Health PEI Recommendations for the Management of Gram Positive Cocci in Clusters Bacteremia

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<td>Gram stain results:
Gram positive Cocci in Clusters

Typically:
Staphylococcus aureus

Other potential pathogens: Coagulase negative Staphylococcus

If pathogen has been identified as Staphylococcus aureus: see below.</td>
<td>Use double therapy initially & reassess when susceptibility results available

<u>DOUBLE THERAPY</u>
1. Cloxacillin 2 g IV q4h
OR
2. Cefazolin (RD) 1 g (<70 kg) or 2 g (≥70 kg) IV q8h (If non-severe PCN allergy)
OR
3. Meropenem (RD) 1-2 g IV q8h (If severe PCN allergy where patient has severe sepsis or greater*)
OR
4. Piperacillin/Tazobactam (RD) 4.5 g IV q6h (If treating another serious infection)

<u>PLUS:</u>

1. Vancomycin 25 mg/kg (max 3 g) IV load, then Vancomycin (RD) 15 mg/kg (max 3 g/dose) IV q12h**
OR
2. Daptomycin (RD) 8 – 10 mg/kg (max 1250 mg) IV q24h (If true allergy to Vancomycin and non-respiratory infection)

*If severe PCN allergy & patient does not have severe sepsis or greater: consider vancomycin monotherapy (dosing as above)
**For patients under age 50, morbidly obese and / or intravenous drug use: consider q8h dosing of Vancomycin IV if normal renal function.</td>
<td>Culture Results:
If only one draw/culture positive (especially if only in one out of two bottles), the positive result may be due to skin contamination. If the patient has not already started on effective therapy consider repeating cultures before antibiotic initiation.

<u>Bacteremia vs. line infection</u>:
If not already done, patients with central IV lines should have aerobic and anaerobic blood cultures performed from the central device (Line or Port) as well as aerobic and anaerobic peripheral blood cultures. Note: re: multi-lumen central device: an aerobic bottle is required for EACH lumen, however no anaerobic bottles are required.
Rationale: To determine, based on a lab calculation, if the patient has a true bacteremia versus only a line infection, and if a true bacteremia, if the central line or port is the most likely source/cause. For patients with more than one lumen anaerobic blood cultures are unlikely to be additive and can lead to excessive blood collection.

<u>Cardiac Imaging:</u>
For patients with prosthetic heart valves and/or pacemaker wires request a TTE even if the organism is later found out to be coagulase negative Staphylococcus. See next page for S. aureus and MRSA.

<u>Source Control</u>:
See next page</td>
<td>Antibiotics:
Do not rely on the following antibiotics to treat a bacteremia, even in the setting of clinical improvement (unless guided by Infectious Diseases):
1. Levofloxacin and Moxifloxacin only have 80% routine susceptibility to Staph aureus and less to coagulase negative Staphylococcus. These agents are not considered effective therapy for bacteremia due to increased chance of developing resistance (even in patients improving on this regimen).
2. Clindamycin is bacteriostatic and levels in the blood are not sufficiently high enough to control a bacteremia.
3. Sulfamethoxazole/Trimethoprim (Septra/Bactrim) is bacteriostatic
4. Doxycycline is bacteriostatic</td>
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RD = dose adjustment required in renal impairment

Health PEI Recommendations for the Management of Gram Positive Cocci in Clusters Bacteremia

