Line infection

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various mechanisms of infection:

- Early infections often arise from the skin:
  - (a) These may occur during line insertion.
  - (b) There may be gradual infection, beginning where the catheter exits the skin.
- Later infection may arise from the catheter hub or luminal surface (fibrin sheath).

prevention

- **Dirty central lines**: It’s OK to place an emergent central line without full sterility. However, it must be removed within <48 hours.
- **Peripheral pressors**: Epinephrine and phenylephrine ([https://emcrit.org/pulmcrit/phenylephrine-epinephrine-central-access/](https://emcrit.org/pulmcrit/phenylephrine-epinephrine-central-access/)) are safe when given peripherally. Norepinephrine can cause extravasation, but it may nonetheless be safe with adequate monitoring ([https://emcrit.org/podcasts/peripheral-vasopressors-extravasation/](https://emcrit.org/podcasts/peripheral-vasopressors-extravasation/)). Patients who require low dose pressors for a limited period of time don't necessarily need a central line.
- **Place central lines with full sterility**: Use a hat, mask, gown, full body drape, etc.
- **Consider delaying central line placement**: Immediate stabilization can often be achieved using peripheral vasopressors and/or intraosseous lines (or a dirty central line if necessary). Subsequently, a fresh central line may be placed in a controlled and meticulously clean manner.
- **Use chlorhexidine**: This is shown to be more effective than povidine iodine in a variety of situations.
- **Discontinue central lines ASAP**: The necessity of the line should be reviewed daily.
- **When inserting a central line, don't make a large nick** with a scalpel along the guidewire. It is better to make a *small* nick, so that the skin incision is nice and tight (this will require using a bit more force to advance the dilator). Using a *small* nick will produce a central line site which remains clean and dry.
- **Use the subclavian site for central lines**: Compared to the internal jugular or femoral sites, the subclavian site has a lower risk of thrombosis or line infection. If possible, this site is recommended by US guidelines ([O'Grady 2011](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3106269/)).
- **Transition to a PICC line** for long-term central access.
- **Consider early placement of tunneled hemodialysis catheter**: For patients who will require chronic dialysis, placement of a tunneled dialysis catheter should be performed sooner rather than later (to allow for removal of the temporary hemodialysis catheter).

diagnosis

when to suspect line infection?

- (1) Fever or septic shock in a patient with a line in place >48 hours (although line infection is rare before one week).
- (2) Local signs of infection involving the line (pain, erythema, purulent exudate).
  - Unfortunately, this is usually absent.
- Obvious evidence of infection at the line site (e.g. purulence) is specific, but insensitive (30241718).
- (3) Dysfunction of the line supports the diagnosis of line infection (this may be due to an infected thrombus occluding the line).

**blood cultures**

- Draw two sets of peripheral blood cultures (from different sites) and one set of cultures from the distal port of the line. All cultures should be obtained using the same volume of blood (e.g. 10 ml).
- Drawing equal volumes of blood from both sites is extremely important. Removal of blood is generally easier from a central line than from a peripheral venipuncture, so there will be a natural tendency to remove more blood from the central line.
- Some evidence suggests that obtaining two sets of blood cultures from two lumens of the central line could increase the sensitivity for central line infection (20455693). However, obtaining more cultures will also serve to increase the likelihood of false-positive cultures due to contamination.
- Four general patterns may be discerned:
  - (1) Peripheral and central line cultures all turn positive within <2 hours of one another: this suggests bacteremia due to another cause (e.g. endocarditis). However, this can definitely occur with catheter infection, so clinical judgement is required. If no obvious source of bacteremia is present, then catheter infection may become increasingly likely (29432818).
  - (2) Central line cultures turn positive first, then subsequently peripheral cultures turn positive >2 hours later. This is fairly diagnostic of central line infection (~85%) but other possible sources still warrant consideration (Safdar 2005).
  - (3) One of the peripheral cultures turns positive, but none of the other cultures do. This suggests a contaminated culture (although gram-negative organisms or candida should always be taken seriously).
  - (4) The central line culture turns positive, but the peripheral blood cultures do not. This presents a bit of a quandary. It might represent contamination, but it could represent early colonization or infection of the line. Line removal is generally indicated here, but systemic antibiotics might not be necessary (depending on the clinical context).
- Quantitative culture techniques can also be used to compare bacterial burden in peripheral versus central cultures. However, most hospitals lack these techniques.
- Some low-virulence skin organisms may be suggestive of line infection (if confirmed from cultures of two different sites):
  - Corynebacterium jeikeium
  - Bacillus spp
  - Malassezia furfur
  - Coagulase negative staphylococci
  - Micrococcus spp.
  - Propionibacterium spp. (the latter now re-named as Cutibacterium!)

