Invasive Group A Streptococcal Infection IGAS We May Have a Problem!

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IPAC-BC Education Day

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Objectives

- Review GAS infection
  - *S. pyogenes* and virulence factors
  - Types of GAS infections
  - Invasive GAS (iGAS)
  - Severe invasive GAS
- Management of invasive GAS: Protecting patients and HCWs
  - Treatment
  - Isolation and precaution
  - Reporting
  - Identification of high risk exposure
  - Chemoprophylaxis
- Case review

Group A Streptococcal infection and health care

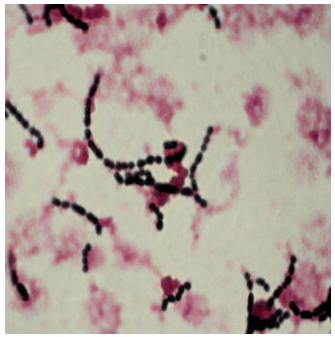
Louis Pasteur

(1822-1895)

"It is the nursing and medical staff who carry the microbe from an infected woman to a healthy one....
This water, this sponge, this lint with which you wash or cover a wound, may deposit germs which have the power of multiplying rapidly within the tissue....
If I had the honour of being a surgeon....not only would I use none but perfectly clean instruments, but I would clean my hands with the greatest care..."

1879

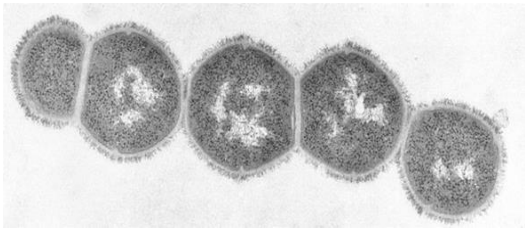
S. pyogenes



- Known reservoirs:
  - human epithelial surfaces of skin and mucous membranes
    - mostly throat / less frequently vagina and rectum
  - can be present at least a week on healthy skin before causing infection
- Highly communicable
  - affects healthy people of all ages

Virulence factors

- Transmission:
  - remain viable for prolonged periods
  - family members/close contacts at higher risk than general population
- Adherence: at least 11 different surface components - adhesins
  - lipoteichoic acid (LTA) → weak reversible adhesion
  - M proteins- major surface protein/tissue specific→ irreversible adhesion
    - > 80 M types, >150 *emm* type genes
    - anchored to cell wall peptidoglycan as hairlike projections
    - binds to fibrinogen, blocks complement inhibits phagocytosis
    - M types 1,3 – severe invasive STSS/necrotizing fasciitis



