

Summary of the situation

Streptococcus pyogenes, also known as group A streptococci of the Langefield classification (GAS), is a group of gram-positive bacteria that cause a wide spectrum of infections. They are estimated to be responsible for more than 500,000 deaths annually worldwide (1).

Generally, GAS causes mild illnesses such as tonsillitis and pharyngitis; rarely, they can cause severe infections, such as necrotizing fasciitis, bacteremia, septic arthritis, puerperal endometritis, or pneumonia. Approximately one third of these invasive infections are complicated by streptococcal toxic shock syndrome (1).

On 15 December 2022, the World Health Organization (WHO) shared information about an increase in cases of invasive GAS disease and scarlet fever in Member States of the WHO European Region, which had resulted in some deaths, especially in children under 10 years of age (1). On 19 December 2022, the Pan American Health Organization/World Health Organization (PAHO/WHO) published an information note on an increase in the occurrence of GAS disease cases in Uruguay (2).

On 28 November 2023, PAHO/WHO issued an epidemiological alert following an increase in cases of invasive GAS disease in Argentina (3).

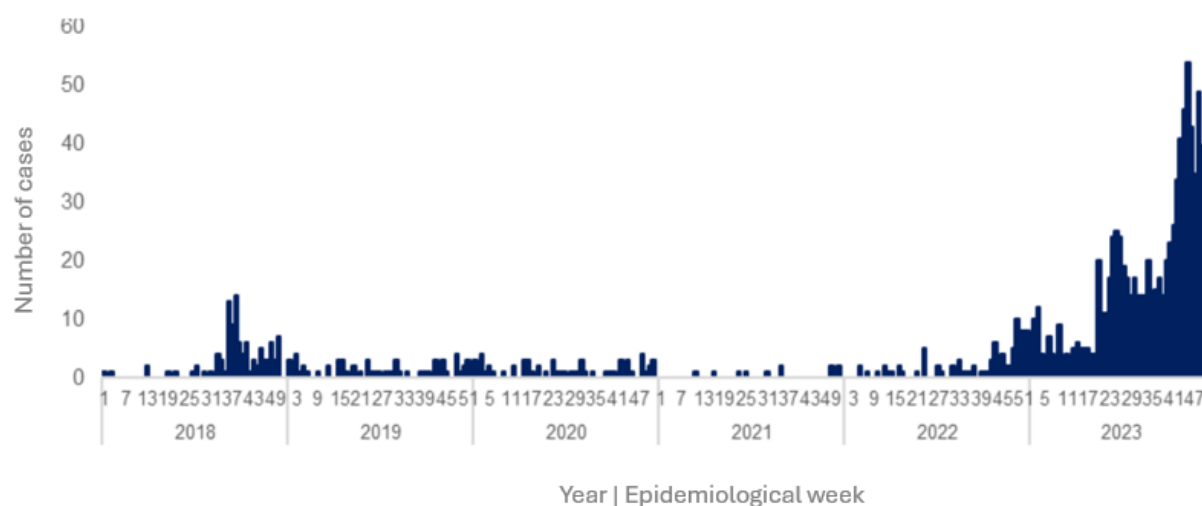
In alphabetical order, the situation of select countries in the Region of the Americas is described below:

In **Argentina**, the national epidemiological bulletin of epidemiological week (EW) 10 of 2024 updates the situation of GAS in the country. Confirmed cases of invasive *S. pyogenes* infection throughout 2023 totaled 926, of which 134 (14.4%) died. Regarding the distribution by age group, 46.7% of the confirmed cases of GAS in 2023 corresponded to children under 16 years of age, and 28.4% to those over 50 years of age, with a median of 20 years. Regarding deceased cases, 32.1% corresponded to children under 16 years of age and 47.0% to those over 50 years of age, with a median of 46.5 years.

The highest incidence rates by age group were observed at the extremes of life: firstly, children under 10 years of age and secondly, adults over 80 years of age. The highest absolute number of cases was observed in children under 10 years of age, followed by the 10 to 19 age group, with 49.6% of cases between both groups. In relation to territorial distribution during 2023, the highest incidence rates were recorded in the regions of Cuyo (4.6 per 100,000 population) and Sur (3.9 per 100,000 population). The cumulative incidence rate for 2023 at the national level was 1.9 cases per 100,000 population and the mortality rate was 0.29 per 100,000 population (**Figure 1**) (4).

