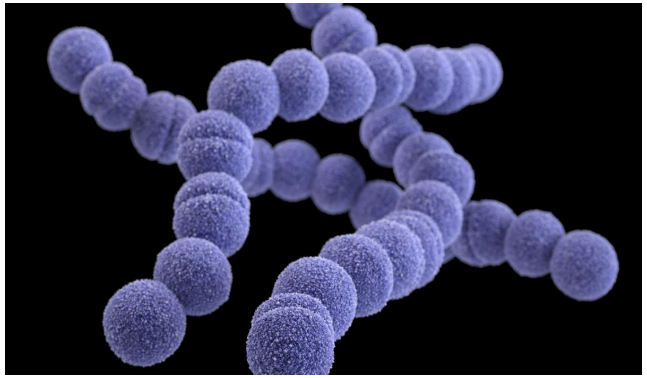
Increasing Rates of Invasive Group A Strep Infections

09/25/2024



Yorgo Zahlanie MD
Pediatric Infectious Diseases
Northern Light Eastern Maine Medical Center
Bangor, ME

None of the planners or speakers for this activity have relevant financial relationships to disclose

Outline:

-General overview

-Epidemiology

-Real-life cases

Case 1:

-8 yo previously healthy boy p/w headaches, facial pain, purulent nasal discharge, abdominal discomfort, fatigue and low-grade fevers

-Positive rapid strep test; prescribed amoxicillin

-However, left eye became progressively swollen and painful

-CT scan with contrast: left postseptal cellulitis, extensive sinusitis, and reactive lymphadenopathy

Case 1:

CT scan:
-Swelling of the superficial soft tissues of left orbit
-Extensive phlegmon vs early abscess (arrows)

Case 1:

-Required I&D

-Grew group A strep from left eye cultures

-Treated with 14-day course of amoxicillin-clavulanate for left orbital cellulitis due to group A strep

Definition:

Streptococcus pyogenes, also known as group A strep (GAS), is a group of gram-positive bacteria which can be carried in human throats or skin

Clinical manifestations:

Noninvasive:

-Pharyngitis (most common of all manifestations)

-Scarlet fever (most often with pharyngitis)

-Skin infection (e.g. pyoderma or impetigo)

2024. "Group A Streptococcal Infections", Red Book: 2024–2027 Report of the Committee on Infectious Diseases, Committee on Infectious Diseases, American Academy of Pediatrics, David W. Kimberlin, MD, FAAP, Ritu Banerjee, MD, PhD, FAAP, Elizabeth D. Barnett, MD, FAAP, Ruth Lynfield, MD, FAAP, Mark H. Sawyer, MD, FAAP

Pharyngitis complications:

Suppurative:

-Peritonsillar or retropharyngeal abscesses
-Suppurative cervical adenitis
-Sinusitis and otitis media (rarely)

Nonsuppurative:

-Acute rheumatic fever
-Acute poststreptococcal glomerulonephritis

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Clinical manifestations:

-GAS pharyngitis is uncommon in children <3 years

-Instead, they may present with rhinitis and a more protracted illness with moderate fever, irritability, and anorexia

-Illness known as streptococcal fever or streptococcosis

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Clinical manifestations:

-Protracted nasopharyngitis is actually the most common presentation of GAS in toddlers

-Inflammation of the skin beneath the nares often is present

https://publications.aap.org/redbook/visual-library

Clinical manifestations:

Invasive:

-Sepsis
-Bacteremia
-Osteomyelitis
-Septic arthritis
-Myositis
-Pneumonia
-Endocarditis
-Pericarditis
-Mastoiditis
-Necrotizing fasciitis

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Invasive group A strep (iGAS) infections:

-Often encompass bacteremia with or without a specific focus of infection

-Less than 5% associated with toxic shock syndrome

-Low death rate in children

-Require prompt treatment

-Notifiable conditions

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iGAS infections:

-Highest in elderly (≥65 years)

-Lowest in children and adolescents

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Molecular physiology:

-More than 240 distinct serotypes or genotypes have been identified based on M-protein serotype or M-protein gene sequence (*emm* types)

-*emm* gene encodes the M virulence protein found on the cell surface of GAS

-Some serotypes or *emm* types are commonly associated with certain clinical manifestations

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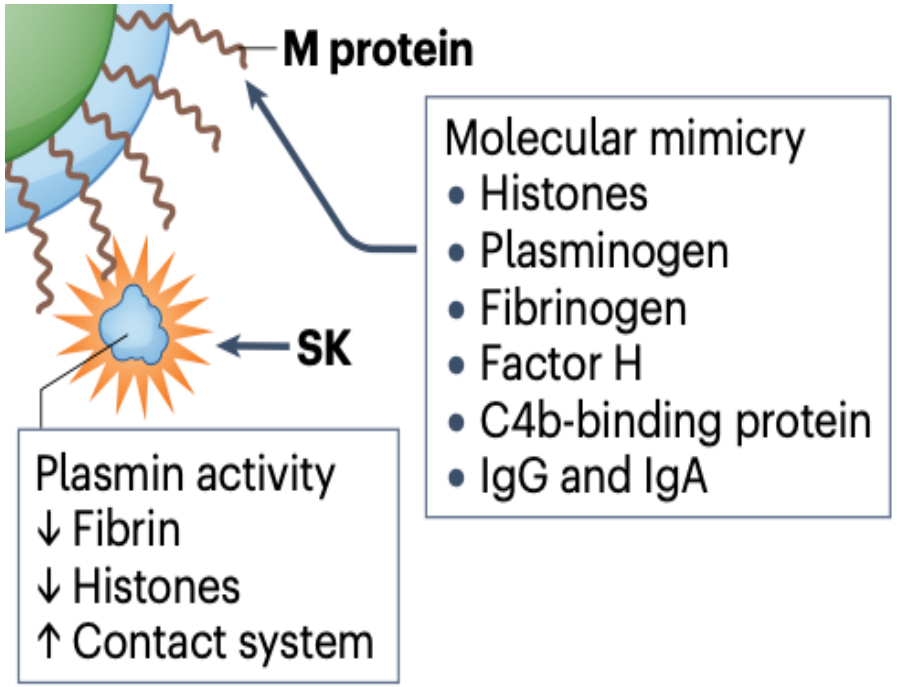
Molecular physiology:



M protein directly binds to ands recruits numerous host components, including plasminogen and fibrinogen, to GAS surface, escaping immune responses

Brouwer S, Rivera-Hernandez T, Curren BF, Harbison-Price N, De Oliveira DMP, Jespersen MG, Davies MR, Walker MJ. Pathogenesis, epidemiology and control of Group A Streptococcus infection. Nat Rev Microbiol. 2023 Jul;21(7):431-447. doi: 10.1038/s41579-023-00865-7. Epub 2023 Mar 9. Erratum in: Nat Rev Microbiol. 2023 Sep;21(9):619. doi: 10.1038/s41579-023-00939-6. PMID: 36894668; PMCID: PMC9998027.