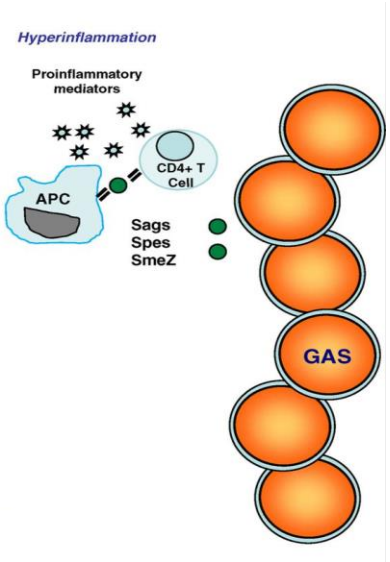
Virulence factors

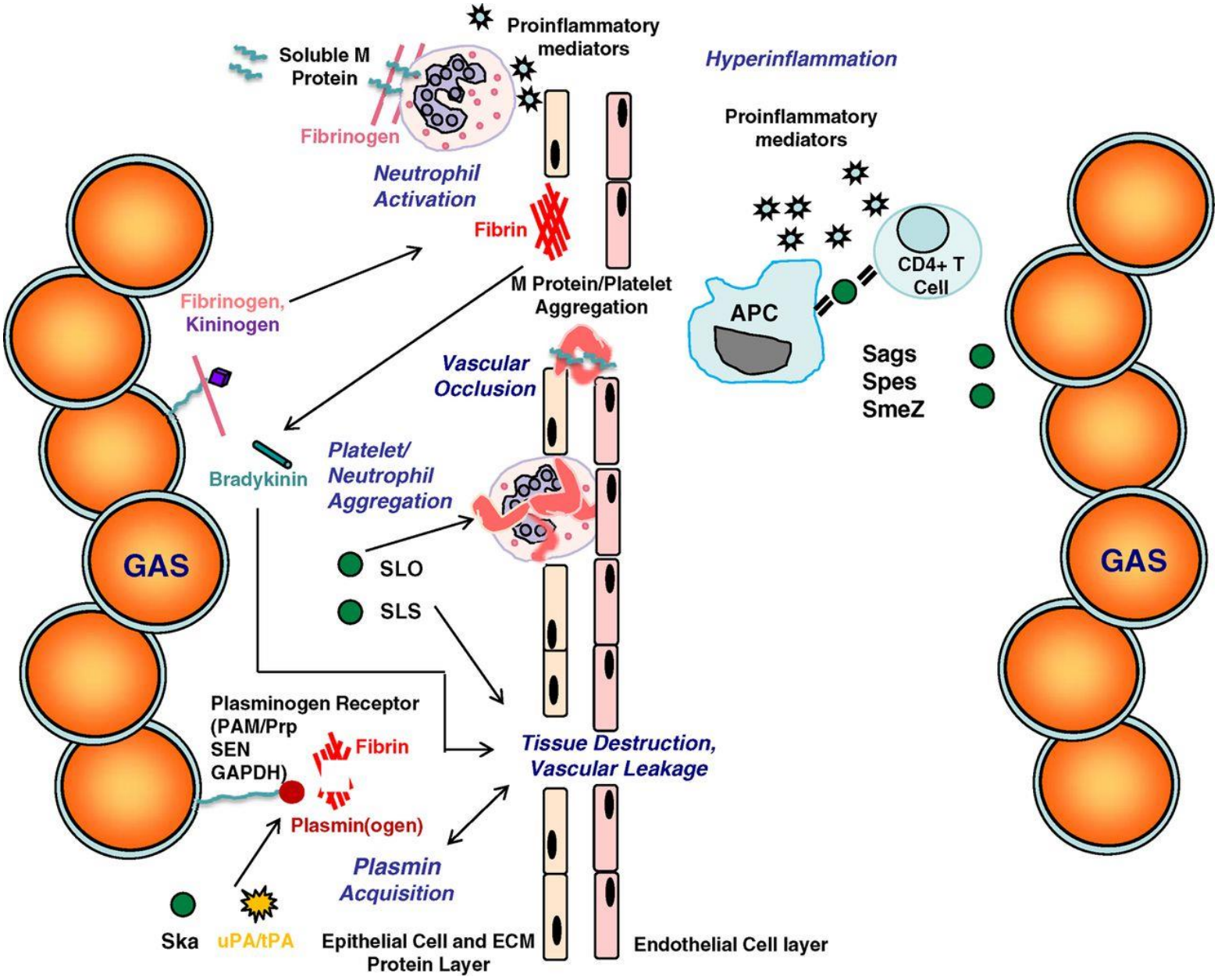
- Extracellular products and toxins
  - Hemolysis
    - Streptolysin-O toxic to many cell types including myocardium
      - Highly immunogenic- antibody response ASOT titre (recent infection)
    - Streptolysin S –damage PMNs/not immunogenic
- Streptococcal pyrogenic exotoxins (SPEs)
  - Pyrogenicity ,cytotoxicity
  - Spe A,C,F – can function as superantigens

    → marked febrile response

    → induce proliferation of T lymphocytes

    → release of multiple cytokines
- Nucleases:
  - liquefaction of pus
  - generate substrate for growth





Walker MJ, CMR 2014, 27:264-301
http://cmr.asm.org/content/27/2/264.full.pdf+html

Types of GAS infection

Wide spectrum of disease:

- Suppurative infections:
  - Superficial
  - Invasive
- Non-suppurative diseases
  - immune mediated sequelae

