

## PedsCases Podcast Scripts

This is a text version of a podcast from PedsCases.com on “**Invasive Group A Streptococcal Infections – CPS Podcast.**” These podcasts are designed to give medical students an overview of key topics in pediatrics. The audio versions are accessible on iTunes or at [www.pedscases.com/podcasts](http://www.pedscases.com/podcasts).

### **Invasive Group A Streptococcal Infections – CPS Podcast**

Developed by Dr. Ola Rydz and Dr. Dorothy Moore for PedsCases.com.  
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#### **Introduction:**

Hello, my name is Ola Rydz and I am a fourth-year General Paediatrics Resident at the Stollery Children’s Hospital in Edmonton, Alberta. This podcast was made in conjunction with PedsCases and the Canadian Paediatric Society (CPS). We will summarize the recently published 2019 CPS Practice Point regarding management and prophylaxis of invasive group A streptococcal infections, which updates the previous practice point published in 2010. This podcast was developed with Dr. Dorothy Moore, Associate Professor of Pediatrics at McGill University in Montreal, Canada. She is the lead author of the CPS statement that we will be reviewing today. For additional information and to view the complete CPS Statement, please visit [www.cps.ca](http://www.cps.ca). The script for this podcast can be viewed at [www.pedscases.com](http://www.pedscases.com).

#### **Clinical case:**

Let’s begin with a case to put this podcast into context.

*You are the junior resident working in the Pediatric Emergency Department. You are assessing Jeremy, a 4 year old boy who has been brought in by his parents for assessment of a rash. The triage note reports that he is previously healthy, although he had recently been sick with a sore throat that was managed symptomatically with acetaminophen.*

*Upon walking into the exam room, you note that Jeremy looks unwell.*

*His temperature is 39.2 degrees Celsius, his HR is 150 bpm, his BP is 100/72, and he is saturating 100% on RA with a RR of 34.*

*He appears drowsy, but upon your entry into the room, begins to cry. You note he is taking care not to move his leg. The anterolateral aspect of his shin is covered by a deeply erythematous lesion with poorly defined margins. Edema extends beyond these margins to the level of his knee. He is exquisitely tender to touch over the lesion, and a rapid head-to-toe assessment reveals no other focus for his fever. You quickly come to the conclusion that this may represent necrotizing fasciitis.*

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Keep this case in mind as we move through the podcast.

### **Objectives:**

The objectives of this podcast are to summarize the CPS guidelines on management and prophylaxis of invasive group A streptococcal infections (IGAS), and specifically to:

1. Review the epidemiology of invasive Group A Strep infections
2. Highlight the various presentations of invasive Group A Strep infection
3. Review management of severe invasive Group A Strep disease
4. Provide case definitions for definite and probable cases of invasive Group A Strep infection
5. Outline the management of close contacts of invasive Group A Strep infection

### **To begin, let's discuss the epidemiology of GAS infections.**

The incidence of invasive Group A Strep disease has been increasing in Canada over the past decades, with the highest rates in infants, young children, and the elderly. Many of the risk factors for invasive Group A Strep among adults, such as HIV infection, alcohol abuse and intravenous drug use, do not apply to children. However, children are at increased risk if they have had recent varicella infection or pharyngitis. For adults and children alike, recent soft tissue trauma and NSAID use are risk factors as well.

Household contacts of those with severe invasive Group A Strep have 20 to 100 times the rate of disease relative to the general population. Most secondary cases occur within 7 days of the index case. Nosocomial transmission is well documented, including transmission to health care workers, but transmission in other settings, such as child care centers and schools, appears rare.

*Let's apply what we've just heard to our case. At 4 years old, Jeremy is of an age with higher rates of IGAS. Furthermore, he has recently had pharyngitis, which confers an increased risk. But, how would we classify his clinical presentation?*

### **This brings us to the various clinical presentations of IGAS.**

IGAS disease can be classified as non-severe or severe.

Non-severe IGAS refers to bacteremia, cellulitis, wound infections, soft tissue abscesses, lymphadenitis, septic arthritis, or osteomyelitis, but without evidence of streptococcal toxic shock syndrome (TSS) or soft tissue necrosis.

By contrast, severe invasive disease refers to one of the following presentations.

