Gram Positive Bacteria in clinical medicine

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USAID PEER/Liberia ID Lecture Series
Objectives

Define the molecular structure of Gram-positive organisms
Highlight differences between Gram-positives and Gram-negatives
Discuss the most important clinically-relevant Gram-positive bacteria
Review treatments for Gram-positives
Illustrate clinical scenarios involving Gram-positive infection
You can approach thinking about causes of infections in two different ways.

One way is by organ system, e.g. pneumonia:

*Streptococcus pneumoniae, Klebsiella pneumoniae, Chlamydophila pneumoniae, Mycoplasma, Moraxella, E. coli, Staph aureus*, etc.

Advantage is that you can memorize various causes in a way that makes sense and not have to review every single organism in your head when you think about an infection, as there are dozens.

*But...could you miss an organism this way?*
You can approach thinking about causes of infections in two different ways.

The second way is by organism, via categories, e.g.:

“Gut Gram-negatives, including *E. Coli, Klebsiella, Salmonella, Shigella, Enterobacter, Citrobacter, Serratia*”

Advantage here is that you can review in your head the major infectious organisms and *not miss an important microbe*

The point is you need to use *both* ways of thinking about infections in order to make sure your differential is complete.

Only a computer can list all the manifestations of disease by organism, or all the infectious causes of a focal infection.

But a human brain can do pretty well if you switch back and forth.
The “ID Differential”

Non-infectious causes

Opportunistic (i.e. HIV)

Infections

"Routine"

Unusual organisms (e.g. Mycoplasma, prions)

Gram Positives

Gram Negatives

Anaerobes

Viruses

Fungi

Parasites & Protozoa

Other bacteria:
--Intracellular
--Acid Fast/Modified
--Spirochetes
What is a Gram stain?

Named after Dr. Gram (1884 paper)

Some bacteria take up crystal violet dye; some don’t

Some take up a counter-stain (safranin), *but some don’t*

(I.E. not *all* bacteria can be seen by Gram stain, e.g. Mycobacteria)
Structural differences

Crystal violet binds the peptidoglycan layer

The differences in the cell wall lead to differing pathogenesis, as well as different targets for antimicrobial (and other) therapy
Gram-negative rod

Gram-positive rod
Gram Positives

*Note: not an exhaustive list

Staphylococcus aureus
Coagulase-negative Staphylococci
Streptococci (many)
Enterococci
Peptostreptococci

Clostridia
Bacillus
Streptococci
Eubacterium
Enterococci

(Actinomyces, Nocardia, Erysipelothrix, Lactobacillus, Gardnerella)
**Staphylococci (esp \( S. \) aureus)**

Lives in nasal passage & skin (axillae)

\( S. \) aureus produces **coagulase** & catalase

Skin and soft tissue infections

Bloodstream infections/endocarditis

Abscesses, osteomyelitis

Toxic shock

Diabetics at high risk (impaired phagocytosis)

“Staph kills, Staph sticks, Staph goes everywhere, Staph recurs”

MRSA: Vanco, TMP/SMX, Doxy, chloramphenicol, +/- Clinda
The Streptococci

Complicated taxonomy
Originated in early 20th century lab methods
Original breakdown based on hemolysis: $\alpha$, $\beta$, and $\gamma$
Streptococci*

**β hemolytic Strep**
Lancefield groups*
- Group A (*S. pyogenes*)
- Group B (*S. agalactiae*)
- Group C
- Group D*

*Note: the Lancefield grouping is *not* done with respect to hemolysis, but *most* useful for the β hemolytic Strep

**All other Strep**

Viridans group (*S. viridans*)
- *S. pneumoniae*
- *S. bovis*

Group D*

Enterococci

*the clinician’s *oversimplified* version

(There’s lots of others)
Strep pyogenes (Group A)

- Pharyngitis (Strep throat)
- Impetigo/Erysipelas/Cellulitis
- Toxic shock
- Myositis & necrotizing fasciitis
- Scarlet fever
- Acute rheumatic fever*
- Glomerulonephritis*
- Tx: PCNs
- No vaccine
Group B Strep

Colonizer of urinary tract

Most common cause of neonatal sepsis (GBS)

Neonatal meningitis

Maternal screening!