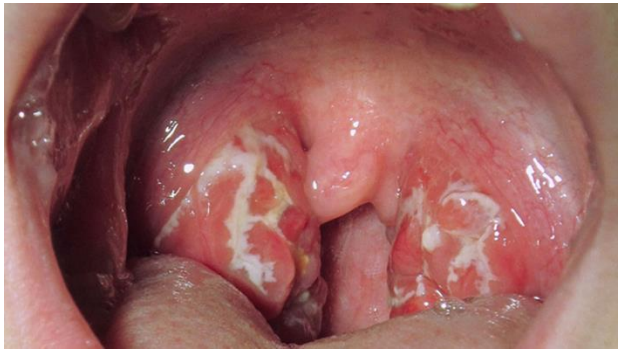
Superficial infections

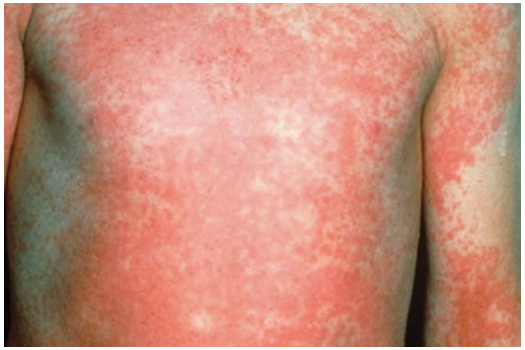
- pharyngitis (Sore throat)
- otitis media
- sinusitis
- scarlet fever
- impetigo
- vulvovaginitis
- urinary tract infections

Invasive GAS infections

- cellulitis
- necrotizing fasciitis/gas gangrene/myositis
- toxic shock syndrome
- postpartum GAS infection—puerperal fever
- bacteremia
- osteomyelitis/septic arthritis
- pneumonia
- endocarditis
- peritonitis
- meningitis/brain abscess

Invasive GAS disease is confirmed through laboratory testing of specimens taken from normally sterile sites.
Puerperal fever: occurring within 7 days of hospital discharge or giving birth.
(BCCDC communicable disease manual –Invasive GAS)



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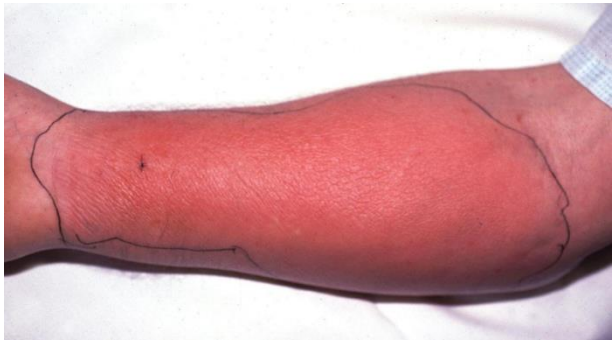
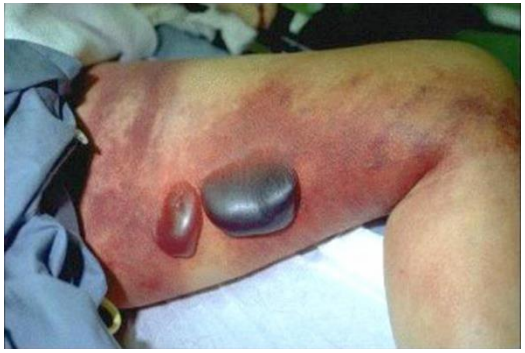
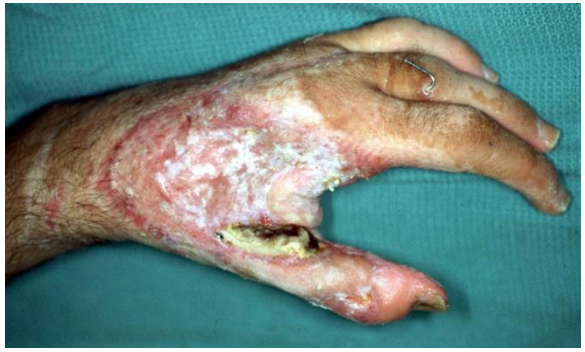






Invasive infections

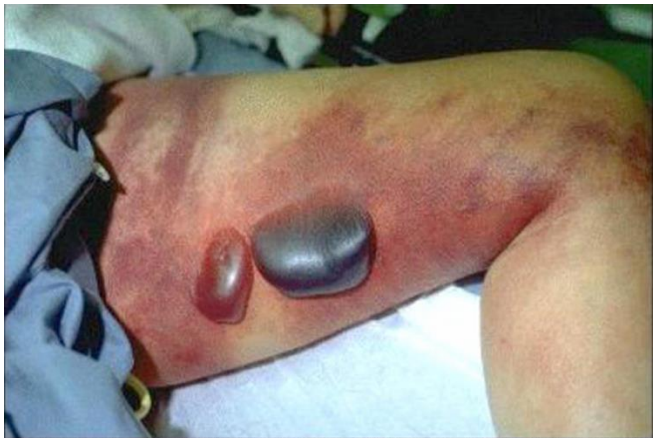
Necrotizing fasciitis " flesh eating disease"

