OFFICE OF THE DEPUTY PRIME MINISTER
MINISTRY FOR HEALTH

Invasive Group A Streptococcus

Dear Doctor,

During 2022, a number of European countries (including Iceland, France, the Netherlands, Sweden and the United Kingdom) have reported an increase the number of cases of **invasive Group A Streptococcus** (iGAS) disease among children less than ten years of age. It is important to emphasise that iGAS is defined as an **infection of a normally sterile body organ** – especially the blood – caused by ***Streptococcus pyogenes***. It does not include typical presentations such as tonsillitis or scarlet fever.
During the same period, especially since September, a number of deaths associated with iGAS in children less than 10 years of age have also been reported, including from Ireland, France, and the UK. The observed increases reported to the European Centre for Disease Prevention and Control (ECDC) and WHO Regional Office for Europe have followed a period of reduced incidence of Group A streptococcus infections observed during the COVID-19 pandemic. The prevalent hypothesis suggests that the increase in iGAS cases in children is **not due to a more virulent or transmissible emm type** of *S. pyogenes*. Rather, children have been kept fairly cloistered from respiratory pathogens throughout the COVID-19 pandemic due to the necessary mitigation efforts, social distancing, and school closures. Now with children attending school without a mask and life largely back to normal, the ability for infections to circulate through the paediatric population has been restored. A significant proportion of children, who have not seen such infections for more than two years, are now being exposed to them. This would also explain the recent increased circulation of respiratory viruses, including seasonal influenza, respiratory syncytial virus (RSV) and adenovirus.

Group A streptococcus (GAS) is a bacterium that can often be found in the throat and on the skin and in most cases does not cause symptoms. Group A streptococcal bacteria can cause pharyngitis/tonsillitis, scarlet fever, impetigo, and cellulitis. In rare cases GAS bacteria can also cause a severe, life-threatening invasive disease (iGAS), which may manifest as bacteraemia, pneumonia, or skin and bone infection (cellulitis, osteomyelitis, necrotising fasciitis). Children with viral infections such as varicella (chickenpox) or influenza are at higher risk of developing iGAS infection.

The symptoms depend on the site of infection. Strep A infection can present in various ways:

- Strep throat causes sore throat and tonsils, fever, cervical lymphadenopathy, muscle pain and tiredness. Coryza and cough (without evidence of a chest infection) are suggestive of a viral and not a bacterial infection.
- Scarlet fever causes sore throat, fever and swollen lymph nodes accompanied by a generalised rash that feels rough to the touch and is accentuated in the flexures
- Impetigo causes skin sores and blisters
- Cellulitis causes pain, redness and swelling in areas of the skin

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Invasive GAS infection is associated with isolation of GAS from a normally sterile site, such as blood, cerebrospinal fluid, joint aspirate, pericardial/peritoneal/pleural fluids, bone, endometrium, deep tissue or abscess at operation or post-mortem.

Early signs and symptoms of necrotising fasciitis include:

- Severe pain and swelling, often rapidly increasing
- Fever (>38°C)
- Redness at wound site

Early signs and symptoms of Streptococcal Toxic Shock Syndrome (STSS) include:

- Sudden onset of generalised or localised severe pain, often in an arm or leg
- Dizziness and /or confusion
- Flu-like symptoms such as fever, chills, muscle aches, nausea, vomiting
- A flat red rash over large areas of the body (only occurs in 1 in 10 cases)

Prevention of viral illnesses is likely to be important in reducing the risk of invasive disease, therefore **vaccination against seasonal influenza and COVID-19** should be promoted. Adequate **hand and respiratory hygiene**, as well as good indoor ventilation, should continue to be emphasized as the most important protective measures during this winter season. Chemoprophylaxis to prevent GAS infection in contacts of an identified case is not recommended other than in cases of invasive disease, and even then primarily to immediate family contacts under public health supervision.