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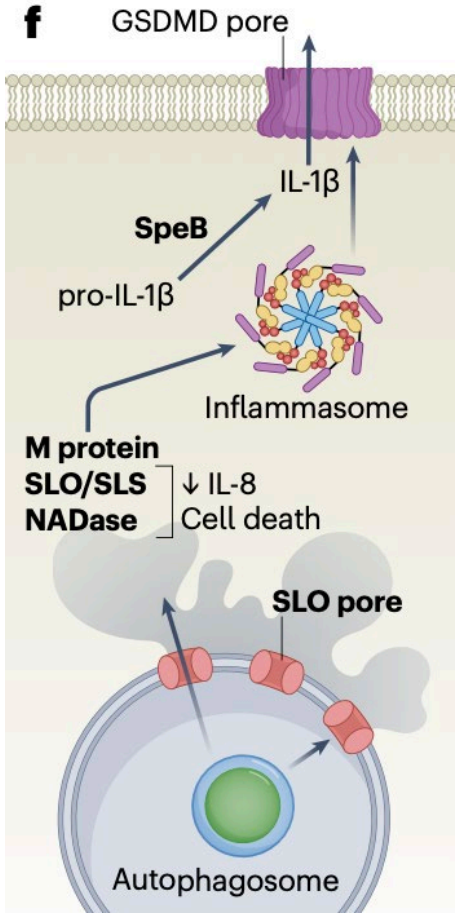

M protein also triggers programmed cell death in macrophages, leading to the secretion of the proinflammatory cytokines

Brouwer S, Rivera-Hernandez T, Curren BF, Harbison-Price N, De Oliveira DMP, Jespersen MG, Davies MR, Walker MJ. Pathogenesis, epidemiology and control of Group A Streptococcus infection. Nat Rev Microbiol. 2023 Jul;21(7):431-447. doi: 10.1038/s41579-023-00865-7. Epub 2023 Mar 9. Erratum in: Nat Rev Microbiol. 2023 Sep;21(9):619. doi: 10.1038/s41579-023-00939-6. PMID: 36894668; PMCID: PMC9998027.

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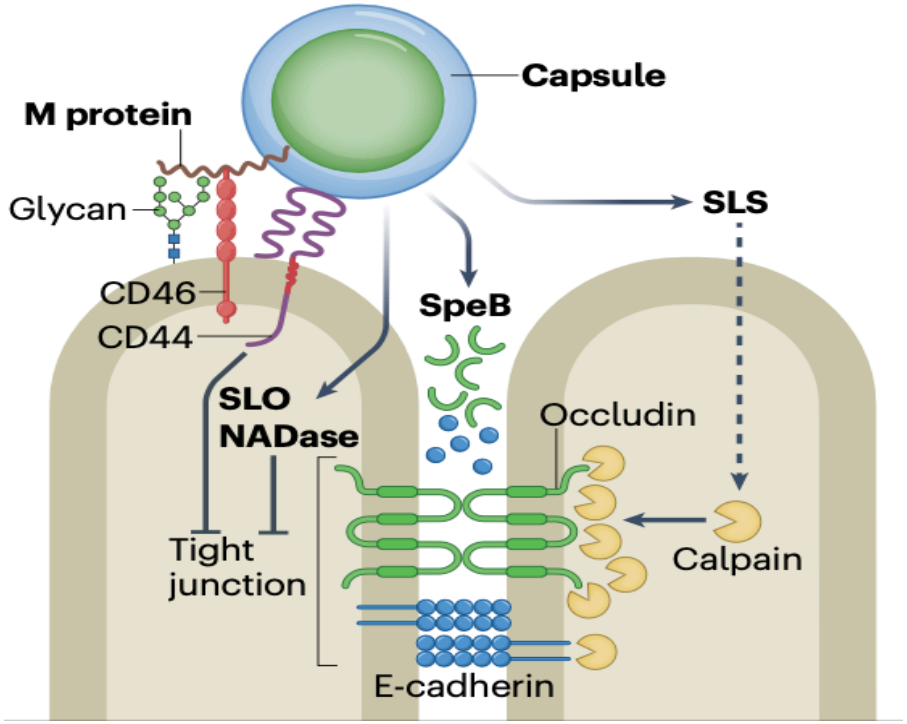

M protein also contributes to host colonization through adhesive interaction with epithelial cell receptors

Brouwer S, Rivera-Hernandez T, Curren BF, Harbison-Price N, De Oliveira DMP, Jespersen MG, Davies MR, Walker MJ. Pathogenesis, epidemiology and control of Group A Streptococcus infection. Nat Rev Microbiol. 2023 Jul;21(7):431-447. doi: 10.1038/s41579-023-00865-7. Epub 2023 Mar 9. Erratum in: Nat Rev Microbiol. 2023 Sep;21(9):619. doi: 10.1038/s41579-023-00939-6. PMID: 36894668; PMCID: PMC9998027.

Transmission:

-Droplet

-Contact with respiratory secretions, wound discharge, surfaces and fomites

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Transmission:

-Close contact in schools, child care centers, contact sports (e.g. wrestling), boarding schools, and military installations facilitates transmission

-Household pets are not vectors

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Case 2:

-6 yo previously healthy girl p/w fevers, neck pain, and b/l LE pain and weakness

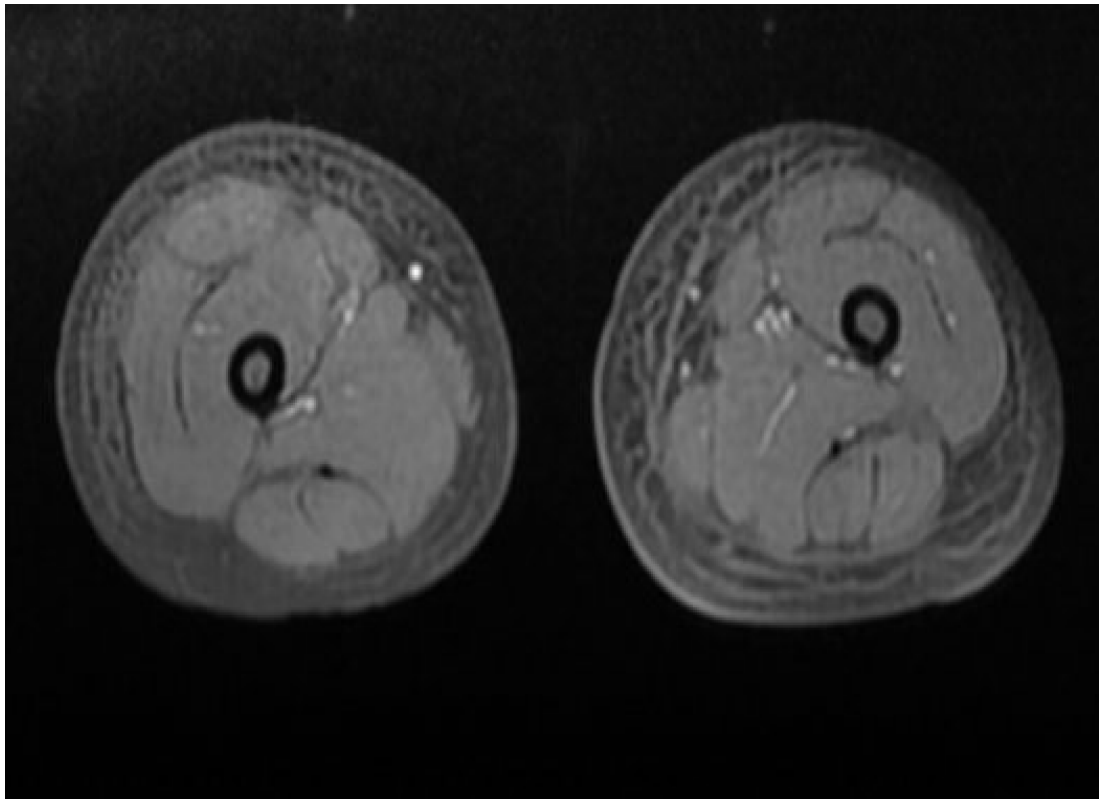
-Tested positive for rapid strep test; prescribed amoxicillin