1. Streptococcal toxic shock syndrome.
  - It is important to know that streptococcal toxic shock is clinically indistinguishable from staphylococcal toxic shock syndrome. It is characterized by hypotension, defined as systolic blood pressure less than the 5<sup>th</sup> percentile for age in children, and at least 2 of the following:

- a. renal impairment (defined as creatinine level of at least 2X upper limit of normal for age or 2X patient's baseline);
  - b. Coagulopathy (platelet count of  $100 \times 10^9/L$  or lower, or disseminated intravascular coagulation);
  - c. Liver function abnormality (levels of aspartate aminotransferase, alanine aminotransferase or total bilirubin  $\geq 2X$  the upper limit of normal);
  - d. Acute respiratory distress syndrome; or,
  - e. Generalized erythematous macular rash that may desquamate later;
2. Soft-tissue necrosis (which includes necrotizing fasciitis (NF), myositis or gangrene);
    - The majority of NF is polymicrobial, but of monomicrobial cases, IGAS is a leading cause. Necrotizing fasciitis presents with severe pain, induration, hemodynamic instability, and rapid progression. Necrotizing fasciitis caused by polymicrobial infection or clostridia is associated with presence of crepitus, while necrotizing fasciitis related to invasive Group A Strep is more commonly associated with a generalized rash, pharyngitis, conjunctivitis, and/or strawberry tongue.
  3. Pneumonia, with isolation of Group A Strep from a sterile site such as pleural fluid. Note that bronchoalveolar lavage (BAL) is not considered to be from a sterile site. Clinically, Group A Strep pneumonia is indistinguishable from other causes of pneumonia, but it tends to progress more rapidly with development of large pleural effusions
  4. Meningitis – which is the rarest presentation of severe invasive Group A Strep.
  5. A combination of the above.
  6. Other life-threatening condition or Infection resulting in death

**Classifying the presentation of the invasive Group A Strep disease is important, because it helps to guide management. So, with that in mind, let's discuss what management looks like.**

The management of severe invasive Group A Strep disease should involve consultation with an infectious disease specialist, and always includes 3 main principles.

1. Supportive treatment with the use of fluid and electrolytes;
2. Specific therapy with antimicrobials; and,
3. The use of measures to minimize or neutralize the effects of toxin production.

Let's discuss antimicrobials further, knowing that specific antimicrobial therapy will vary according to the clinical presentation.

For TSS, empiric antimicrobial therapy should include coverage of both *Staphylococcus aureus* and GAS with a beta-lactamase stable beta-lactam, i.e. cloxacillin or a first generation cephalosporin. Due to increasing rates of MRSA, consideration should also be given to addition of vancomycin depending on local prevalence and risk factors.

By comparison, necrotizing fasciitis is often polymicrobial in etiology, and thus empiric regimens should offer broader coverage, including either a beta-lactam-beta-lactamase inhibitor combination (i.e. piperacillin-tazobactam) or a carbapenem, again with consideration of the addition of vancomycin for MRSA coverage. In otherwise healthy children with no risk factors for organisms other than Group A Strep, penicillin may suffice as the initial beta-lactam antibiotic.

All suspected or confirmed severe invasive Group A Strep cases should also receive clindamycin as part of empiric therapy. It is a potent inhibitor of toxin production and its antimicrobial activity is unaffected by inoculum size. Use of clindamycin has been associated with improved outcomes in severe invasive Group A Strep. However, due to high rates of resistance to clindamycin, it is not recommended for monotherapy of IGAS.

Finally, IVIG should be considered on the day of clinical presentation in the treatment of streptococcal TSS or other severe invasive toxin-mediated disease, particularly if the patient is severely ill or the condition is refractory to initial fluid therapy. Besides neutralizing toxin, IVIG also works to improve phagocytic killing and suppress inflammation.

It is very important to know that, in early stages, both TSS and necrotizing fasciitis may pose diagnostic challenges, as full criteria may not yet be met. However, in any situation where either of these diagnoses is suspected, urgent empiric therapy with antibiotics and clindamycin is warranted. Progression is often rapid, and very close follow-up is required.

The above summarizes empiric therapy for presumptive invasive Group A Strep infection. For necrotizing fasciitis, definitive diagnosis is based on emergent surgical exploration which, in addition to therapeutic debridement, yields material for gram stain and culture; these results allow antibiotics to be tailored to a specific organism.

For all confirmed cases of invasive Group A Strep, the treatment of choice is penicillin, as to date there has been no documented Group A Strep resistance to penicillin. If the patient is hemodynamically stable, the blood is sterile, and there is no further necrosis, clindamycin may be discontinued after 48-72 hours of treatment.