Reducing the transmission of GAS will help to reduce the risk of severe iGAS infection. Prompt testing and treatment of GAS infections is encouraged. Group A Streptococcus can be effectively treated with several first line antibiotics. Indeed, **local isolates of *S. pyogenes* are 100% sensitive to penicillin, amoxicillin and co-trimoxazole**. Unfortunately, local **resistance to macrolides has increased to almost 25%**. Therefore, empiric treatment of potential GAS infections with formulations such as clarithromycin or azithromycin should be done with laboratory guidance. When first line options are available, use of extensively broad-spectrum antibiotics - such as third generation cephalosporins - to treat GAS is unnecessary and only serves to encourage antibiotic resistance.
At the same time, it is essential that antibiotic prescribing remains judicious and avoided in situations which suggest a viral, rather than bacterial, infection.
Annex 1 includes specialist advice to support you in **determining whether pharyngitis is likely to be due to GAS** and when antibiotics are therefore indicated. As always one is to use his clinical acumen in managing cases and refer to further specialist advice as necessary.

Regards

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Annex 1: Guidelines for doctors to detect Group A streptococcal pharyngitis

The Centor scoring system is a useful tool to aid in diagnosing pharyngitis caused by Group A streptococcus (*Streptococcus pyogenes*) in children from 3 years of age and adults. The tool also provides guidance when antibiotics should be prescribed. A Centor Score calculator is available in the "Calculators" section of the National Antibiotic Committee's "Antibiotics Malta" app, which many GPs and paediatricians already use in their practice. The Antibiotics Malta app can be downloaded in either android or Apple format, from Play or App Stores respectively. It can also be found online at: https://www.mdcalc.com/calc/104/centor-score-modified-mcisaac-strep-pharyngitis.
The tool should not be used in children below 3 years of age. Individuals with cough and coryza, without signs of a chest infection, are very likely to have a viral infection and should not be given antibiotics. Every doctor should use his or her clinical acumen when assessing a patient and should not solely rely on this tool.
The Centor score assigns points for specific criteria, as follows

Age	
3-14 years	1
15- 44 years	0
≥ 45 years	-1
Fever >38°C (during previous 24 hours)	1
Absence of cough or coryza (inflammation of the nasal mucous membranes)	1
Pus or exudate on tonsils	1
Tender/swollen anterior cervical lymph nodes	1

The following interpretation should be used:

Score	Risk of Strep infection	Management
0	1 - 2.5%	No antibiotics
1	5 - 10%	No antibiotics
2	11 - 17%	Throat swab for culture & sensitivity or rapid antigen test.
3	28 - 35%	Consider delayed antibiotic prescription
4/5	51 - 53%	Treat immediately with antibiotics

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The FeverPain scoring system is another useful tool to aid in diagnosing pharyngitis caused by Group A streptococcus (*Streptococcus pyogenes*) in children from 3 years of age and adults. The tool provides guidance when antibiotics should be prescribed. On online FeverPAIN Score calculator is available at https://www.mdcalc.com/calc/3316/feverpain-score-strep-pharyngitis). The tool should not be used in children below 3 years of age. Individuals with cough and coryza, without signs of a chest infection, are very likely to have a viral infection and should not be given antibiotics. Once again, every doctor should use his or her clinical acumen when assessing a patient and should not solely rely on this tool.

These are the FeverPAIN criteria

- Fever ≥38°C (during previous 24 hours)
- Onset of symptoms within last 3 days
- No cough or coryza (inflammation of the nasal mucous membranes)
- Pus on tonsils
- Severely inflamed tonsils

Each criterion is worth 1 point with a maximum score of 5

Score	Risk of Strep infection	Management
0-1	13-18%	No antibiotics
2	30-35%	Consider delayed antibiotics
3	39-48%	Consider delayed antibiotics
4/5	62-65%	Treat with antibiotics

Higher scores would suggest a likely bacterial (streptococcal) cause.