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Current scenario of recently rising up cases of invasive group A streptococcal (iGAS) infections in younger children in many European nations: clinical management and prospective counteracting measures – an update

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Dear Editor,

The frequency of cases of invasive group A streptococcal (iGAS) infections in children younger than 10 years of age has been rising in many European nations this year, especially since September 2022. These countries include France, Ireland, The Netherlands, Sweden, and the UK. In the same time frame, multiple fatalities in children under the age of 10 due to iGAS illness have been recorded from countries including France, Ireland, and the UK as reported by WHO[1]. For a same time span, the number of documented cases of iGAS in children in both France and the UK is much greater than it was before the epidemic[1].

Group A *Streptococcus* (GAS) infection rates dropped during the COVID-19 pandemic, but recent reports to WHO/Europe and the European Centre for Disease Prevention and Control (ECDC) indicate an uptick in GAS infections. As coinfection of viruses with GAS may enhance the risk of iGAS illness, it is probable that the recent increase in the circulation of respiratory viruses is also related to the rise in instances of iGAS disease in children. This includes seasonal influenza and respiratory syncytial virus.

Although most patients don't have a localized source of infection, skin lesions caused by trauma, surgery, or persistent skin disorders are the most often reported risk factors[2–5]. Heart disease, diabetes, and cancer are just some of the pre-existing illnesses linked to an increased risk of infection as reported in literature[6–8]. The H1N1 outbreaks provided more evidence that influenza has a significant effect on susceptibility to iGAS infection[9,10]. Studies have indicated that injection drug users had a higher risk of iGAS infection than the general population. This is likely owing to the greater vulnerability of injection drug users, both directly and indirectly, due to their compromised immune systems and substandard living circumstances[11,12].

Among children, varicella infection is a major risk factor for necrotizing fasciitis and other infections of the soft tissues[13,14]. It is unclear how varicella increases susceptibility to necrotizing fasciitis[14]. Varicella infection is associated with immunosuppression, especially a decline in humoral immunity, which may be caused by the illness itself or by the pox lesions that facilitate a portal of entry to the dermal and fascial layers[15]. This second theory is backed up by the fact that patients seldom develop secondary pox lesions on top of the necrotizing fasciitis[16] and by the fact that streptococcal toxic shock syndrome (TSS) and iGAS illness without necrotizing fasciitis may occur after varicella infection[17,18].

Treatment of severe iGAS illness includes supportive care, such as intravenous fluids and electrolytes; targeted medication, such as antibiotics; and steps to reduce or neutralize the consequences of bacterial toxin production, if needed. For treatment of possible iGAS, one should see a specialist in infectious illnesses. Management of *Staphylococcus aureus* and GAS with a beta-lactamase stable beta-lactam (i.e. cloxacillin) in combination with clindamycin is recommended for ameliorating TSS or suspected TSS as part of an empiric antimicrobial treatment plan. For populations or regions with high rates of methicillin-resistant *Staphylococcus aureus* (MRSA) colonization, it may be wise to administer empiric vancomycin awaiting culture findings due to the link between TSS and MRSA.

Clinical manifestations and risk factors for iGAS, MRSA colonization risk, exposure to potential water-borne pathogens,

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and predisposing risk factors to clostridial or polymicrobial myonecrosis, all these together influence the decision to initiate empiric antibiotic therapy for necrotizing fasciitis (linked with chemotherapy, recent gastrointestinal surgery, penetrating trauma, intra-abdominal or pelvic focus of infection, or pregnancy associated complications). As a rule, the first line of treatment is effective against a wide variety of gram-positive, gram-negative, and anaerobic bacteria, with GAS and Clostridia receiving specific attention. The microbiological identification of infections may be speeded up and early debridement can be performed, all thanks to urgent surgical exploration for necrotizing fasciitis diagnosis. A beta-lactam-beta-lactamase inhibitor (such as piperacillin–tazobactam) or a carbapenem along with clindamycin, may be used as an empiric regimen, with the addition of vancomycin for MRSA coverage being considered based on local incidences and risk factors[19]. Some specialists recommend penicillin with clindamycin for first-line treatment in otherwise healthy youngsters who have none of the predisposing risk factors for organisms other than GAS. When possible, data from Gram staining, culture, and antibiotic sensitivity testing should be used to individualize antibiotic treatment.

For confirmed instances of GAS, penicillin is still the go-to therapy[20]. All severe iGAS cases, both those treated emphatically and those confirmed by culture, should be treated with clindamycin, a powerful inhibitor of toxin production with potent antimicrobial action that is independent of inoculum size. There is evidence to suggest that this combination may enhance results in severe iGAS infection[21]. After 48–72 hours of therapy with clindamycin, the drug may be stopped if the patient is hemodynamically stable, blood becomes sterile, and no further advancement of necrosis is observed.

The danger of fatal iGAS infection may be reduced by cutting down on the spread of GAS. Patients with iGAS disease have a better chance of survival if their condition is diagnosed early and treatment with a combination of targeted and supportive care is begun without delay. Therefore, it is important for public health officials to think about ways to educate doctors and the public about GAS infections and to promote timely diagnosis and treatment in accordance with national recommendations. Children with severe respiratory symptoms, a history of viral illness (including chickenpox), or close contact with a scarlet fever patient should have GAS infections to be considered in their differential diagnosis. National criteria should be used to identify, evaluate, and manage close contacts of iGAS patients.

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Conflicts of interest disclosure

The authors declare that they have no financial conflict of interest with regard to the content of this report.

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