Suggested citation: Pan American Health Organization / World Health Organization. Epidemiological Update: Invasive disease caused by group A streptococci. 21 June 2024. Washington, D.C.: PAHO/WHO; 2024.

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



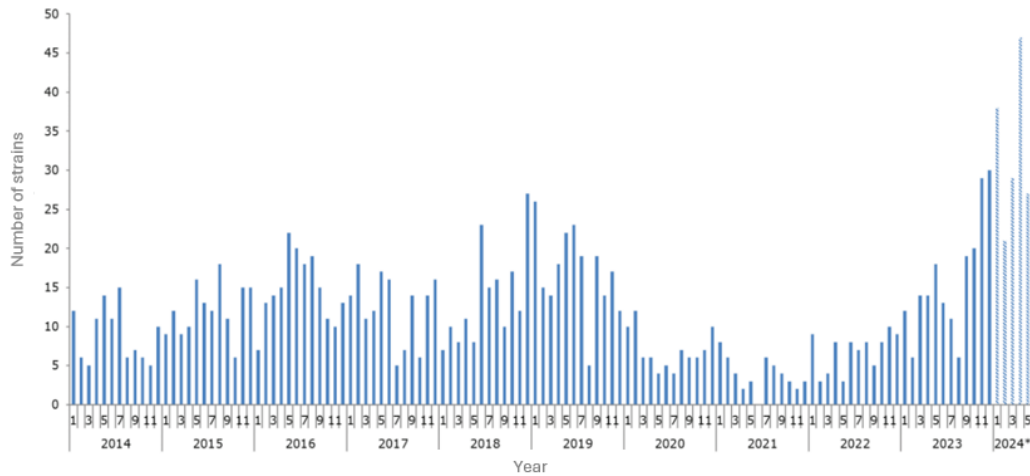
Source: Adapted from Ministerio de Salud de la República Argentina. Boletín epidemiológico nacional, N 695, EW 10 of 2024. Buenos Aires: Msa; 2024. Available in Spanish from: <https://bancos.salud.gob.ar/recurso/boletin-epidemiologico-nacional-n-695-EW-10-2024>

In **Chile**, on 27 May 2024, the Chile Ministry of Health issued an alert due to the increase of strains confirmed by the Institute of Public Health (ISP per its acronym in Spanish) during the year 2024 (5).

In the laboratory surveillance bulletin of invasive disease by *S. pyogenes* published on 31 May by the INS, with updated information as of 15 May 2024, a progressive increase of confirmed strains is described between 2014 and 2019, recording 108 and 204 strains, respectively (6). During the COVID-19 pandemic years, a decrease in the number of confirmed strains was reported for 2020 (n= 83), 2021 (n= 46), and 2022 (n= 82), respectively. However, the year 2023 saw an increase with 192 confirmed GAS strains, mainly during the last months of the year. During 2024, between January and as of 15 May, 162 strains have been confirmed, mainly concentrated in the Metropolitan, Valparaíso, and Biobío regions (**Figure 2**) (6).

Between 2014 and 2023, the dominant phenotype was resistant to macrolides, lincosamines, and streptogramins B in their inducible expression (MLSB_{ind}) with 84.6% of the strains analyzed, followed by the same phenotype, but with their constitutive expression (MLSB_{const}) with 12.1% and a phenotype where only macrolides (M) are affected with 3.4%. In relation to the MLSB_{ind} phenotype, serotype M4T4 presented the highest frequency with 67.5%. Regarding the total number of strains analyzed in the period, the most frequent serotypes were: M1T1 (21.0%), M12T12 (12.4%) and M4T4 (10.3%). Of note was the increase in serotypes M12T12, M49T14/49, M43T13, and M76T12 between 2014 and 2023 (6).