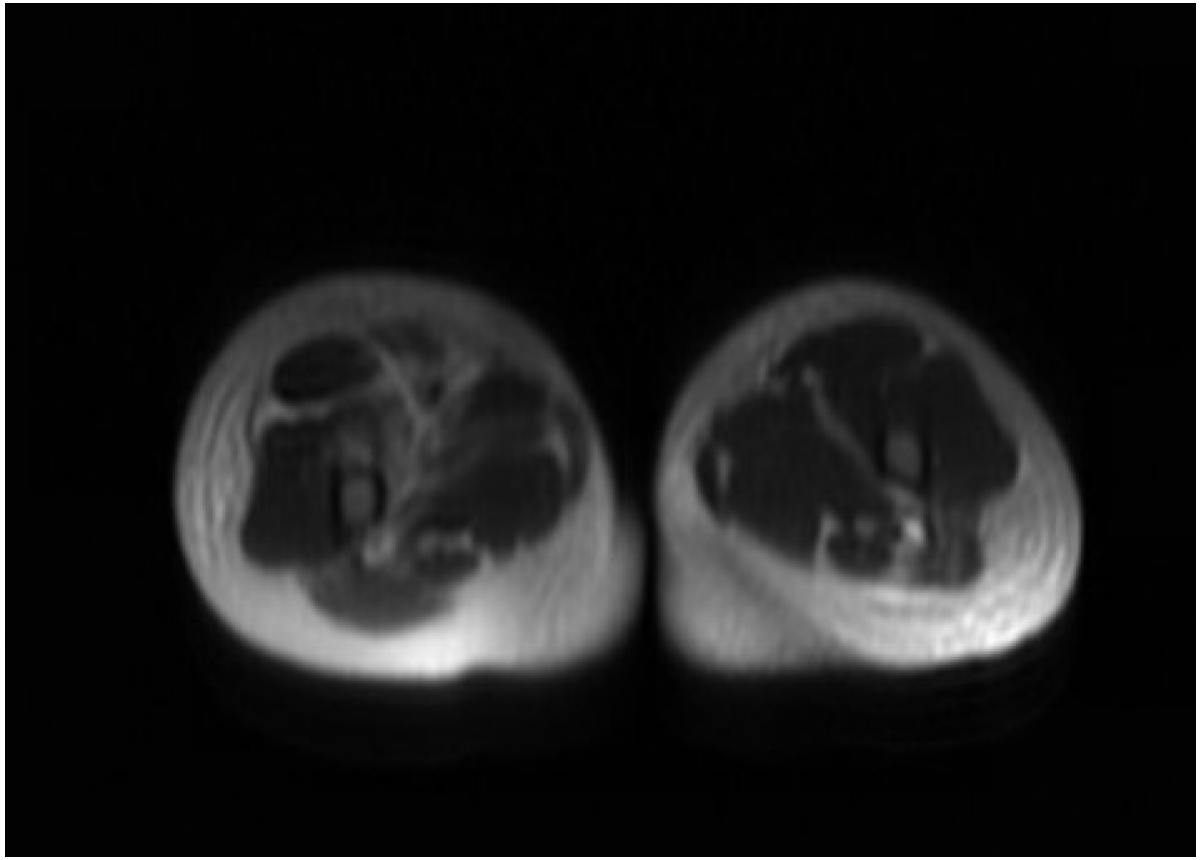
-Persistent Sx with swelling/redness over right thigh

-CT scans with contrast: cellulitis and myositis in thighs

-MRI with and without contrast: bilateral myositis in thighs with abscess in right vastus medialis muscle

Case 2:





MRI: fat stranding in both thighs

Case 2:

-I&D performed

-Grew AS from right thigh abscess

-Treated with 3-week course of amoxicillin for myositis due GAS

Risk factors:

-Concurrent or preceding viral infections such as influenza and varicella

-People ≥65 years

-American Indian and Alaska Native populations

-Residents of long-term care facilities

-People with medical conditions such as diabetes, malignancy, immunosuppression, chronic kidney, cardiac, or respiratory disease

-People with wounds or skin disease

-People who inject drugs or who are experiencing homelessness

https://emergency.cdc.gov/han/2022/han00484.asp

Risk factors:

Before varicella vaccine, chickenpox was the most commonly identified predisposing factor for iGAS infection in children

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Case 3:

-5 yo previously healthy boy had a closed supracondylar fracture of right elbow after tripping

-S/P reduction with percutaneous pinning

-Pins removed 1 month later

-The next day, started having fevers, fatigue and poor oral intake

-I&D performed

Case 3:

04/23/2023 11:46:00 ...	Culture Anaerobic/Aerobic ...	SeeReport	Auth (Veri...	STREPTOCOCCUS PYOGENES, GRO...	Completed	04/26/2023 10:46:19 EDT	ELBOW-RIGHT
04/23/2023 11:45:00 ...	Culture Anaerobic/Aerobic ...	SeeReport	Auth (Veri...	STREPTOCOCCUS PYOGENES, GRO...	Completed	04/26/2023 10:46:07 EDT	ELBOW-RIGHT
04/23/2023 11:37:00 ...	Culture Anaerobic/Aerobic ...	SeeReport	Auth (Veri...	STREPTOCOCCUS PYOGENES, GRO...	Completed	04/26/2023 10:45:56 EDT	ELBOW-RIGHT

Treated with a 4-week course of cephalexin for right elbow osteomyelitis due to GAS

Epidemiology:

-More than 500,000 deaths/year worldwide

-1,800-2,400 deaths/year in the U.S.

https://www.who.int/emergencies/disease-outbreak-news/item/2022-DON429
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Epidemiology:

-Peak incidence is during Dec-Ap

-However, some infections are more common in certain seasons:

- Pharyngitis and scarlet fever: late fall, winter and spring *(due to close contact in schools)*
- Impetigo and pyoderma: summer *(due to insect bites and other minor skin trauma)*

https://www.cdc.gov/group-a-strep/php/surveillance/index.html
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Recent epidemiology:

-The U.S. rates of iGAS disease began increasing in 2014

-This increase was largest among adults 18-64 years, but the rate also increased among older adults

-Substantial increases in cases among 2 groups appear to account for much of the change:

- People experiencing homelessness
- People with injection drug use

https://www.cdc.gov/group-a-strep/php/surveillance/index.html

Surge in Vermont:

-During 2022–2023, the University of Vermont Medical Center experienced a substantial increase in the number of GAS bacteremia