- extensive , rapidly spreading infection of subcutaneous tissue and fascia

→ necrosis and gangrene

- erythema → 24/48 hrs purplish/blisters/bullae→ gangrene/tissue necrosis
- blunt trauma - major risk factor
- mortality - 24-32%
  - higher in low income countries
  - without surgery- 86%

Both host and bacterial proteases involved



http://img.medscapestatic.com/pi/meds/ckb/55/37455.jpg

Invasive infections

Toxic shock syndrome

- can occur with any of the invasive GAS infections
- response to superantigen production
- rapid progression
  - high fever, hypotension multi-organ failure
  - Massive cytokine response by T cells
  - widespread tissue damage/ DIC /organ dysfunction

MHC class II haplotype influences host susceptibility haplotype
DR14/DQ5 more common with STSS
DR15/DQ6 less common with STSS

Invasive infections

Puerperal sepsis

- GAS: increased incidence attributable to pregnancy
  - 20 fold increased incidence vs non-pregnant women
  - 85% cases occur post partum (within 4 days) most after vaginal delivery
  - altered immunity of pregnancy
- transmission
  - ascending from colonized vagina
  - Infected /colonized contacts including HCWs
- debate about need to report/treat GAS in colonized women
  - low rates of vaginal colonization- 1/3472 deliveries
- infections:
  - bacteremia, endometritis, peritonitis, abortions, STSS, chorioamnionitis
- delivery incidence 0.5/10,000 deliveries
  - mortality rate of STSS – 49%

Immune mediated sequelae

- acute rheumatic fever
- acute post streptococcal glomerulonephritis

Management: protect patients and HCWs

- Treatment
  - Antibiotics
  - surgery
- Infection Control considerations
  - Isolation
  - Contact tracing
  - prophylaxis

Treating Invasive Group A Strep

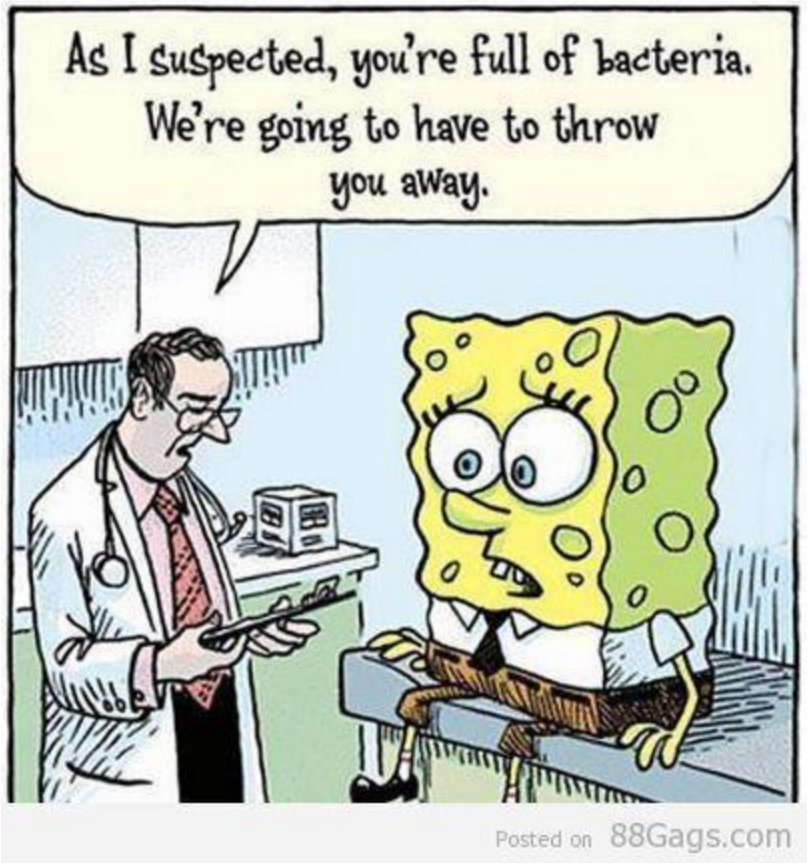
Penicillin + clindamycin

Eagle effect

- Penicillin decreased efficacy when GAS at high inoculum
  - PBPs are not expressed during stationary phase growth of GAS
  - Stationary phase occurs when exhaustion of nutrients or accumulation of toxins so that growth ceases
  - Inability to eradicate at source of infection

- Clindamycin/linezolid:
  - direct effect on toxin production
  - not susceptible to Eagle effect
  - Continues to kill bacteria even in stationary phase

Infection Control Issues



Infection Control

- Invasive GAS:
  - confirmed through laboratory testing of specimens taken from normally sterile sites.
- Severe invasive GAS:
  - Clinical evidence of severe invasive disease may be manifested as:
    - streptococcal toxic shock syndrome (STSS);
    - soft tissue necrosis, including necrotizing fasciitis (NF), myositis or gangrene;
    - meningitis;
    - death directly attributable to GAS in a confirmed case.