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

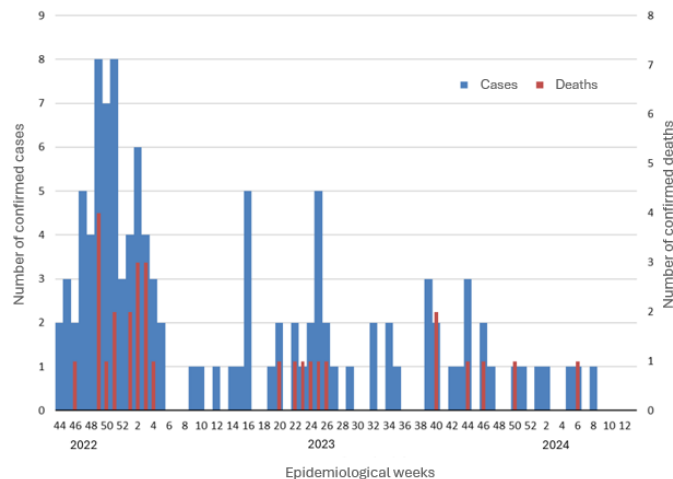


2024* Data for 2024 are preliminary.

Source: Adapted from Ministerio de Salud de Chile. Instituto de Salud Pública. Vigilancia de laboratorio de enfermedad invasora por *Streptococcus pyogenes*, Chile 2014-2023/May 2024. Santiago, Chile: IPS; 2024. Available in Spanish from: <https://www.ispch.cl/wp-content/uploads/2024/05/Streptococcus02-31052024A-1.pdf>

In **Uruguay**, during 2023, 66 cases of invasive *S. pyogenes* infection were detected, of which 20 (30.3%) died. The most affected age groups were those between 6 and 10 years of age (19.9%) and those over 60 years of age (28.8%). The incidence rate was 1.85 cases per 100,000 population and the mortality rate was 0.56 per 100,000 population. The most affected departments were Montevideo with 42 cases and Soriano with five cases. In 2024, as of EW 8, five cases and one death were reported (**Figure 3**) (7).

Figure 3. Distribution of cases and deaths with confirmed invasive disease due to *S. pyogenes*. Period between EW 44 of 2022 and EW 12 of 2024.



Source: Adapted from the Uruguay International Health Regulations National Focal Point (IHR NFP). E-mail communication dated 14 June 2024. Montevideo: 2024. Unpublished.

Recommendations

The main recommendations for surveillance, clinical management, prophylaxis and risk communication that were published in the 28 November 2023 PAHO/WHO epidemiological alert (3) are reiterated below and remain in effect:

Clinical and genomic surveillance

- Strengthen activities for detection, characterization and trend monitoring of invasive GAS infection cases.
- Report to the surveillance system any unusual and unexpected form of infections by this agent (invasive forms, outbreaks).
- Notify the International Health Regulations National Focal Point (IHR NFP) of any unexpected spike in the national or regional incidence of such invasive infections.
- Ensure that all strains isolated from patients with invasive forms are sent to the National Public Health Laboratory for further characterization and genomic surveillance of lineages (clones) and sub-lineages.

Clinical management, infection prevention and control and prophylaxis

- Health care professionals should maintain a high clinical suspicion for GAS infection, especially when evaluating patients with previous viral infection, direct contact with scarlet fever cases, or invasive GAS infection.
- Encourage the consultation of all suspected symptomatic cases of GAS, as well as the diagnosis, isolation, and adequate and timely treatment.
- In case of hospital admission due to invasive infection, precautions should be taken to avoid transmission by respiratory droplets and standard precautions should always be observed. In case of tissue involvement (necrotizing fasciitis, infected wounds, skin lesions) contact precautions are required. Respiratory droplet and contact precautions can be discontinued after 24 hours of antimicrobial treatment.
- Although there is no general recommendation on the administration of prophylaxis, this measure could be considered depending on the degree of exposure and the immune status of the contacts. For example, prophylaxis could be considered in close family members who have shared a bed or who have had close contact, as well as in caregivers who have spent many hours with an infected person. It could also be evaluated in immunocompromised contacts, pregnant women, those who have had recent surgery, wounds, or those with a family history of rheumatic fever. It could also be considered during outbreaks of pharyngitis, acute rheumatic fever, or post-streptococcal glomerulonephritis in closed communities.
 - The regimen consists of penicillin (adults, 250 mg vo / 6 h for 10 d; children, 25mg/kg - maximum 250 mg per dose - vo / 6 h for 10 d). If penicillin allergy is present, clindamycin or azithromycin may be chosen, after confirming the sensitivity of the index patient's isolate to these antimicrobials (8).