In adults, GBS causes pneumonia, bacteremia, abscess

Can be seen in immunocompromised

No vaccine
*Streptococcus pneumoniae* ("pneumococcus")

Colonizes nasopharynx (~30-50%)
Polysaccharide capsule
Pneumonia, meningitis, bacteremia
CXR: more than just lobar
Empyema/parapneumonic effusion
*Diplococci* on Gram stain
Tx: 3\(^{rd}\) gen cephalosporin
Vaccines (PCV13; PPSV23)—but there are ~90 serotypes!
Other *Strep*

*-* *viridans* (endocarditis)

*-* *bovis* (colon malignancy)

Group C Strep (bacteremia)

*Strep anginosus* group

...there are many others!

Note: Enterococci (urinary pathogen, gut pathogen, bacteremia) is not considered in the Strep family proper
Gram Positives

Gram Positive Cocci

- Staphylococcus aureus
- Coagulase-negative Staphylococci
- Streptococci (*many*)
- Enterococci
- Peptostreptococci

Gram Positive Bacilli

- Clostridia
- Bacillus
- Listeria
- Corynebacteria
  (Actinomyces, Nocardia, Erysipelothrix, Lactobacillus, Gardnerella)
**Clostridia**

*Anaerobic, spore-forming*
*Live in soil, human gut*
*Often in polymicrobial infection*
*Gas forming*
*C. perfringens* (wounds, shock)
*C. tetani* (tetanus)
*C. botulinum* (botulism)

Tx: abx, call a surgeon fast (wounds)
Also *C. difficile*: abx use/diarrhea
Bacillus

“Bamboo stick”

Anthrax—livestock in West Africa
Pulmonary anthrax—high mortality
Gastrointestinal anthrax
Cutaneous anthrax—eschar formation
Tx: ciprofloxacin, doxycycline, antitoxin
B. cereus: diarrheal disease assoc w rice
Listeria

Intracellular
Young, old, immune suppressed at greatest risk
Meningitis (neonatal esp)
Sepsis/bacteremia
Abscesses
Milk products, meats, other foods
Tx: ampicillin +/- gentamicin
Corynebacteria

Diphtheria

Frequent contaminant of blood cultures ("diphtheroids")
A 58 yo M presents with fever, cough productive green sputum, dyspnea x 36 hrs. Temp 102F, HR 120, Sats 90%. He coughs up sample, which you take to the laboratory and perform Gram stain.

Which of the following is TRUE about this organism?

A. This is a Gram-positive rod.
B. This is a mycobacteria seen under AFB staining.
C. This is pneumococcus.
D. This bacteria does not have a thick peptidoglycan layer.
E. This is a Gram-positive coccus closely related to *Staph aureus*. 
A 65 yo M presents with a RLE tenderness and a lesion draining pus. You do not have Gram staining available and must treat him empirically. Which of the following stains is the MOST LIKELY to represent the MOST COMMON organism causing this presentation?
A 70 yo F presents with confusion and fever of 24 hours duration. You perform a spinal tap: the pressure appears high, and there are 300 WBCs. Protein is 120 mg/dl. Which of the following Gram stains are NOT likely causes?
Online resources

Basics of Gram stains:
http://www.uphs.upenn.edu/bugdrug/antibiotic_manual/Gram3.htm

Medical Microbiology (with StatPearls including brief reviews):
https://www.ncbi.nlm.nih.gov/books/NBK7627/

Staphylococci (brief) review:

And Streptococci review: https://www.jfmed.uniba.sk/fileadmin/jlf/Pracoviska/ustav-mikrobiologie-a-imunologie/VLa/STREPTOCOCCI.pdf