-Predominantly in persons who inject drugs

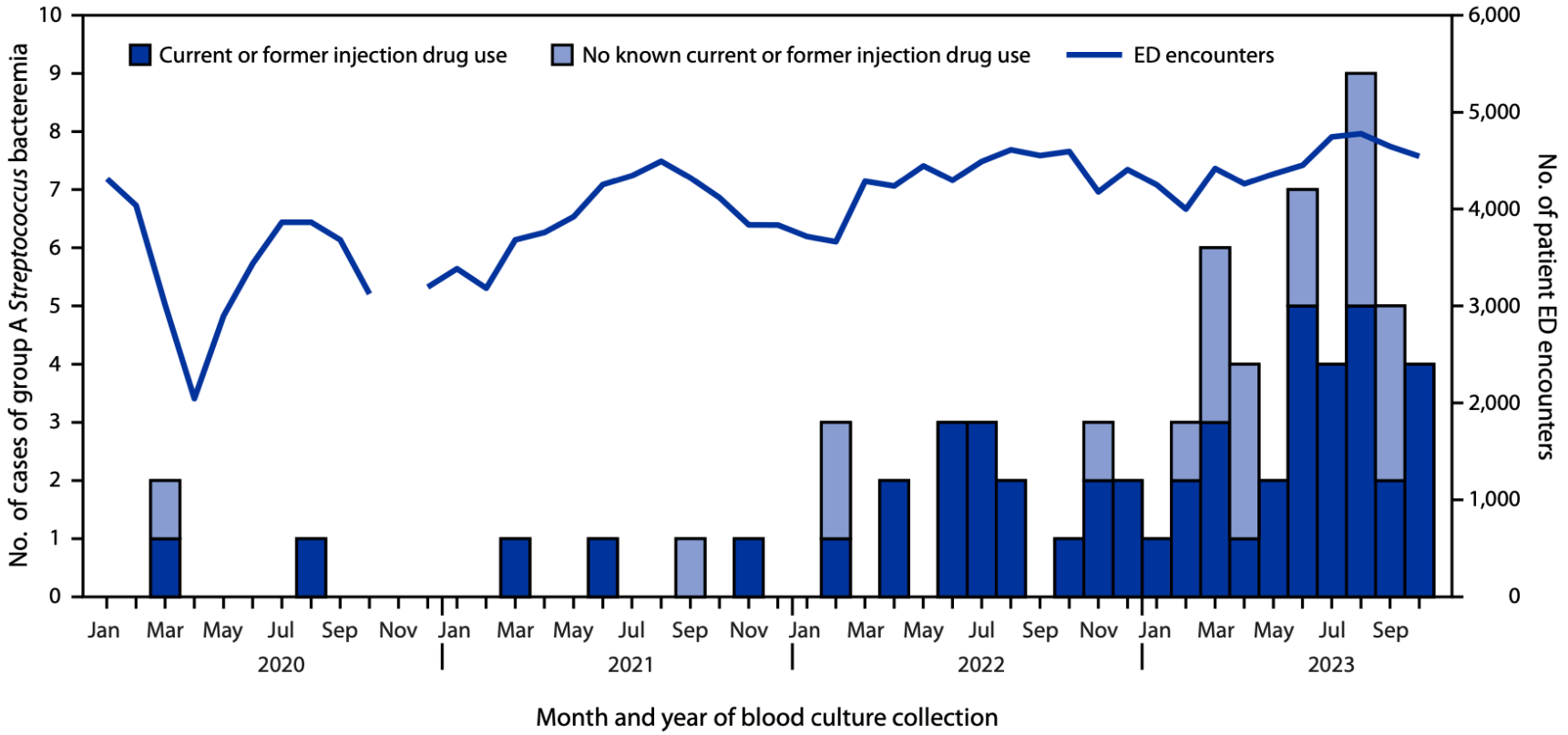
-This increase coincided with the introduction of xylazine into the drug supply

-Xylazine causes peripheral vasoconstriction and ischemia, leading to necrosis at injection sites and noninjection sites

-Xylazine-related wounds might serve as portal of entry for bacteria into the bloodstream

https://www.cdc.gov/mmwr/volumes/73/wr/mm7316a5.htm#print

FIGURE. Cases of community-acquired group A *Streptococcus* bacteremia, by month of blood culture collection, patient history of injection drug use, and emergency department encounters — University of Vermont Medical Center, January 2020–October 2023*,†



https://www.cdc.gov/mmwr/volumes/73/wr/mm7316a5.htm#print

Recent epidemiology:

-Nov 2022: CDC was notified of possible increase in iGAS infections among children at a hospital in Colorado

-Increase in pediatric iGAS infections was noted in other states

-Occurred in the setting of increased circulation of RSV, influenza, SARS-CoV-2, and other respiratory viruses

https://emergency.cdc.gov/han/2022/han00484.asp

Recent epidemiology:

-During the COVID-19 pandemic, both invasive and less severe infections caused by GAS decreased by ~25% in the U.S.

-Likely due to the steps taken to prevent the spread of respiratory diseases (e.g., school and workplace closures, masking, physical distancing)

https://archive.cdc.gov/www_cdc_gov/groupastrep/igas-infections-investigation.html

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CDPHE monitoring increase in invasive group A strep cases, other bacterial infections, in Colorado

-12/15/22: 11 pediatric cases since 11/1/22

-Including 2 deaths

https://cdphe.colorado.gov/press-release/monitoring-increase-in-invasive-group-a-strep-cases-other-bacterial-infections

DEPARTMENT OF HEALTH

Health Advisory: Group A Streptococcal Infections

Minnesota Department of Health, Thurs, Dec 8 14:00 CST 2022

-Nov 2022: 46 cases compared to 20 cases/month in 2022

-All age groups but mostly in pediatric and elderly patients

https://www.health.state.mn.us/communities/ep/han/2022/dec8strep.pdf

Department of Health and Human Services
Maine Center for Disease Control and Prevention
286 Water Street
11 State House Station
Augusta, Maine 04333-0011
Tel: (207) 287-8016; Fax (207) 287-9058
TTY Users: Dial 711 (Maine Relay)

Maine Health Alert Network (HAN) System

PUBLIC HEALTH ADVISORY

To: Health Care Providers
From: Dr. Isaac Benowitz, State Epidemiologist
Subject: **U.S. CDC: Increase in Pediatric Invasive Group A Streptococcal Infections**
Date / Time: Thursday, January 5, 2023 at 4:26PM
Pages: 2
Priority: Normal
Message ID: 2023PHADV001

11/1/22-12/31/22:
-Maine CDC identified 25 cases of iGAS infections, one of which was in a pediatric patient
-Higher than seen in this time frame in the 5 preceding years

https://www.maine.gov/dhhs/mecdc/health-advisory.shtml?id=10047616#:~:text=The%20United%20States%20has%20seen,cases%20in%20November%20and%20December).

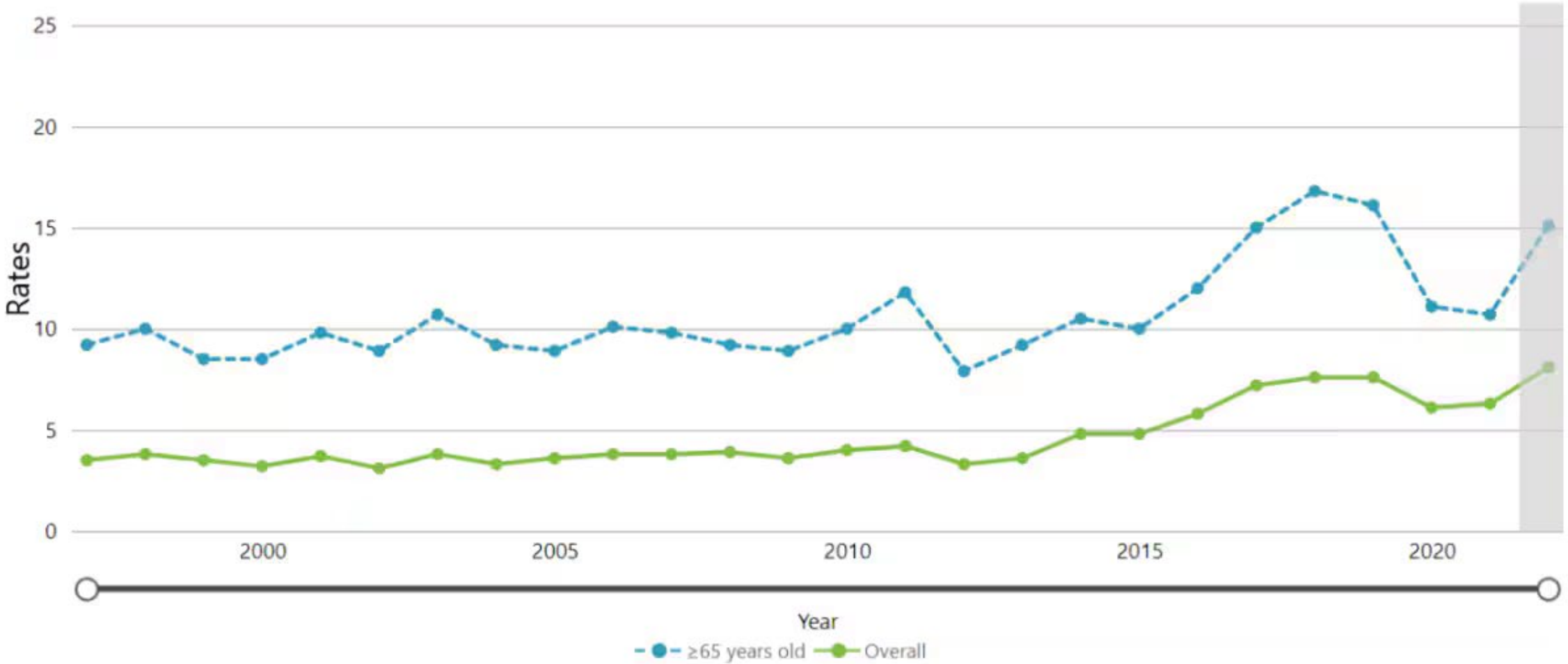
Recent epidemiology:

-Dec 2022: CDC issued an advisory to notify clinicians and public health authorities of a recent increase in iGAS infections

-2023: incidence remained high in some areas of the country even after decrease in respiratory viruses

https://emergency.cdc.gov/han/2022/han00484.asp

Rates* of invasive group A strep infections, by age, in ABCs areas



* Rates are calculated as cases per 100,000 population.
Preliminary data denoted by gray bars.

ABC: Active Bacterial Core surveillance

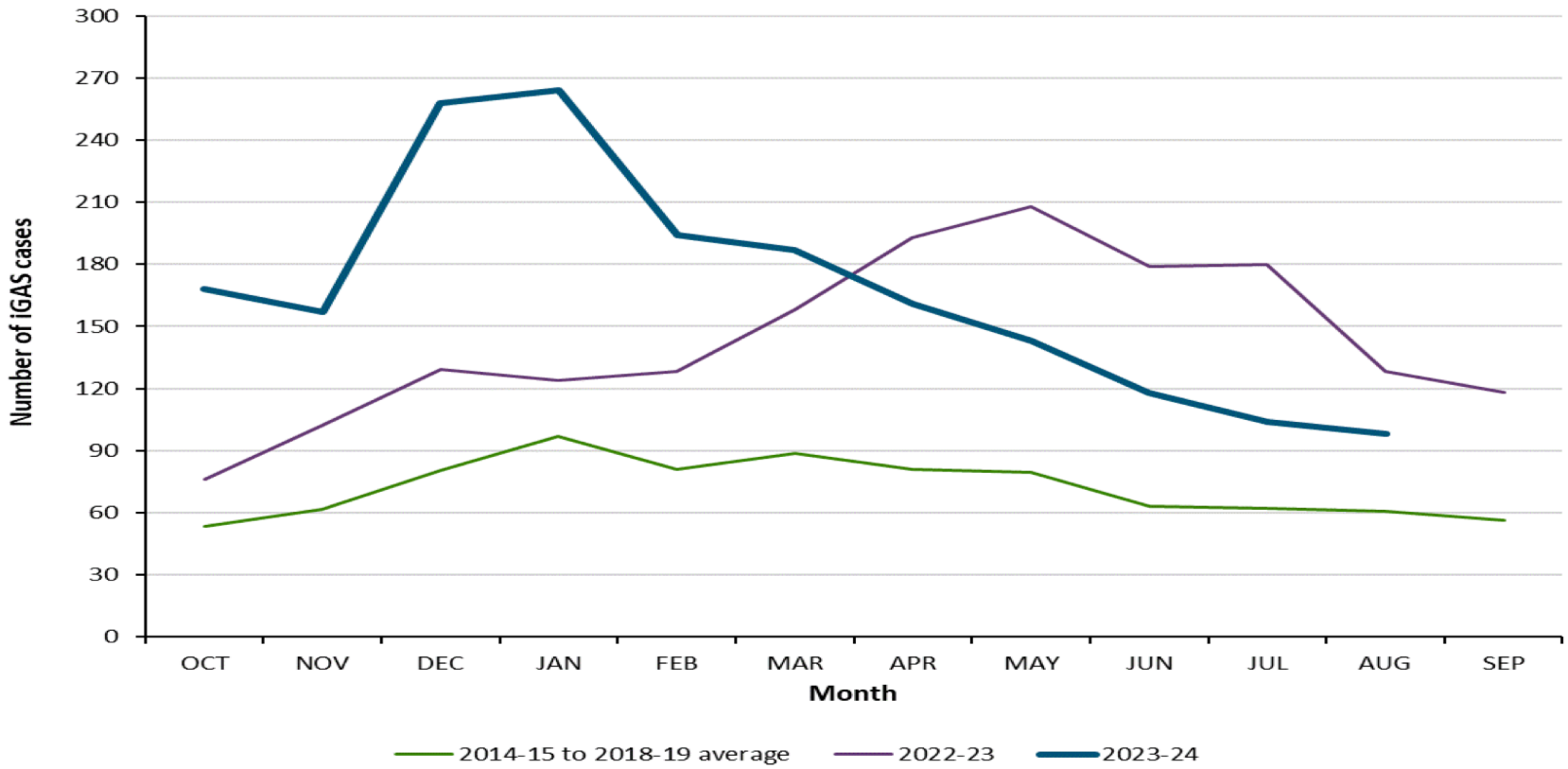
https://www.cdc.gov/group-a-strep/php/surveillance/index.html

Recent epidemiology:

2024: no reported surges in iGAS infections in the U.S. so far

https://emergency.cdc.gov/han/2022/han00484.asp

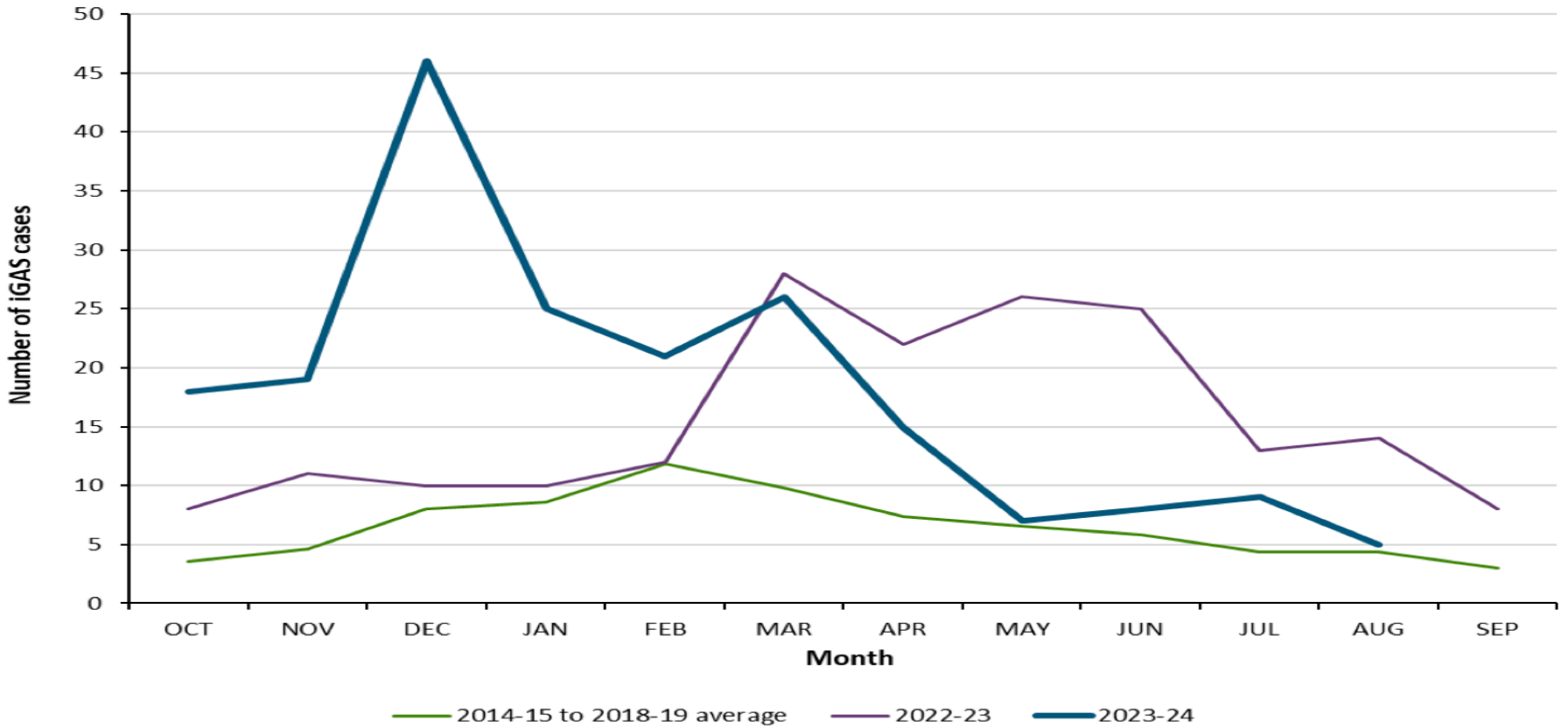
Figure 1: Confirmed iGAS Case Counts by Month for all Ages: Current Season (October 1, 2023 – August 31, 2024)* Compared to the 2022-23 Season (October 1, 2022 – September 30, 2023) and the Five Pre-Pandemic Season Average (October 1, 2014 – September 30, 2019)