❷ Streptococcal toxic shock syndrome (STSS) is characterized by hypotension (systolic blood pressure ≤ 90 mmHg in adults or < 5th percentile for age in children) **and at least two** of the following signs:

(i) renal impairment: creatinine level ≥ 177 umol/L for adults

(ii) coagulopathy: (platelet count ≤ 100,000/mm^3 or disseminated intravascular coagulation

(iii)liver function abnormality: serum glutamic oxaloacetic transaminase (SGOT), aspartate aminotransferase (AST), serum glutamate pyruvate transaminase (SGPT), alanine aminotransferase (ALT) or total bilirubin ≥ 2x upper limit of normal

(iv) adult respiratory distress syndrome (ARDS)

(v) generalized erythematous macular rash that may desquamate

❸ NF (necrotizing fasciitis) may or may not be associated with STSS. NF is characterized by isolation of Group A streptococci (*Streptococcus pyogenes*) from a normally sterile body site or taken under sterile conditions from deep tissue (aspirate or deep tissue exploratory) **AND** at least one of the following:

(i) histopathologic diagnosis: necrosis of superficial fascia and polymorphonuclear infiltrate and edema of reticular dermis, subcutaneous fat and/or superficial fascia (this should be distinguished from necrosis that

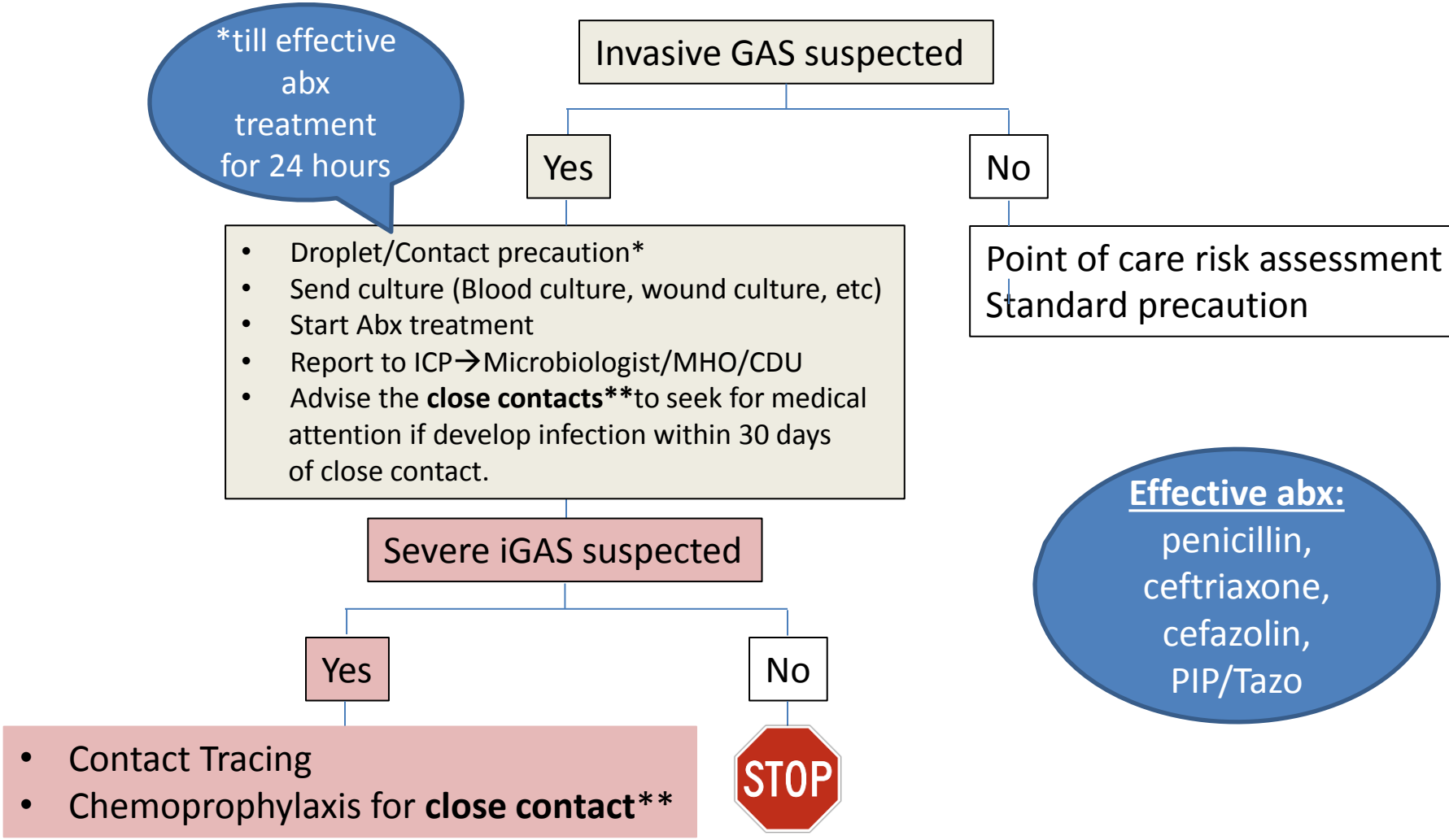
- **Mode of transmission**
  - Primarily by large droplet contact of the oral or nasal mucous membranes with respiratory secretions or with exudates from wounds or skin lesions
  - by direct or indirect contact with non-intact skin with exudates from skin or wound or infectious respiratory secretions
  - transmission by contaminated equipment has rarely been reported