Antibiotic treatment (8, 9)

Antibiotic treatment is indicated in group A streptococcal infections; the choice of drug, dose and route of administration depends on the clinical manifestations, location of the infection and patient characteristics.

In cases of **invasive infection** (e.g., bacteremia, necrotizing fasciitis) or **toxic shock**, the support of a clinical team with infectious disease experts, surgeons, and intensivists is required, as treatment includes immediate administration of intravenous antimicrobials, fluid management and hemodynamic support, surgical evaluation if needed for resection of necrotic tissue, and other supportive measures, such as possible administration of immunoglobulin G (8). In the initial presentation of invasive infection or toxic shock due to group A Streptococci, it cannot be distinguished from sepsis due to other pathogens, so empirical treatment should also cover *Staphylococcus aureus* (including methicillin-resistant), as well as gram-negative bacilli. The duration of antimicrobial treatment should be adjusted to the patient's characteristics, including the origin of the infection and the clinical course. Patients with bacteremia should be treated for at least 14 days.

Table. Antimicrobial Treatment for Invasive Group A Streptococci (GAS) Infections

Infection	Treatment
Necrotizing fasciitis/myositis	Early and extensive surgical debridement, plus: Empirical treatment -Adults: piperacillin/tazobactam 4.5 g/IV q8h+ clindamycin 600 mg/IV q8h + vancomycin 1 g/IV q12h or linezolid 600 mg/IV q12h. -Children: penicillin G crystalline 200,000 UI/kg/IV/d divided in four doses (q6h) + clindamycin 40 mg/kg/IV/d divided in three doses (q8h) + third generation cephalosporin in usual doses. ¹ If GAS confirmed , de-escalate to: -Penicillin G (adults 4 million units / q4h IV, children, 200,000 units /kg iv daily, divided in q4-6h, maximum daily dose 24 million units) + clindamycin (adults, 900 mg IV / q8h, children 40 mg IV divided in 3 doses (q8h), maximum daily dose 2.7 g).

¹ In case of suspicion of methicillin-resistant *S. aureus*, add vancomycin 60mg/kg/iv/d divided in 3 doses (q8h).

Infection	Treatment
Streptococcal toxic shock	<p>Patient with community-acquired sepsis, empirical treatment:</p> <p><u>-Adults:</u> piperacillin/tazobactam 4.5 g/IV q6-8h or ertapenem 1 g/IV q24h; consider add vancomycin 1 g q12h, according to local epidemiology.</p> <p><u>-Children (> 1 month of age):</u> ceftriaxone 100 mg/kg/IV/d in one dose q24h or cefotaxime 200 mg/kg/IV/d divided in four doses (q6h) + ampicillin 200 mg/kg/IV/d divided in four doses (q6h).</p> <p>Patient with sepsis/toxic syndrome, confirmed GAS, de-escalate to:</p> <p>-Penicillin G (adults 4 million units / q4h IV, children, 200,000 units /kg IV daily, divided in q4-6h, maximum daily dose 24 million units) + clindamycin (adults, 900 mg IV / q8h, children 40 mg IV divided in 3 doses (q8h), maximum daily dose 2.7 g).</p> <p>-Consider adding adjuvant treatment with immunoglobulin G (dose in adults and children: 1 g/kg IV on day 1, followed by 0.5 g/kg IV on days 2 and 3).</p>
Bacteremia (in the absence of shock, organ failure or necrotizing infection)	<p>Confirmed GAS:</p> <p>-Penicillin G (adults 4 million units / q4h IV, children, 200,000 – 400,000 units /kg IV daily, divided in q4-6h, maximum daily dose 24 million units) + clindamycin (adults, 900 mg IV / q8h, children, 40 mg IV divided in 3 doses (q8h), maximum daily dose 2.7 g).</p>

Disclaimer: Antimicrobial treatment recommendations are for informational purposes only and are in no way a substitute for the advice, diagnosis, treatment or recommendations of health care professionals.

Risk communication

- Promote the dissemination of public health messages to physicians and the general population to improve early recognition, reporting and prompt initiation of treatment of these cases.
- Inform and educate about the risk of invasive disease among household contacts of scarlet fever cases, emphasize proper hand hygiene and adequate indoor ventilation as additional protective measures.

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