Data source: iPHIS
*Data for the 2023-2024 season includes cases reported up to August 31, 2024. Data for the most recent reporting month should be interpreted with caution due to reporting and/or data entry lags.

https://www.publichealthontario.ca/-/media/Documents/I/2023/igas-enhanced-epi-2023-2024.pdf?rev=20675675fd0b443a9bf8e4f71ca1f4d5&sc_lang=en&hash=E852E904A9E8B1D83BF2D26D9253C5D9

Figure 2: Confirmed iGAS Case Counts by Month in Children 0-17 Years of Age: Current Season (October 1, 2023 – August 31, 2024)* Compared to the 2022-23 Season (October 1, 2022 – September 30, 2023) and the Five Pre-Pandemic Seasons (October 1, 2014 – September 30, 2019)



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https://www.publichealthontario.ca/-/media/Documents/I/2023/igas-enhanced-epi-2023-2024.pdf?rev=20675675fd0b443a9bf8e4f71ca1f4d5&sc_lang=en&hash=E852E904A9E8B1D83BF2D26D9253C5D9

Increase in Invasive Group A streptococcal infections among children in Europe, including fatalities

Press release

12 Dec 2022

-Several European countries had an increase in iGAS infections during 2022, particularly since Sep 2022, among children <10 years

-In France and the UK, the increase in iGAS cases in children was 4-fold than pre-pandemic levels

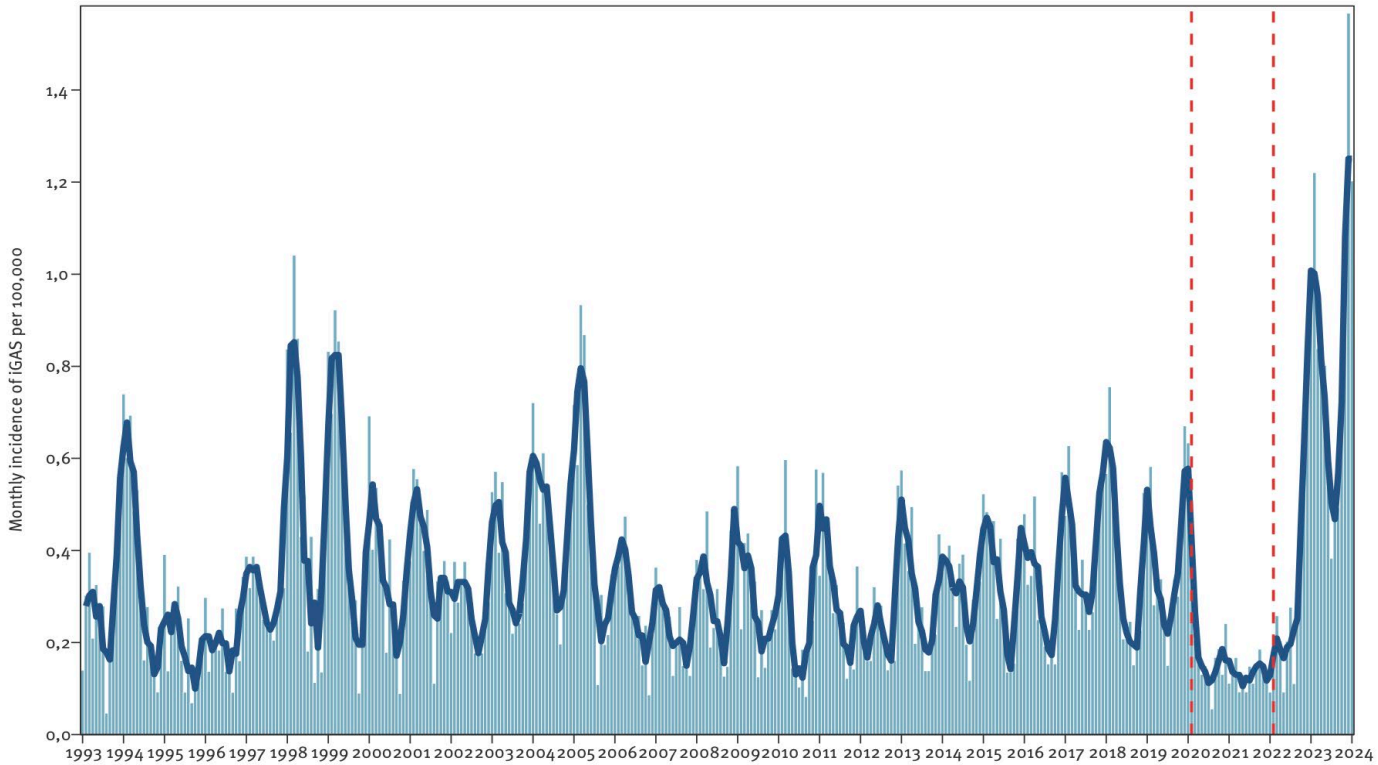
-Several deaths in France and the UK

-Likely due to increase in circulating respiratory viruses

https://www.ecdc.europa.eu/en/news-events/increase-invasive-group-streptococcal-infections-among-children-europe-including