- **Incubation Period**
  - The incubation period for invasive GAS infection has not been determined
  - The incubation period for non-invasive GAS infection is usually 1-3 days

- **Period of communicability**
  - In untreated cases 10 – 21 days
  - Transmissibility generally ends within 24 hours of appropriate antibiotic therapy
  - Use of prophylaxis in close contacts may prevent severe illness

- **EPIDEMIOLOGY of iGAS**
  - occur sporadically, most common during winter months.
  - nosocomial, long term care facility(LTCF), daycare/preschool, community, educational facility and household outbreaks have been documented.
  - risk factors for invasive disease include: HIV/AIDS, cancer, heart and lung disease, diabetes, IDU and alcohol abuse, and varicella infection, >60 yr or <4 yr

If you have a patient suspected iGAS



Purpose of chemoprophylaxis for close contact: to prevent severe iGAS

Not everybody who contacts the patient is at risk

Table 1: Definition of close contacts

• Household contacts of a case who have spent at least 4 hours/day on average in the previous 7 days or 20 hours/week with the case
• Non-household persons who share the same bed with the case or had sexual relations with the case
• Persons (including HCW) 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
• Children and staff of family or home day care centres

http://www.bccdc.ca/resource-gallery/Documents/Guidelines%20and%20Forms/Guidelines%20and%20Manuals/Epid/CD%20Manual/Chapter%201%20%20CDC/iGAS.pdf

- **HCW Close Contact**
  - Exposure to the case during the period from 7 days prior to onset of symptoms in the case to 24 hours after the case's initiation of antibiotics
  - HCWs who have had direct mucous membrane contact with the oral or nasal secretions of a case (e.g. mouth-to-mouth resuscitation) or unprotected direct contact with an open skin lesion of the case
    - Who have not worn mask when do mouth-to-mouth resuscitation
    - Who have not had gloves on when contact with open wound.

- **Chemoprophylaxis**
  - indicated only for close contacts of cases presenting with clinical evidence of severe invasive GAS disease
  - not routinely recommended for contacts of cases that are not severe (such as bacteremic illness or septic arthritis cases).
  - the purpose of chemoprophylaxis is to reduce the risk of subsequent episodes of severe disease in close contacts. This may also contribute to reducing transmission of GAS to others.
  - timing: give chemoprophylaxis as soon as possible and preferably within 24 hours of case identification and up to 7 days after the last contact with a severe invasive case (This recommendation is based on the finding that most subsequent cases occur within 7 days after the last contact with a case.)