Culture Results	Management Recommendations		Comments
	Medications	Investigations	
Staphylococcus aureus (**Not** MRSA)	1. Cloxacillin 2 g IV q4h OR 2. Cefazolin (RD) 1 g (<70 kg) or 2 g (≥70 kg) IV q8h (If non-severe PCN allergy) Note: Cloxacillin preferred 3. For severe PCN allergy: obtain Infectious Diseases opinion <u>Duration of therapy</u>: Minimum of 2 weeks IV from official Day 1 of therapy. <u>Note</u>: Official Day 1 of therapy is the day the first negative blood cultures were drawn, unless there is another source control issue (see Comments).	• Consider early Infectious Diseases opinion • Request a TTE initially and will frequently require a TEE especially if prosthetic valve, pacemaker wire, or blood cultures fail to clear after 4 days of effective therapy. • Repeat blood cultures after 48 hours of effective therapy and every 48 hours until clearance. **Note**: persistent bacteremia from blood cultures obtained 4 days after initiation of antibiotics suggests inadequate source control or warrants reassessment of current antibiotic therapy. Consider Infectious Diseases consultation (on or off Island). • If prosthetic heart valve and any bacteremia: consider early Infectious Diseases formal consultation (e.g role of additional antibiotics including rifampin and low dose gentamicin).	**Source control** involves consideration of the following: 1) Removal of any plastic such as Foley Catheters, Central/PICC lines etc. 2) Endocarditis: new/ decompensating HF, prolonged PR interval, rheumatoid factor, increasing cardiac markers. 3) MSK: rule out infected prosthetic joints/septic arthritis including the sternoclavicular and sacroiliac joints, abscesses (see below) Bone: spine (discitis) 4) Abscesses: psoas, epidural, pleural, subhepatic, suprahepatic, prostate, cardiac etc.
MRSA	1. Vancomycin 25 mg/kg (max 3 g) IV load, then Vancomycin (RD) 15 mg/kg (max 3 g/dose) IV q12h OR 2. Daptomycin (RD) 10 mg/kg (max 1500 mg) IV q24h (If true allergy to Vancomycin and non-respiratory infection)	• As above • Consider Infectious Diseases formal consultation. **Rationale**: patient specific characteristics (e.g. minimum inhibitor concentration to vancomycin may warrant the use of alternatives such as linezolid or daptomycin); infection control intervention such as reducing bioburden of the patient may be recommended.	• As above

RD = dose adjustment required in renal impairment

Health PEI Recommendations for the Management of Gram Positive Cocci in Clusters Bacteremia

References:

1. Liu C, Bayer A, Cosgrove SE, Daum RS, Fridkin SK, Gorwitz RJ, et al. Clinical practice guidelines by the infectious diseases society of America for the treatment of methicillin-resistant Staphylococcus aureus infections in adults and children. *Clin Infect Dis*. 2011;**52**(3):e18-55.
2. McConeghy KW, Bleasdale SC, Rodvold KA. The empirical combination of vancomycin and a β-lactam for Staphylococcal bacteremia. *Clin Infect Dis*. 2013;**57**(12):1760
3. Providence Health Care P&T Committee. Management of *Staphylococcus aureus* Bacteremia. June 2014.
4. MSH + UHN Antimicrobial Stewardship Program. Clinical Summary: *S. aureus* Bacteremia. Accessed May 18, 2016. http://www.antimicrobialstewardship.com/sites/default/files/asp_simple_messaging_--_staphylococcus_aureus_bacteremia.pdf
5. Blondel-Hill E and Fryters S. Bugs & Drugs 2012.
6. The Johns Hopkins POC-IT ABX Guide App ©2000-2013. The Johns Hopkins University.
7. The Sanford Guides to Antimicrobial Therapy App ©1969-2016. Antimicrobial Therapy, Inc.
8. Health PEI Antibiogram 2014
9. Ng JK, Schulz LT, Rose WE, Fox BC, Andes DR, et al. Daptomycin dosing based on ideal body weight versus actual body weight: comparison of clinical outcomes. *Antimicrobial Agents and Chemotherapy*. 2014;**58**(1):88.
10. Shank BR, Zimmerman DE. *Demystifying Drug Dosing in Obese Patients*. Bethesda, MD: American Society of Health-System Pharmacists; 2016:20-21.

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Provincial Drugs & Therapeutics
Antimicrobial Stewardship Subcommittee

To:	All Island Physicians, Nurse Practitioners, Nurse Educators, Nurse Managers, and Pharmacists
From:	Provincial Drugs & Therapeutics Antimicrobial Stewardship Subcommittee
Date:	July 22, 2016
Re:	**Management of Gram Positive Cocci in Clusters Bacteremia including *Staphylococcus aureus***

The Provincial Drugs & Therapeutics Antimicrobial Stewardship Subcommittee (PD&T ASSC) has developed the attached **Health PEI Recommendations for the Management of Gram Positive Cocci in Clusters Bacteremia** in conjunction with several PEI Physicians and Pharmacists. The guidelines were approved by the Provincial Drugs & Therapeutics Committee on June 7, 2016.