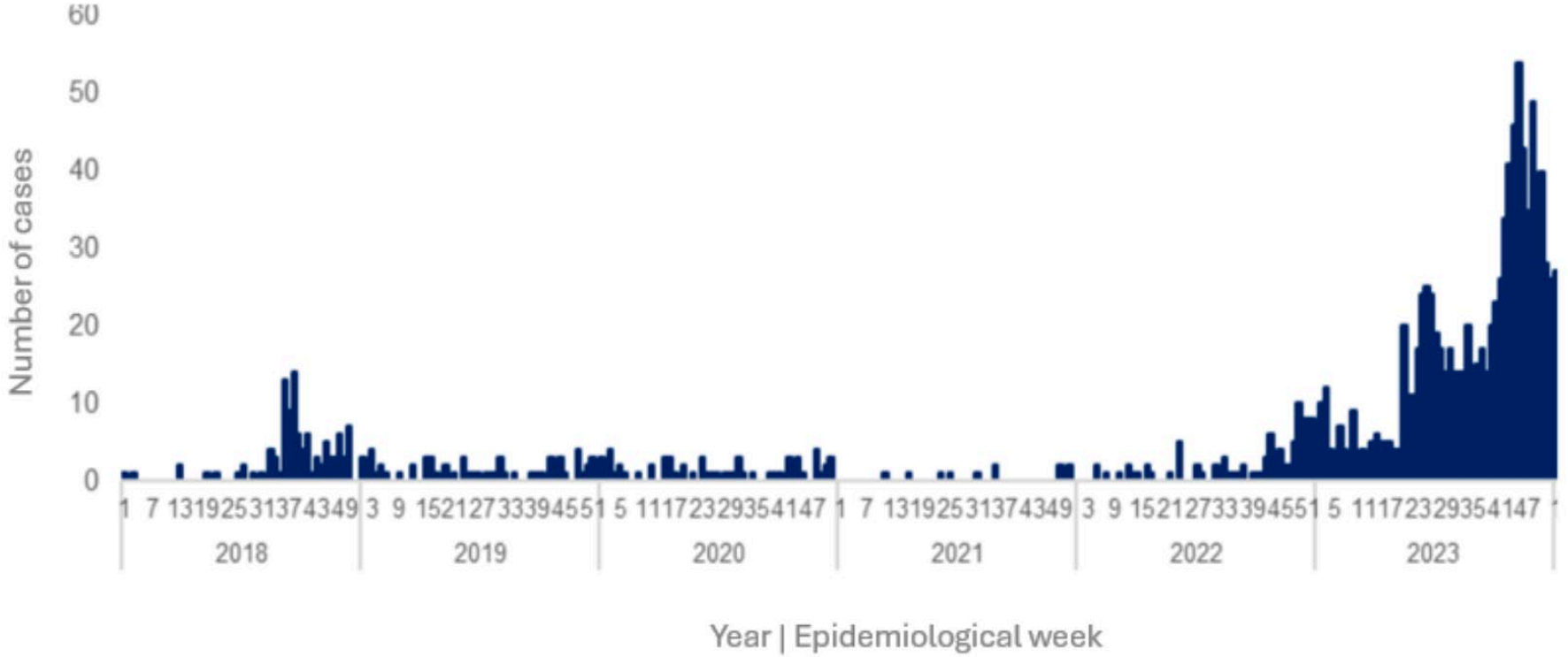
FIGURE 1

Monthly incidence of invasive group A streptococcal infection for all ages, Norway, January 1993– February 2024 (n = 6,219)



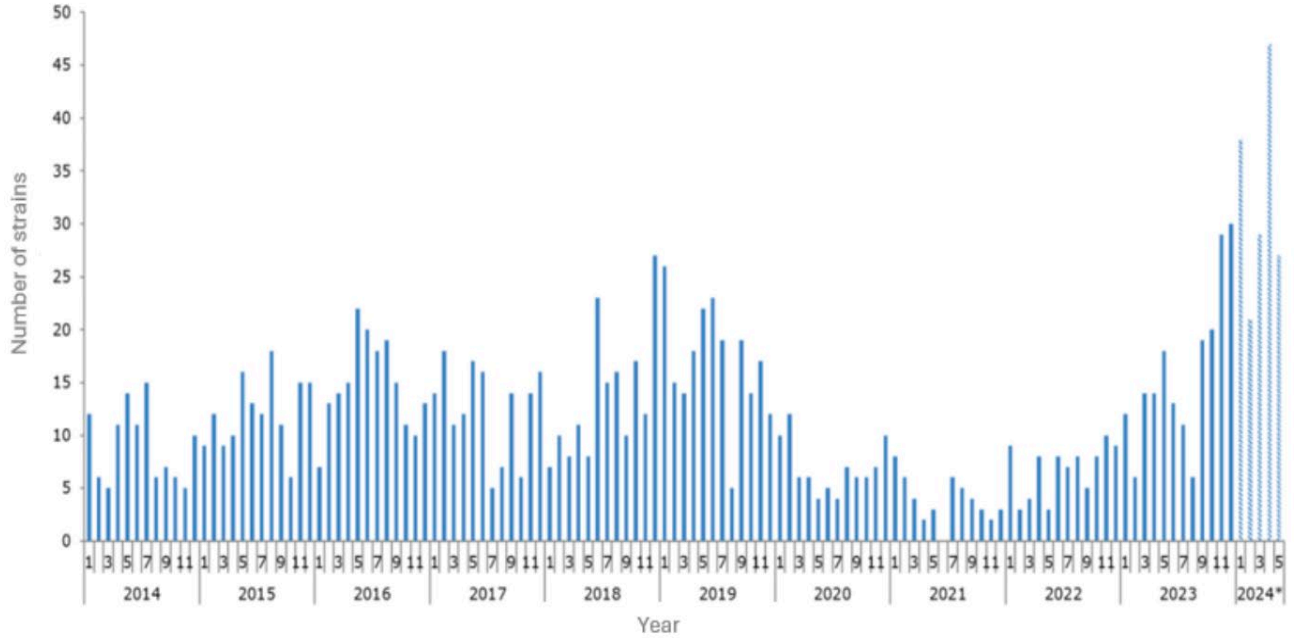
-Mostly in children 0-9 years and older adults ≥70 years
-Strep pharyngitis rates had similar pattern compared to iGAS rates

Figure 1. Number of cases of invasive GAS infection, according to EW and year in Argentina, 2018-2023.



https://www.paho.org/en/documents/epidemiological-update-invasive-disease-caused-group-streptococci-21-june-2024

Figure 2. Number of confirmed *S. pyogenes* strains, by year and month. Chile, 2014 until 15 May 2024.



https://www.paho.org/en/documents/epidemiological-update-invasive-disease-caused-group-streptococci-21-june-2024

Likely explanations of increased iGAS infections:

-Increasing circulating respiratory viruses after reduced circulation during the COVID-19 pandemic

-SARS-CoV-2 reinfection following the pandemic

-Shift in *emm* types

-Increased homelessness and IV drug use

Eurosurveillance | Increase in invasive group A streptococcal infections (iGAS) in children and older adults, Norway, 2022 to 2024
emm Typing Overview and Guidelines | Strep Lab | CDC

Case 4:

-17 yo previously healthy girl p/w fatigue, abdominal pain, vomiting, diarrhea, low back pain, and rash on ankles/wrists

-Labs showed normal WBC, left shift, hyponatremia and elevated ALT/bilirubin

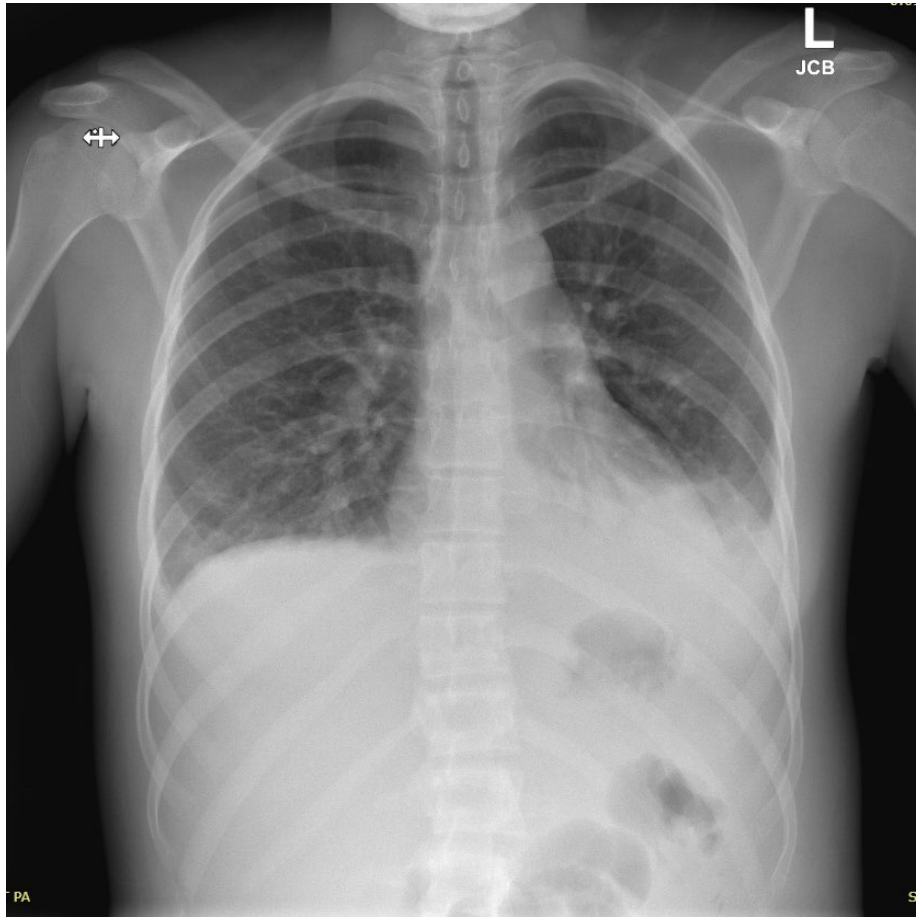
-Started on doxycycline for suspected tickborne illness