Table 3: Recommended chemoprophylaxis regimens for close contacts

Drug	Dosage	Comments
FIRST LINE REGIMEN		
First-generation cephalosporins: cephalexin, cephadroxil, cephradine	**Children and adults**: 25 – 50 mg/kg daily, to a maximum of 1 g/day in 2 to 4 divided doses x 10 days	Recommended drug for pregnant and lactating women. Should be used with caution in patients with allergy to penicillin. Use of cephalosporins with nephrotoxic drugs (e.g. aminoglycosides, vancomycin) may increase the risk of cephalosporin-induced nephrotoxicity.
SECOND LINE REGIMENS		
Erythromycin	**Children:** 5 to 7.5 mg/kg every 6 hours or 10 to 15 mg/kg every 12 hours (base) x 10 days (not to exceed maximum of adult dose). **Adults:** 500 mg every 12 hours (base) x 10 days	Erythromycin estolate is contraindicated in persons with pre-existing liver disease or dysfunction and during pregnancy. Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be ≥ 10%.❶
Clarithromycin	**Children:** 15 mg/kg daily in divided doses every 12 hours, to a maximum or 250 mg po bid x 10 days **Adults:** 250 mg po bid x 10 days	Contraindicated in pregnancy. Sensitivity testing is recommended in areas where macrolide resistance is unknown or known to be ≥ 10 %.❶
Clindamycin	**Children:** 8 to 16 mg/kg daily divided into 3 or 4 equal doses x 10 days (not to exceed maximum of adult dose). **Adults:** 150 mg every 6 hours x 10 days	Alternative for persons who are unable to tolerate beta-lactam antibiotics.

❶ Since 2002, erythromycin and clarithromycin resistance for iGAS isolates has exceeded 10% in BC (data from the National Streptococcal Laboratory)

Also…

- Alert close contacts of **all** confirmed invasive cases (i.e., regardless of whether the case is a severe one) to signs and symptoms of invasive GAS disease.
- Advise them to seek medical attention immediately should they develop febrile illness or any other clinical manifestations of GAS infection within 30 days of diagnosis in the index case.
- This may be done by the case or the attending physician.

4.3 Special settings

Table 2 outlines the criteria for special settings that warrant further investigation and consideration of chemoprophylaxis.

Table 2: Special settings

Group Child Care Centres	Children and staff of group child care centres and pre-schools when there is: • Occurrence of a confirmed or probable iGAS case, followed by a 2nd confirmed or probable iGAS case or a non-invasive case (e.g. pharyngitis, impetigo, wound or skin infections, cellulitis) within 1 month **or** • A case of varicella 2 weeks prior to a case of GAS or within 1 month of a case of GAS❶ ❷
Long-term care facility	• An incidence rate of culture-confirmed invasive GAS infections of > 1 per 100 residents per month **or** • At least 2 cases of culture-confirmed invasive GAS infection in 1 month in facilities with fewer than 200 residents **or** • An incidence rate of suspected invasive or non-invasive GAS infections of > 4 per 100 residents per month
Hospital	Patients and staff of hospitals when there is: • Occurrence of a confirmed or probable iGAS case, followed by a 2nd confirmed or probable iGAS case or a non-invasive case (e.g. pharyngitis, impetigo, wound or skin infections, cellulitis) within 1 month

❶ Assess children and staff for varicella susceptibility and offer varicella vaccine as needed.

❷ Recommend chemoprophylaxis for individuals with acute varicella.

Case review

- 50 yo M patient,
- Previously healthy, developed back discomfort after plumbing, the pain became worse after a dirt biking,
- The symptoms progressed over the following 24 hours and developed fever, rigors, and severe back pain,
- PE: He was a little hypotensive and tachycardia that improved by hydration, no wound, some soft tissue tender in back,
- CT showed non-obstructive kidney stone
- Urine showed hematuria
- Query Kidney stone or discitis
- Blood culture was collected
- PIP/TAZO was started
- No month-to-month resuscitation
- Patient was not on isolation

Then…

- 22 hours after PIP/TAZO started, Blood culture became positive for GAS:
  - Droplet and contact precaution till 24 hours of pip/tazo treatment.
  - Abx was switched to penicillin and clindamycin for invasive GAS case
- 36 hours after admission, necrotizing fasciitis was diagnosed.
- I&D was done

Questions:

1. Should this patient restart isolation when necrotizing fasciitis was diagnosed?
2. Was there any risk for OR staff for exposure?

- Pip/Tazo: broad spectrum antibiotic agent actively for Gram positive and Gram negative bacteria including aerobic and anaerobic bacteria.

- Question?

Thank You