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Consideration of some other specific indications: Bacteremia

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Definitions: Bacteremia

Bacteremia (Bacteræmia in British English, also known as ‘blood poisoning’ or ‘toxemia’) is **the presence of viable bacteria in the blood.**

Bacteremia is most commonly diagnosed by blood culture.

From Wikipedia, the free encyclopedia

Definitions: Bacteremia

True bacteremia = clinically significant

Contamination = clinically not significant

Pseudobacteremia = systematic contamination

Transient, intermittent, or persistent bacteremia

Bacteremia is a microbiologic finding, it is <u>not an infection</u> per se

CDC Definitions: Bloodstream infection

Clinical definition

Bacteremia with at least one positive blood culture

+

clinical manifestations of infection

(such as fever, chills and/or hypotension)

→ clinically always significant

CDC Definitions: Primary bloodstream infection

Laboratory-confirmed bloodstream infection must meet at least one of the following criteria:

Criterion 1: Patient has a recognized pathogen cultured from one or more blood cultures

and

organism cultured from blood is *not related* to an infection at another site.

Horan TC, Gaynes RP. Surveillance of nosocomial infections. In: Hospital Epidemiology and Infection Control, 3rd ed., Mayhall CG, editor. Philadelphia: Lippincott Williams & Wilkins, 2004:1659-1702.

CDC Definitions: Primary bloodstream infection

Criterion 2: Patient has at least *one* of the following signs or symptoms: fever (38°C), chills, or hypotension

and at least *one* of the following:

a. Common skin contaminant (e.g., diphtheroids, *Bacillus* sp., *Propionibacterium* sp., coagulase-negative staphylococci, or micrococci) is cultured from two or more blood cultures drawn on separate occasions

b. Common skin contaminant is cultured from at least one blood culture from a patient with an intravascular line, and the physician institutes appropriate antimicrobial therapy

and signs and symptoms and positive laboratory results are *not* related to an infection at another site.

CDC Definitions: CLABSI and CR-BSI

Central Line-Associated Bloodstream Infection (CLABSI)

Primary laboratory confirmed bloodstream infection that is central line-associated (i.e., a central catheter was in place at the time of, or within 48 hours before, onset of the event).

Definition is used for infection-control surveillance purposes, no microbiological proof required.

O'Grady NP et al. Guidelines for the prevention of intravascular catheter-related infections. Am J Infect Control. 2002; 30:476-89.
Mermel L, et al. Clinical Practice Guidelines for the Diagnosis and Management of Intravascular Catheter-Related Infection: 2009 Update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 49:1–45

CDC Definitions: CLABSI and CR-BSI

Catheter-Related Bloodstream Infection (CR-BSI)

Bacteremia or fungemia in a patient who has an intravascular device and ≥1 positive blood culture result obtained from the peripheral vein, clinical manifestations of infection (e.g., fever, chills, and/or hypotension), and no apparent source for BSI except the catheter.

One of the following should be present (as microbiological proof):

(i) positive result of semiquantitative (>15 cfu per catheter segment) or quantitative (>10^2 cfu per catheter segment) catheter culture, whereby the same organism (species) is isolated from a catheter segment and a peripheral blood culture;
(ii) simultaneous quantitative cultures of blood with a ratio of > 3:1 cfu/mL of blood (catheter vs. peripheral blood);
(iii) differential time to positivity >2h (catheter vs. peripheral blood)

CDC Definitions: Secondary bloodstream infection

Laboratory-confirmed bloodstream infection must meet at least one of the following criteria:

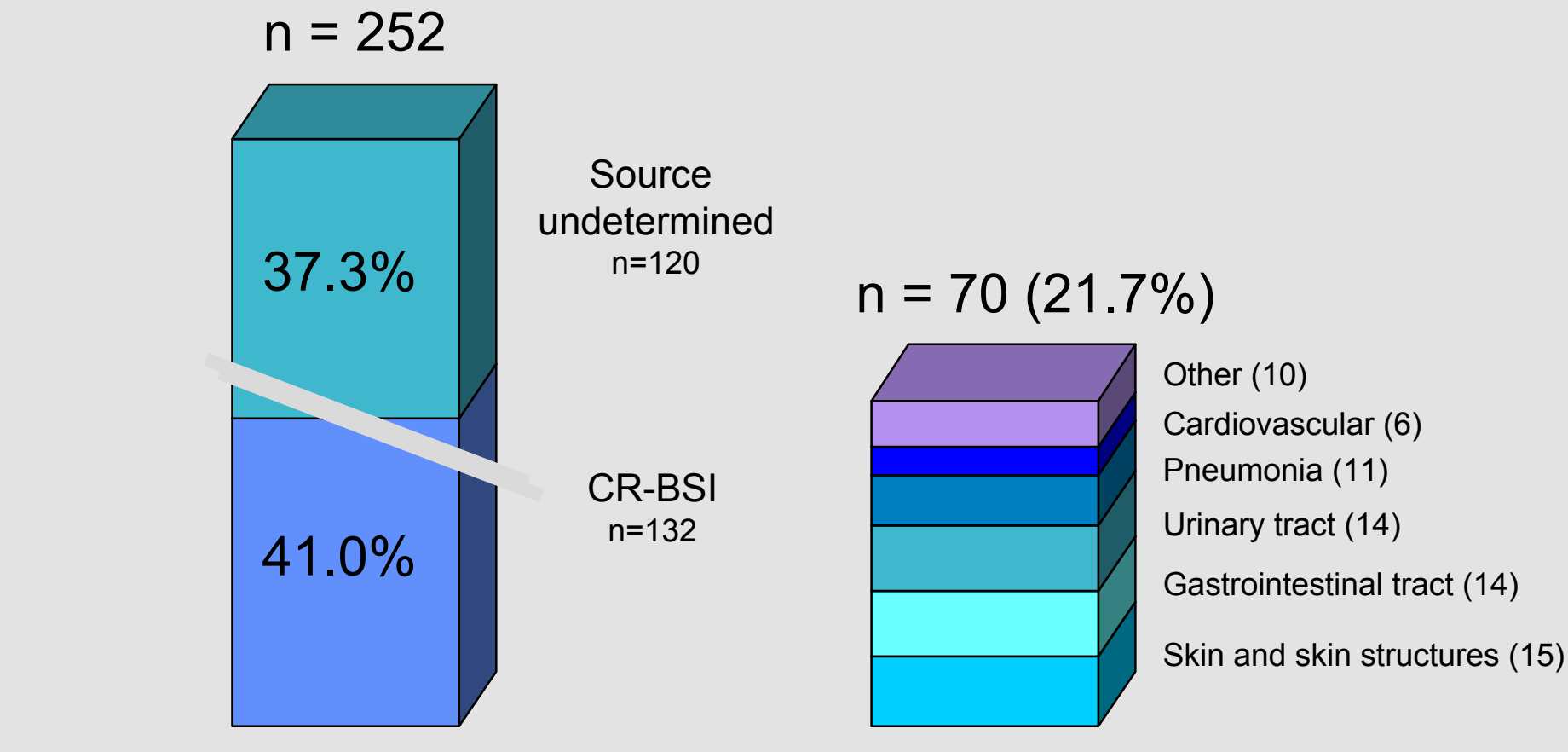
Criterion 1: Patient has a recognized pathogen cultured from one or more blood cultures

and

organism cultured from blood is *related* to an infection at another site.

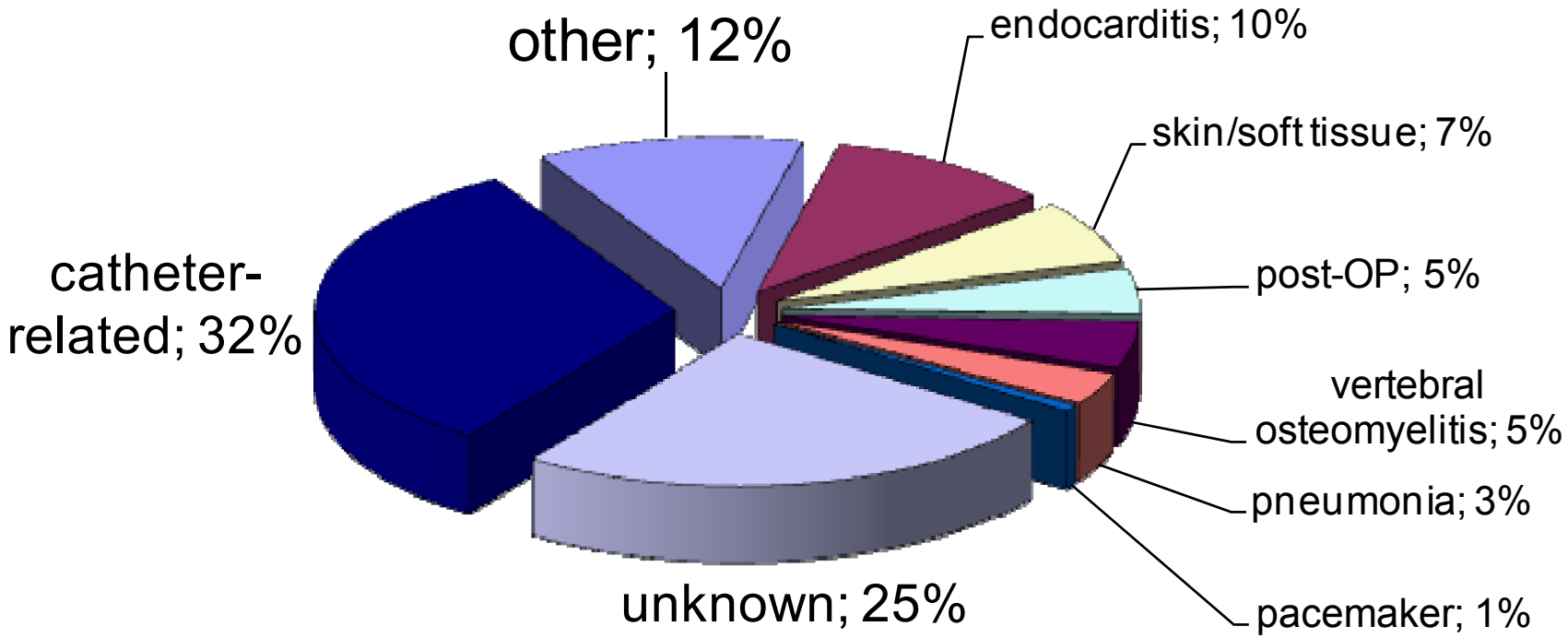
Horan TC, Gaynes RP. Surveillance of nosocomial infections. In: Hospital Epidemiology and Infection Control, 3rd ed., Mayhall CG, editor. Philadelphia: Lippincott Williams & Wilkins, 2004:1659-1702.

