Surge of strep A infections, including more dangerous type, has affected Denmark since 2022, especially in the elderly

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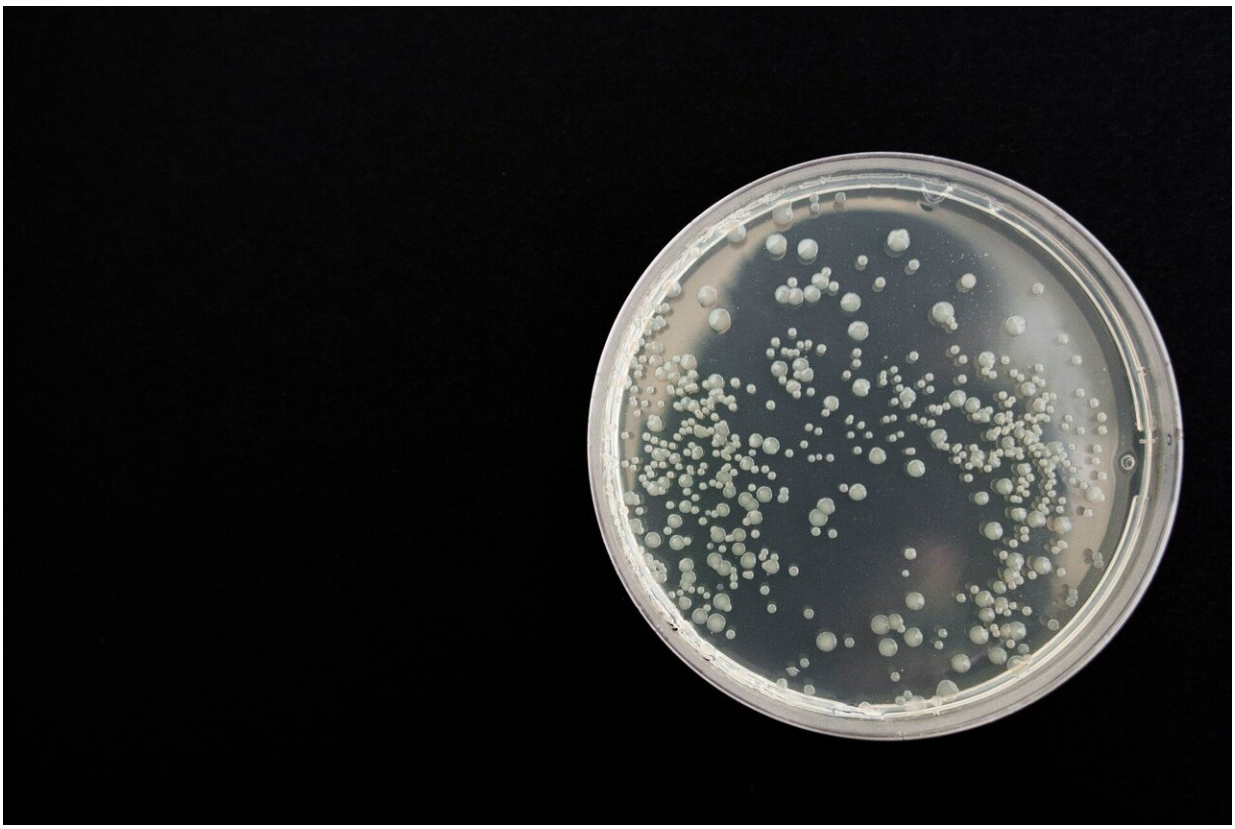

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During the 2022-2023 winter season Denmark experienced a surge in infections caused by group A streptococci (GAS), including the more

dangerous, invasive types of infections (iGAS). Incidence of iGAS is highest among the elderly, but the largest relative increase from previous seasons was seen among children. The study is being presented to the European Congress of Clinical Microbiology & Infectious Diseases (ECCMID 2023, Copenhagen, 15-18 April), by Thor Bech Johannesen and Steen Hoffmann, Statens Serum Institut, Copenhagen, Denmark, and colleagues.

Following the implementation of lockdown measures to prevent spread of COVID-19 in March 2020, the number of invasive infections caused by GAS, including more dangerous invasive types (iGAS), decreased. However, during November 2022, an increasing number of these infections occurred in all regions of Denmark, with incidence rates reaching three times the pre-lockdown levels in January-March 2023. While there is no policy on mandatory reporting of GAS infection in Denmark, clinical microbiology laboratories nationwide submit isolates of iGAS to Statens Serum Institut (SSI) for further characterization on a voluntary basis.

Since 2018 approximately 90% of all iGAS cases in Denmark have been submitted to SSI for whole genome sequencing (WGS). For the period 2018 through March 2023, the authors extracted these WGS data and all records from the Danish Microbiology Database (MiBa) with culture-proven GAS and iGAS (invasive GAS being defined as GAS isolated from an anatomical region that should be sterile). Repeated specimens from the same patient of either GAS or iGAS within a 30-day-period were excluded. Potential date of death was collected from the Danish Civil Registration System.

Incidence of GAS as well as iGAS decreased notably following the restrictions in March 2020. The incidence of both remained at low levels until October 2022 and then dramatically increased in December 2022, peaking between January and March 2023. The incidence of iGAS was

highest in the age groups 65-84 years (4.0/100,000) and 85+ years (5.2/100,000). Fatalities from iGAS in absolute numbers have also increased, but the case fatality rates for all age groups were similar to previous seasons (approximately 15% overall, and 30% in those aged 85 years and older—rates in children are low and vary due to low absolute numbers).

The strains ST28 *emm*1 (also known as M1) and ST36 *emm*12, which have both been virtually absent since April 2020, accounted for 53% and 28%, respectively, of iGAS infections in 2023. A new subvariant of M1 emerged in 2022 and has become the dominant subvariant in 2023, accounting for 30% of all iGAS cases. In addition to a distinct core genome, this variant is characterised by its acquisition of a bacteriophage carrying the virulence factor *SpeC*, a known key exotoxin. From initial analyses, the novel M1 subvariant does not appear to be significantly more virulent than other M1 variants circulating in Denmark, however, M1 variants in general are more likely to cause invasive disease, and iGAS patients infected with M1 variants are more often in need of intensive care. No significant difference was found in mortality rates for individual variants.

The authors conclude: "Since December 2022, the incidence of iGAS-cases in Denmark has been unusually high, partly driven by the emergence of a new M1 subvariant, which has been responsible for 30% of iGAS cases in 2023. Although a large proportion of the variants currently circulating in Denmark have a high capacity for virulence, we estimate that the current surge is largely due to extensive community spread, possibly combined with a low level of immunity in the general population following two years of extraordinarily low incidence rates."

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