*Returning to our case: you have given Jeremy a bolus of 40 ml/kg NS, and initiated therapy with piperacillin-tazobactam plus clindamycin pending emergent plastic surgery consult. You know that surgical debridement is a crucial component of management of necrotizing fasciitis. Jeremy's hemodynamics stabilized, and he has been rushed to the OR, so you go home for the night. When you return the next day, there is a new result flagged on his chart: cultures from tissue obtained in the OR are growing only one organism: Gram positive cocci in chains consistent with Group A Strep. What are your next steps, with regards to notifying Public Health and offering prophylaxis to contacts?*

The first thing to know is that confirmed cases of invasive Group A Strep are reportable in **all** provinces and territories in Canada, and they are also reported to the Public Health Agency of Canada. In some regions, probable cases are also reportable. So, how are confirmed and probable cases defined?

A **confirmed case** requires isolation of Group A Strep from a normally sterile site, with or without clinical evidence of severe invasive disease. This means that even non-severe cases of invasive Group A Strep should be reported, assuming that invasive Group A Strep has been isolated from a sterile site.

By contrast, the consensus definition for a **probable case** of invasive Group A Strep requires invasive disease in the absence of another identified etiology, and with isolation of Group A Strep from a non-sterile site, such as a bronchoalveolar lavage.

Once a case of invasive Group A Strep been confirmed, close contacts must be notified.

Close contacts are defined as:

- Household contacts who, in the previous seven days, have spent at least 4 hours per day on average or a total of 20 hours with the case.
- Non-household persons who shared the same bed with the case or had sexual relations with the case.
- Persons who have had direct mucous membrane contact with the oral or nasal secretions of a case (e.g., mouth-to-mouth resuscitation, open mouth kissing) or unprotected direct contact with an open skin lesion of the case.
- Injection drug users who have shared needles with the case.
- Contacts in selected child care settings (mainly family or home daycare settings)
- Selected hospital contacts
- Selected contacts in long-term care facilities

(For more information on what qualifies as close contact in child care, hospital or a long-term care facility, please see the PHAC website – the link will be made available in the transcript of this podcast <http://www.phac-aspc.gc.ca/publicat/ccdr-rmtc/06vol32/32s2/index-eng.php>).

All close contacts of any confirmed case of invasive Group A Strep, whether the disease was severe or non-severe, should be educated about signs and symptoms of invasive Group A Strep, and counseled to seek medical attention should they develop symptoms or a febrile illness within 30 days of diagnosis of the index case.

By contrast, chemoprophylaxis is only offered to close contacts of confirmed cases of **severe** invasive Group A Strep, who have been exposed to the index case anytime from 7 days prior to symptoms, to 24 hours after initiation of antimicrobial therapy. Chemoprophylaxis is ideally offered within 24 hours of diagnosis in the index case, but is recommended up to 7 days after last contact with the case.

First-generation cephalosporins are the chemoprophylactic agents of choice, as they are more effective than penicillins in eradicating Group A Strep colonization. Second line agents include macrolides or clindamycin. The duration of therapy for any of these agents is 10 days.

*Let us apply these concepts to our case. Jeremy has necrotizing fasciitis with isolation of Group A Strep, so he is classified as having a confirmed case of severe invasive Group A Strep. Jeremy attends day care 2 mornings per week, and is otherwise cared for at home by his mother. He has no siblings and his father works full time.*

*You notify regional Public Health authorities of the diagnosis. They approach Jeremy's parents and prescribe a 10-day course of cephalexin to each parent; as close household contacts, they qualify for chemoprophylaxis. Public Health then reaches out to the daycare, as the decision to provide education around symptoms of invasive Group A Strep versus offering chemoprophylaxis to other attendees will rely on information provided to them by the daycare.*

### **Summary:**

Let us conclude this PedsCases podcast with a few take home points on invasive Group A Strep management.

- Invasive Group A Strep incidence has been increasing, with children and the elderly at greatest risk
- Invasive Group A Strep causes a wide spectrum of disease, most often TSS, necrotizing fasciitis, bacteremia with no focal infection, and pneumonia
- Empiric therapy should always include a beta-lactam antibiotic and clindamycin
- All invasive Group A Strep, regardless of severity, is reportable
- All close contacts of those with invasive Group A Strep need to be alerted to signs and symptoms of invasive Group A Strep, but only a subset of these require chemoprophylaxis
- Where chemoprophylaxis is indicated, a 10 day course of a first generation cephalosporin is the recommended first line therapy

That concludes our PedsCases podcast on invasive Group A Strep management and chemoprophylaxis, brought to you by PedsCases and the Canadian Pediatric Society. Thanks for listening to PedsCases podcasts!

### **References:**

Moore D, Allen U, Mailman T. Canadian Paediatric Society, Infectious Diseases and Immunization Committee. Invasive group A streptococcal disease: Management and chemoprophylaxis. \*\*

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