03/07/2024 10:51:00 EST	Bacterial Identification	SeeReport	Auth (Verified)	STREPTOCOCCUS PYOGENES, GROUP A
03/07/2024 10:28:00 EST	Bacterial Identification	SeeReport	Auth (Verified)	STREPTOCOCCUS PYOGENES, GROUP A

-Switched to ampicillin

-Then, developed tachypnea and hypoxia

Case 4:



Chest X-ray:

-Left lung base consolidation

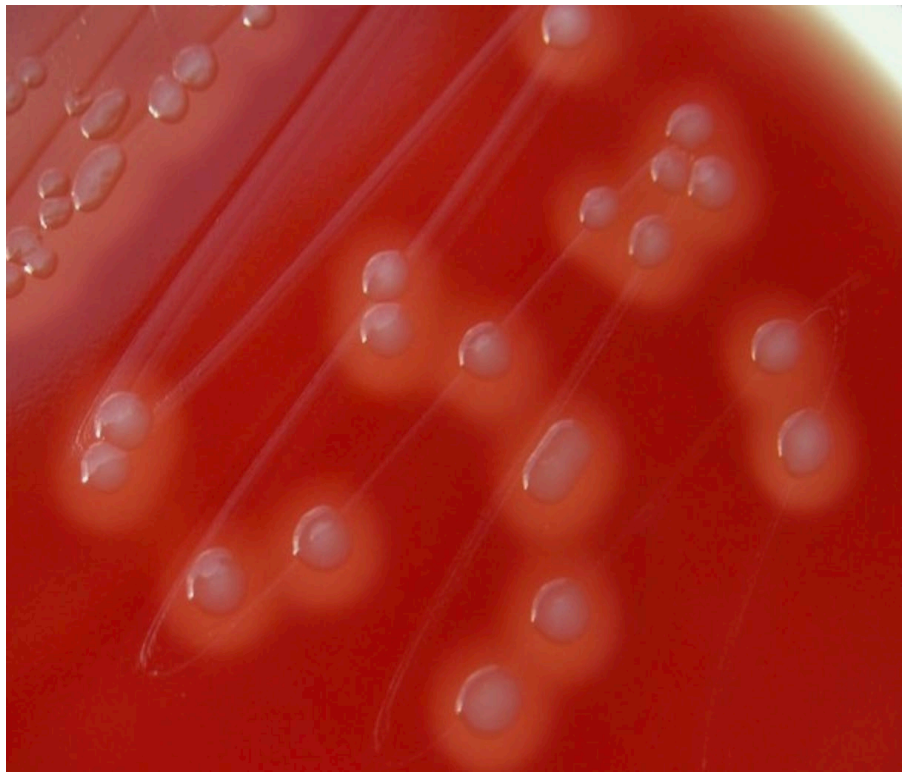
-Bilateral small pleural effusions

Case 4:

Treated with 10-day course of ampicillin for bacteremia and pneumonia due to GAS

Diagnosis:

Cultures of blood and focal sites of possible infection



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Treatment:

Supportive care

-Management of respiratory and cardiac failure (if present)

-Fluid resuscitation (if needed)

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Treatment:

Antibiotics

-GAS is universally susceptible to penicillin and thus to all other beta-lactam antibiotics

-Susceptibility testing is needed only for non–beta-lactam agents, such as a macrolide or clindamycin, to which some strains are resistant

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Antibiotics

-GAS is universally susceptible to penicillin

-Might need however to treat with broader-spectrum antibiotics if suspecting polymicrobial infection (e.g. ampicillin-sulbactam) or for ease of use (e.g. IV ceftriaxone)

Treatment:

Antibiotics

-Clindamycin should be added in toxic shock syndrome to inhibit bacterial protein synthesis

-Clindamycin should not be used alone in serious infections because of potential for resistance (~1/3 of isolates can be resistant to clindamycin)

-Linezolid can be used instead if isolate is resistant to clindamycin

-Clindamycin (or linezolid) may be discontinued after few days if there is adequate source control and clinical improvement

2024. "Group A Streptococcal Infections", Red Book: 2024–2027 Report of the Committee on Infectious Diseases, Committee on Infectious Diseases, American Academy of Pediatrics, David W. Kimberlin, MD, FAAP, Ritu Banerjee, MD, PhD, FAAP, Elizabeth D. Barnett, MD, FAAP, Ruth Lynfield, MD, FAAP, Mark H. Sawyer, MD, FAAP
https://www.cdc.gov/group-a-strep/php/surveillance/index.html

Treatment:

Surgical debridement

-Aggressive drainage and irrigation of accessible sites of infection

-Immediate surgical debridement in case of necrotizing fasciitis

2024. "Group A Streptococcal Infections", Red Book: 2024–2027 Report of the Committee on Infectious Diseases, Committee on Infectious Diseases, American Academy of Pediatrics, David W. Kimberlin, MD, FAAP, Ritu Banerjee, MD, PhD, FAAP, Elizabeth D. Barnett, MD, FAAP, Ruth Lynfield, MD, FAAP, Mark H. Sawyer, MD, FAAP

Treatment:

IVIG

-Should be strongly considered as adjunctive therapy for toxic shock syndrome or necrotizing fasciitis if patient is moderately to severely ill

-Use however is supported by limited data

2024. "Group A Streptococcal Infections", Red Book: 2024–2027 Report of the Committee on Infectious Diseases, Committee on Infectious Diseases, American Academy of Pediatrics, David W. Kimberlin, MD, FAAP, Ritu Banerjee, MD, PhD, FAAP, Elizabeth D. Barnett, MD, FAAP, Ruth Lynfield, MD, FAAP, Mark H. Sawyer, MD, FAAP

Treatment:

Often requires a multidisciplinary approach involving Pediatric ID, ICU and Surgery

Prevention:

-Adequate hand and respiratory hygiene

-Adequate cleaning of surfaces

-Good indoor ventilation

-Vaccinations for SARS-CoV-2 and influenza

https://www.ecdc.europa.eu/en/news-events/increase-invasive-group-streptococcal-infections-among-children-europe-including

Conclusion:

-It is important to treat GAS infections, such as pharyngitis or impetigo, to avoid invasive infections and reduce onward transmission

-Prompt testing and treatment of iGAS infections with antibiotics and supportive care +/- surgery are essential

-Continued monitoring of the epidemiological situation at the national and international levels is needed to detect new surges of iGAS infections

-It is important to get immunized for influenza, SARS-CoV-2 and VZV in order to avoid secondary bacterial infections such as GAS