Strep Infections Rising Among Children

at Vanderbilt

Dec 24, 2022, 11:48am EST

## **Timeline of invasive GAS infections**







Centers for Disease Control and Prevention CDC 24/7: Saving Lives, Protecting People™



Morbidity and Mortality Weekly Report (MMWR)

#### *Notes from the Field:* Increase in Pediatric Invasive Group A Streptococcus Infections — Colorado and Minnesota, October–December 2022

Weekly / March 10, 2023 / 72(10);265-267

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#### Texas



Invasive cases increased in the October-December quarter in 2022 (36.5%) compared to 2014-2018 (29.7%)



Alboulhosn et al, CID 2023 77: 351

#### London, Nov-Dec 2022



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#### Alcolea-Medina Clin Microbiol Infect 2023, 29: 887

#### Netherlands



FIGURE 1. Quarterly number of pediatrics cases of iGAS infections (iGAS) in 2018–2019 and between July 2021 and June 2022. Quarterly number of pediatric iGAS infections in 2018–2019 and between July 2021 and June 2022. The in-between period was characterized by COVID-19 restrictions and not taken into account. Cases per time period (quarter) for both periods were available from 5/7 hospitals.

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# England, 2022



<sup>a</sup> This figure compares the first 12 weeks of the season, all of which fall into the first year the season covers.



Guy et al, Eurosurveillance 2023 28: 2200942

## England, 7 day mortality



Numbers of dealths • Seasonal case fatality rate



Guy et al, Eurosurveillance 2023 28: 2200942

#### Vanderbilt University Medical Center Data

Outpatient ICD-10 codes for streptococcal pharyngitis (Oct-Mar)



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#### **iGAS** at **MCJCHV**

- 51 patients, Oct 2022-May 2023
- Positive GAS culture from any of these specimens:
  - Blood
  - CSF
  - Pleural Fluid
  - Surgical specimens
  - Urine (if >100K cfu/ml)





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#### Viral infections within prior 2 weeks



Respiratory GI None



## **Clinical Severity**



\*\* children's Hospital at Vanderbilt

#### Outcomes

• 8 patients on pressors or mechanical ventilation during admission



	Length of Stay
Average	6.2 days
Median	4 days
Mode	0 days

\*Does not include the 3 patients still admitted (all >14 days)



## Molecular epidemiology of iGASemm type distribution unchanged

 In high income countries (1990-2009), *emm1* and 12 were most common<sup>1</sup>



- CDC<sup>2</sup>
  - 26 isolates were typed
  - 50% emm12
  - 35% emm1
- London outbreak<sup>3</sup>
  - 113 isolates had WGS
    - 59% emm12
    - 16% emm1 → most M1<sub>UK</sub> clone which has high superantigen production

#### <sup>1</sup>Steer et al, Lancet 2009, 9:611

<sup>2</sup>Barnes M et al. *Notes from the Field:* Increase in Pediatric Invasive Group A *Streptococcus* Infections — Colorado and Minnesota, October–December 2022. MMWR Morb Mortal Wkly Rep 2023;72:265–267. <sup>3</sup>Alcolea-Medina Clin Microbiol Infect 2023, 29: 887



# Changes in *emm* types associated with invasive infections in adults in Spain



Figure. emm type distribution of 61 culture-confirmed invasive group A Streptococcus infections, by month, Lleida, northeast Spain, January 2019–May 2023

Bellés-Bellés A, Prim N, Mormeneo S, Villalón-Panzano P, Valiente-Novillo M, Jover-Sáenz A, et al. Changes in Group A Streptococcus emm Types Associated with Invasive Infections in Adults, Spain, 2023. Emerg Infect Dis. 2023;29(11). https://doi.org/10.3201/eid2911.230857

# *emm*1 is causing most of iGAS pulmonary infections in adults in Scotland



Figure 2. Microbiologic features of pulmonary invasive group A Streptococcus infections, central Scotland, UK, December 2017–February 2023. A) Streptococcus pyogenes isolate M type results, where available, comparing **historical data (December 2017–November 2022)** with **2022–23 cohort (December 2022–February 2023)**. B) Results of respiratory virus testing, where available, comparing historical data with 2022–23 cohort.

# Why are we seeing increased iGAS infections?

↓ GAS exposure
 during the pandemic
 (waning protective
 immunity, increased
 # of susceptibles)

÷.

 respiratory virus activity "post-pandemic"
 ↑↑↑ iGAS
infections after
mitigation
efforts were
lifted



## Conclusions

- 1) iGAS infections increased post COVID-19 but are still rare
- 2) To reduce risk of transmission and limit possible complications, prompt recognition and treatment of GAS is important
- 3) Benefits of vaccination against respiratory viruses
  - $\circ$  Influenza
  - SARS-CoV-2
  - $\circ \text{RSV}$
- 4) Importance of local, national, and global surveillance



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## Thank you

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