**procalcitonin**

| Table 1 | Characteristics of included studies. | | | | |
|---|---|---|---|---|---|---|
| Author (Year) | Regime | Design | No. of patients | GBS/GPA/Augmenta | Cutoff value (ng/mL) | Procalcitonin (ng/mL) | Study period |
| CASS | Non-CASS |
| Chen et al 2012* | China | Prospective | 56 | 13/11/1 | 3.1 | 5.48 ± 4.30 | 1.32 ± 1.19 | 2009-2009 |
| Harle and Andrew 2011** | Egypt | Prospective | 31 | NA | 16.5 | 49.2 ± 21.9 | 1.1 ± 1.0 | NA |
| Kassim et al 2012*** | USA | Prospective | 62 | 10/59 | 0.3 | 19.16 ± 6.85 | 2010 |
| Gurnani et al 2016 | Turkey | Prospective | 49 | 10/39 | 0.96 | 1.18 ± 0.57 | 2013-2014 |
| Theodorou et al 2012 | Greece | Prospective | 46 | 23/39 | 0.70 | 7.76 ± 10.10 | 2013-2011 |
| Zhao et al 2014 | China | Prospective | 68 | NA | 2.98 | NA | 2014 |

* Focal infection, **Blood culture, ***Procalcitonin

- Available data is summarized above.
  - A very low procalcitonin argues against bacteremia (e.g. procalcitonin <0.3 ng/mL).
  - Elevated procalcitonin is nonspecific (e.g. it could represent line infection, infection elsewhere, or renal dysfunction).
- Use of procalcitonin in suspected line infection?
  - Procalcitonin should not be used in the decision of whether to initiate antibiotics.
  - Low procalcitonin may be used to support a decision to discontinue antibiotics (in combination with clinical judgement).
- The evidentiary basis supporting procalcitonin here remains weak, so this should be interpreted judiciously. For example, in a patient with known systemic infection (e.g. pneumonia), procalcitonin will likely be positive whether or not there is a line infection – so it’s not worth obtaining.

**line tip culture**

https://emcrit.org/ibcc/line/
This involves cutting off the line tip and sending it for culture (after removing the line).

Limitations to this technique:

i) It requires removing the line.

ii) The tip can get contaminated during line removal, leading to a “false-positive” diagnosis of line infection.

Reasonable approach?

Generally, avoid culturing line tips (the preferred technique for diagnosis of line infection is differential time to blood culture positivity, as discussed above).

Line tip culture may be rarely utilized in unusual situations (e.g. inability to obtain peripheral blood cultures).

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**indications for line removal and empiric antibiotics:**

- **[1] Definite line infection**
  - Unequivocal local signs of infection (e.g. purulent drainage).
  - Positive blood cultures from the line.

- **[2] Possible infection – plus – increased risk of harm from leaving the line in, due to:**
  - i) Septic shock.
  - ii) Neutropenia.
  - iii) Prosthetic valve, other endovascular hardware (e.g. pacemaker), or fresh arterial graft. These increase the risk of an infection spreading to a site where it would be difficult to eradicate.

**are there situations where the line can be left in place despite infection?**

- Occasionally, for patients with infected ports or tunneled hemodialysis lines, it might be possible to treat with antibiotics alone (without hardware removal). This should be considered only if all of the following conditions are met:
  - (1) Patient isn’t in septic shock.
  - (2) Organism isn’t Staphylococcus, Pseudomonas, a multi-drug-resistant gram-negative, Candida, Acinetobacter, Micrococcus spp., or Propionibacterium spp.
  - (3) Infectious disease consultant agrees that this is a wise course of action.

**can the line be exchanged over a guidewire?**

- Line exchange over a guidewire has been shown to increase the risk of subsequent infection (compared to placement of a fresh line) ([9267959](https://www.ncbi.nlm.nih.gov/pubmed/9267959)).
- Reasons that guidewire exchange may increase infection risk:
  - i) It's very difficult to do this with true 100% sterility.
  - ii) The skin tract may be infected, so even if perfect sterility is achieved, the new line may immediately be contaminated by residual bacteria.
- In the modern era of ultrasound-guided line placement, guidewire exchange is a highly dubious practice (placement of a fresh line can generally be accomplished safely & effectively).

**empiric antibiotic selection**

**microbiology of line infections**

- Mostly gram-positives (~75%)
  - Coagulase negative staphylococci (~17-37%)
  - Staph aureus (13%)
  - Enterococcus (~14%)
- Gram-negative bacilli (~14-20%)
  - Klebsiella spp. (8%)
  - Escherichia coli (5%)
  - Enterobacter spp. (4%)
  - Pseudomonas spp. (4%)
  - Serratia spp.
  - Acinetobacter spp.
- Candida (8-12%)

(empirical regimen for line infection (prior to any culture results)