Rationale behind developing these guidelines:

- Gram positive cocci in clusters growing in blood cultures is typically caused by *Staphylococcus aureus*.
- *Staphylococcus aureus* bacteremia is associated with a 20% mortality rate and delay in treatment and inappropriate choice of antibiotics are linked with decreased survival[1].
- There is an opportunity to improve patient outcomes for a serious condition using peer developed management guidelines.

The guidelines offer suggestions on medications and investigations for 2 points in time:

1) Initial guidance when only the Gram stain is available (when result is Gram positive cocci in clusters).
2) Further guidance if the organism has been identified as *Staphylococcus aureus* - either methicillin-susceptible *Staphylococcus aureus* (MSSA) or methicillin-resistant *Staphylococcus aureus* (MRSA).

You will soon notice that blood culture reports for Gram positive cocci in clusters will include a note directing the healthcare provider to this new guidance document. When the positive blood culture report is communicated from nursing to the treating physician, it would be appreciated if this note can be conveyed as well.

This guideline can be found on the following website: www.healthpei.ca/micro . For CIS users: a reminder that there is a quick link to the website on one of the toolbars at the top of the PowerChart screen.

Please direct questions to the co-chairs of the PD&T ASSC, Dr. Greg German (Medical Microbiologist & Infectious Disease Consultant; 894-2515; GJGerman@ihis.org) and Jennifer Boswell (Antimicrobial Stewardship Pharmacist; 894-2587; JLBoswell@ihis.org).

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Highlights of the document include*:

- When the Gram stain shows Gram positive cocci in clusters, double therapy is recommended until the organism is known. Rationale: In PEI, 10% of *Staphylococcus aureus* bacteremia is MRSA. For the remaining 90%, beta-lactams are superior to vancomycin for the definitive treatment of methicillin-susceptible *Staphylococcus aureus* (MSSA)[2].
- A list of antibiotics not to trust for treatment of Gram positive cocci in clusters bacteremia.
- Repeat blood cultures are required to determine clearance of bacteremia for MSSA/MRSA.
- Duration of therapy for MSSA/MRSA bacteremia is a minimum of 2 weeks of IV antibiotics from the date of the first negative blood cultures.
- Determining if a central line is the cause of infection based on how fast the blood cultures grow.
- Cardiac imaging and the need for a transthoracic echocardiogram (TTE).
- MSSA/MRSA blood stream infections frequently develop abscesses and other complications for which source control is paramount.
- Loading doses for Vancomycin at 25mg/kg IV initially with the time between future doses dependent on renal function.
- For MSSA bacteremia early ID opinion should be considered and for MRSA bacteremia early ID formal consultation is recommended. ID involvement in *Staphylococcus aureus* bacteremia is associated with improved patient management and better outcomes[1,3].

*See References within the guidelines.

References mentioned above:

1. Paulsen JP, Solligård E, Damås JK, DeWan A, Åsvold BO, Bracken MB. The Impact of Infectious Disease Specialist Consultation for *Staphylococcus aureus* Bloodstream Infections: A Systematic Review. Open Forum Infect Dis. 2016 Mar 1; **3**(2):ofw048. doi: 10.1093/ofid/ofw048.
2. McDanel JS, Perencevich EN, Diekema DJ, Herwaldt LA, Smith TC, Chrischilles EA, et al. Comparative Effectiveness of Beta-Lactams Versus Vancomycin for Treatment of Methicillin-Susceptible *Staphylococcus aureus* Bloodstream Infections Among 122 Hospitals. Clin Infect Dis. 2015;**61**(3):361-7.
3. Bai AD, Showler A, Burry L, Steinberg M, Ricciuto DR, Fernandes T, et al. Impact of Infectious Disease Consultation on Quality of Care, Mortality, and Length of Stay in *Staphylococcus aureus* Bacteremia: Results From a Large Multicenter Cohort Study. Clin Infect Dis. 2015;**60**(10):1451-61.

Peers involved: Dr. Alex MacLean, Dr. Paul Seviour, Wendy Cooke, Trent Ferrish; PD&T ASSC (Dr. Lenley Adams, Jennifer Boswell, Amanda Burke, Dr. Jill Cunniffe, Christine Drummond, Dr. Greg German, Barb Inman, Dr. Michael Irvine, Beverly Martin). This guideline was presented on June 17, 2016 at PEI's 7th Annual ER/Critical Care Summit.