

## Antibiotic treatment for streptococcal pharyngitis: time for a new approach?

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### To the Editor,

We would like to draw attention to the need to make appropriate antimicrobial prescriptions in regard to Group A *Streptococcus* (GAS) *pharyngitis*. Furthermore, we would like to encourage the public at large to follow official guidelines, not to fall for misinformation, and pediatricians to follow appropriate antimicrobial stewardship.

Acute pharyngitis in children is one of the most common causes of pediatric evaluation. It is often caused by a viral infection, but in 20-30% of cases the etiological agent is GAS (1). Nevertheless, a wide range of studies has shown that 20 up to 50% of antibiotic prescriptions are needless or inappropriate, with patients receiving broad-spectrum antibiotics for viral infections or antibiotic treatment courses significantly longer than needed (2). Therefore, the management of antibiotic therapy in this scenario could be improved. Italy is indeed one of the countries with the highest rate of antibiotic prescriptions for children in Europe. Selective pressure due to inappropriate prescriptions is the leading cause of arising antibiotic resistance. The main way to make appropriate therapeutic prescriptions starts with an appropriate diagnosis. Differential diagnosis based only on clinical features could be hard for physicians. Scoring systems are a valid point of care tool for risk assessment and management of patients with pharyngitis. There is no unanimous international consensus regarding the utility of microbiological confirmation. The throat culture is the gold standard technique, but it has high costs and delayed

outcomes; conversely, Rapid Antigen Detection Test (RADT) nowadays has adequate accuracy, lower costs and, therefore, is preferred. Because GAS colonization occurs in 5%–20% of healthy children, GAS detection is not definitive proof of disease. Moreover, Italy lacks national guidelines for the management of acute GAS pharyngitis.

Because of its narrow spectrum, low cost, palatability, and effectiveness in preventing complications, amoxicillin is the antibiotic of choice used (50 mg/kg, max 1000 mg) (3). Although all these recommendations are present in every treatment guideline, co-amoxiclav and cephalosporins are often overly prescribed for pharyngitis by pediatricians.

The natural history of untreated streptococcal pharyngitis is clinical resolution and antibiotics only partially relieve symptoms. The goal of therapy is to prevent suppurative complications, such as peritonsillar and retropharyngeal abscesses, and non-suppurative ones, such as acute rheumatic fever (ARF) and post-streptococcal glomerulonephritis. Other reasons include reducing acute morbidity and avoiding transmission to close contacts.

ARF is a multisystemic autoimmune reaction to GAS infection with a low incidence in high-income countries. The incidence of ARF in Italy has been scarcely investigated and limited to the main regions of Northern and a single region of Central Italy. A multicenter and retrospective study conducted in Tuscany in the period between 2010 and 2019 stated an ARF annual incidence ranged from 0.91 to 7.33 out of 100,000 patients (4). Antibiotics played a main

role in determining the reduction of ARF but they were not the only agent since this decrease in incidence started previously, before their administration on large scale numbers. The improvement of socio-economic conditions may be considered a main factor as well. A 2005 meta-analysis showed that the number of pharyngitis cases needed to treat with penicillin to prevent one case of ARF is 53 (5). These data may reflect an overtreatment if compared to a minimum reduction of the relative risk of ARF. On the other side, the chance of harming patients by administering inappropriate antibiotics is consistent. Inappropriate antibiotic prescriptions are harmful on a large-scale level because they boost antimicrobial resistance and on an individual level because they are related to adverse drug events, such as allergic reactions (e.g., anaphylaxis, skin rash) and microbiome disruption-related conditions (e.g., *Clostridium difficile* infection). Their clinical management requires an expensive healthcare burden, which is in most cases avoidable. Taking these considerations into account, it may be time in Italy to consider a more selective treatment.

Since December 2022 increasing numbers of GAS infections among children have been stated across the United Kingdom (UK) and other European countries such as Ireland, France, Netherlands, Spain, and Sweden (6). At the same time in Italy from January-February 2023 a peak of GAS infections (pharyngotonsillitis and scarlet fever) was referred by clinicians and the epidemiological examination is still in progress. This peak could probably be due to a reduced immune stimulation secondary to the SARS-COV2 pandemic, causing the so-called “immune debt”. In fact, several public health interventions had been put in place during the COVID-19 pandemic including border control, quarantine, rapid contact tracing, hand hygiene, community-wide wearing of face masks and social distancing measures in order to avoid the risk of transmission. These measures not only contained the pandemic but also limited the transmission of respiratory viruses and bacteria, quite limiting the immunity stimulation. Subsequently, now that pandemic restrictions are over, a sort of “rebound effect” of infections could have happened. This is in line with the concomitant enhancement of other respiratory

infections. Another theory suggests that COVID-19 infections could have caused immune dysregulation in children (the so-called “immune theft”), thus leaving children more susceptible to infections (6). Thus, at this historic moment with the peak of streptococcal infection in Europe, despite its mild clinical manifestations, therapy represents a determining controversial issue. On one hand, we are now aware of the huge burden and impact of inappropriate antibiotic administrations, on the other we are facing a boosting peak of infections which will probably lead to massive antibiotic prescriptions. From this point of view, we would like to draw attention towards the need to make appropriate antimicrobial prescriptions.

Screening of contacts and start of post-exposure prophylaxis is another key element. As a matter of fact, during the SARS-COV2 pandemic massive swab testing was applied to maximize case detections. In this setting, diagnostic GAS testing or an empiric treatment of asymptomatic contacts of patients with acute streptococcal pharyngitis is not recommended. A microbiological test should only be applied in case of onset of clinical signs or symptoms. An indiscriminate amount of swab tests could detect GAS pharyngeal chronic carriers who are unlikely to spread the infection and have no risk of developing suppurative or nonsuppurative complications. Hence, children identified as chronic pharyngeal GAS carriers do not generally require antibiotic treatment. We would encourage the public at large to follow official guidelines, not to fall for misinformation, avoiding massive testing of contacts, and pediatricians to follow appropriate antibiotic stewardship. We suppose that after the immune debt will be paid the number of GAS infections will be back to pre-COVID-19 standards. Meanwhile, strict prescription protocols should be followed, quite limiting wide-spectrum drugs and leaving viral infections untreated. Otherwise, we should probably face harder challenges in terms of the onset of antimicrobial resistance, drugs’ adverse effects, and increasing costs of healthcare systems.

**Conflict of Interest:** Each author declares that he or she has no commercial associations (e.g. consultancies, stock ownership, equity

interest, patent/licensing arrangement etc.) that might pose a conflict of interest in connection with the submitted article.

**Authors Contribution:** The authors confirm contribution to the paper as follows: A Chiaretti and AG contributed to the conception and design. The first draft of the manuscript was written by LDS, A Caroselli, A Curatola and VP. All authors reviewed the draft and approved the final version of the manuscript.

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Received: 10 June 2023

Accepted: 10 July 2023

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