- (1) Agent that covers drug-resistant gram positives (vancomycin, daptomycin, or linezolid).
  - Vancomycin shouldn't be used in patients colonized with vancomycin-resistant enterococci (VRE).
  - Linezolid use here is a bit controversial, but it's probably fine (discussed further here).
- (2) Anti-pseudomonal beta-lactam (e.g. piperacillin-tazobactam, meropenem, cefepime).
- (3) Empiric coverage of candida may be considered for patients with multiple risk factors (listed below). The initial antibiotic of choice is generally an echinocandin (e.g. caspofungin or micafungin). When candidemia is a concern, consider obtaining a (1,3)-Beta-D-Glucan level (FUNGITELL) as well.
  - Risk factors:
    - Colonization with candida at multiple sites
    - Prolonged exposure to broad-spectrum antibiotics
    - ICU stay >1 week
    - Total parenteral nutrition
    - Immunosuppression (chemotherapy, neutropenia, transplantation, hematologic malignancy)

**pathogen-specific treatments**

**key factors to consider:**

- [1] Presence of any hardware (especially endovascular hardware, such as mechanical heart valves).
- [2] Indicators of endocarditis or deep-seated infection:
  - i) Signs/symptoms of endocarditis (more on this in the endocarditis chapter).
  - ii) Persistent fever or bacteremia >72 hours after catheter removal.
  - iii) Recurrence of culture positivity or clinical deterioration after stopping antibiotics.
  - iv) Evidence of suppurative thrombophlebitis (e.g. adjacent deep vein thrombosis).
**rough guide to treatment duration (in uncomplicated infections)**

- Coagulase-negative staphylococci (not including S. lugdunensis): Generally treat for 5-7 days.
- Staph aureus & Staph lugdunensis ("slug"): 2-6 weeks.
- Enterococcus: 7-14 days.
- Gram-negative organisms:
  - Pseudomonas or multi-drug resistant organism: 10-14 days
  - Other gram-negatives: 7-14 days

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**septic thrombophlebitis**

**diagnosis**

- May be suggested by:
  - Signs of DVT (e.g. extremity swelling/erythema, palpable cord).
  - The line stops working (occluded by clot).
  - Persistent sepsis, fever, or positive blood cultures >72 hours after line removal.
  - Septic pulmonary emboli (which typically cause a multifocal nodular-distribution pneumonia with cavitation).
- Diagnosis is based on ultrasonography.

**management**

- Line must be removed.
  - There may be concern that line removal will dislodge the clot. This is a theoretical concern. Ultimately the line must be removed – just take it out.
- Antibiotic therapy duration may need to be extended (e.g. to 4-6 weeks).
- Anticoagulation may be indicated if the thrombus is within a deep vein (i.e. a deep vein thrombosis).

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**arterial line infection**

**radial arterial catheter**

- Radial arterial catheters seem to have an extremely low rate of infection.
  - One meta-analysis found the infection rate to be 0.3% (1 in 333) (24413576). However, determining the true infection rate is challenging, given that line infection is often a clinical diagnosis (without a single definitive gold-standard diagnostic).
- A major factor driving the low rate of line infections may be that arterial lines often stop working after a couple of days, leading to their removal.

**femoral & axillary arterial catheters**

- Femoral arterial lines are associated with a higher rate of infection than radial arterial lines (24413576). Drivers of this higher rate of infection may be:
  - It is difficult to keep groin lines clean and dry over several days.
  - Femoral lines often stay in longer than radial lines, because femoral arterial lines tend to function well for a longer period of time.
- The infection rate of axillary arterial catheters is unclear. These lines can function well for prolonged periods of time, which could increase the risk of infection.
- Both axillary and femoral arterial catheters should be placed under full sterile conditions, similar to those of a central line.

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**septic shock from an infected chest port**
This is uncommon, but definitely happens. Make sure to always consider any hardware in the patient's body when evaluating for the source of sepsis.

- This can occur even if the port isn't being actively used (due to seeding of the catheter).
- Diagnosis is similar to that of a central line infection, based on some combination of the following:
  1. Local signs of infection (erythema, warmth, pain).
  2. Positive blood cultures (especially with a gram-positive organism, but a gram-negative organism may be involved as well).
  3. Lack of any other clear focus of active infection.

For patients in shock, immediate removal is necessary (source control).

- This is a fairly minimal bedside procedure, which can be done under local anesthesia (perhaps with mild sedation).
- Both surgeons and interventional radiologists are entirely capable of performing the procedure. If a patient is actively dying and neither are available, the procedure could probably be done by anyone with basic procedural skills.

Key point: Saving the patient's life is always more important than saving the port. When facing a septic patient, it's generally safest to err on the side of port removal.
Don't ignore blood cultures showing organisms that are typically contaminants in patients with indwelling lines (e.g. coagulase-negative staphylococcus, bacillus spp.). If multiple cultures are positive for one of these organisms, it may reflect a line infection.

When treating a line infection, repeat cultures after 72 hours to ensure sterilization of the blood. Failure to achieve this may suggest endocarditis or septic thrombophlebitis.

**Going further:**