Sources of nococomial bloodstream infections Cologne, 1997/1998 (n=322)



Unpublished data

S. aureus bloodstream infection (SAB): source of infection



N=417, January 2006 – December 2008

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Daptomycin versus Standard Therapy for Bacteremia and Endocarditis Caused by *Staphylococcus aureus*

Daptomycin (Cubicin) is approved in the U.S. and in Europe, at 6 mg/kg, for the treatment of *S. aureus* bloodstream infections, including right-sided IE caused by MRSA and MSSA.

Cubicin is the only I.V. antibiotic approved for this indication based on results of a prospective, randomized, controlled registration trial.

Daptomycin vs. standard therapy for bacteremia and endocarditis caused by *S. aureus*

Study design:

Open-label, randomized trial conducted between August 2002 and February, 2005.

Eligible patients were ≥ 18 y of age and had ≥ 1 blood cultures positive for *S. aureus* within two days before initiating study medication.

Patients were ineligible if they had a creatinine clearance of ≤ 30 ml/min, osteomyelitis, polymicrobial bacteremia, or pneumonia.

Fowler V et al. N Engl J Med 2006;355:653-65.

Daptomycin vs. standard therapy for bacteremia and endocarditis caused by *S. aureus*

Clinical outomes:

The primary outcome was the clinical success rate in each of the two treatment groups in the MITT population at the visit 42 days after the end of therapy. Non-inferiority margin: 20%

Failure at this visit was defined as clinical failure, microbiologic failure, death, failure to obtain blood culture, receipt of potentially effective non-study antibiotics, or premature discontinuation of the study medication because of clinical failure, microbiologic failure, or an adverse event.

Fowler V et al. N Engl J Med 2006;355:653-65.

Ceftarolin (Teflaro, Forest Laboratories)

- Drug class: Cephalosporin (with anti-MRSA activity)
- Approval: FDA 29.10.2010
- Indications: Community-acquired pneumonia; cSSST
- Dosing: 600mg IV bid

Ceftaroline (Teflaro, Forest Laboratories)

Clinical studies

- FOCUS I and FOCUS II studied adult patients who were hospitalized with moderate to severe CAP (PORT III-IV); Ceftaroline 600mg iv bid vs. ceftriaxone1g iv od
- Exlusion: CAP suitable for outpatient tx with an oral agent
- Clinical cure in the MITT population: 82.6% vs 76.6%
- **Bacteremia rate 3.5%** (43/1225 patients included)
- **Death-rate 2.2%** (27 of 1225 patients included)

File TM et al. Integrated Analysis of FOCUS 1 and FOCUS 2: Randomized, Doubled-Blinded, Multicenter Phase 3 Trials of the Efficacy and Safety of Ceftaroline Fosamil versus Ceftriaxone in Patients with Community-Acquired Pneumonia. Clin Infect Dis 2010; 51:1395–1405

Ceftaroline (Teflaro, Forest Laboratories)

Clinical studies

- The CANVAS I and CANVAS II trials evaluated ceftaroline monotherapy (600mg iv bid) versus vancomycin plus aztreonam (each, 1g iv bid) in adult patients with complicated skin and skin structure infections (cSSSI)
- Clinical cure in the MITT population: 85.9% vs 85.5%
- **Bacteremia rate 4.0%** (55/1378 patients included)
- **Death-rate 0.2%** (3/1378 patients, none related to cSSSI)

Corey GR et al. Integrated analysis of CANVAS 1 and 2: phase 3, multicenter, randomized, double-blind studies to evaluate the safety and efficacy of ceftaroline versus vancomycin plus aztreonam in complicated skin and skin-structure infection. Clin Infect Dis. 2010;51:641-50.

Ceftaroline (Teflaro, Forest Laboratories)

What ceftaroline dosage would you use if you had to treat a patient with a serious infection?

Do we need new drugs such as ceftaroline for CAP and cSSSI?

We need new drugs for serious and life-threatening infections.

We need clinical studies in patients with serious infections such as patients with BSI.

We need to know what dose to be used to treat these patients.