Universitair Ziekenhuis Gent

UNIVERSITEIT GENT

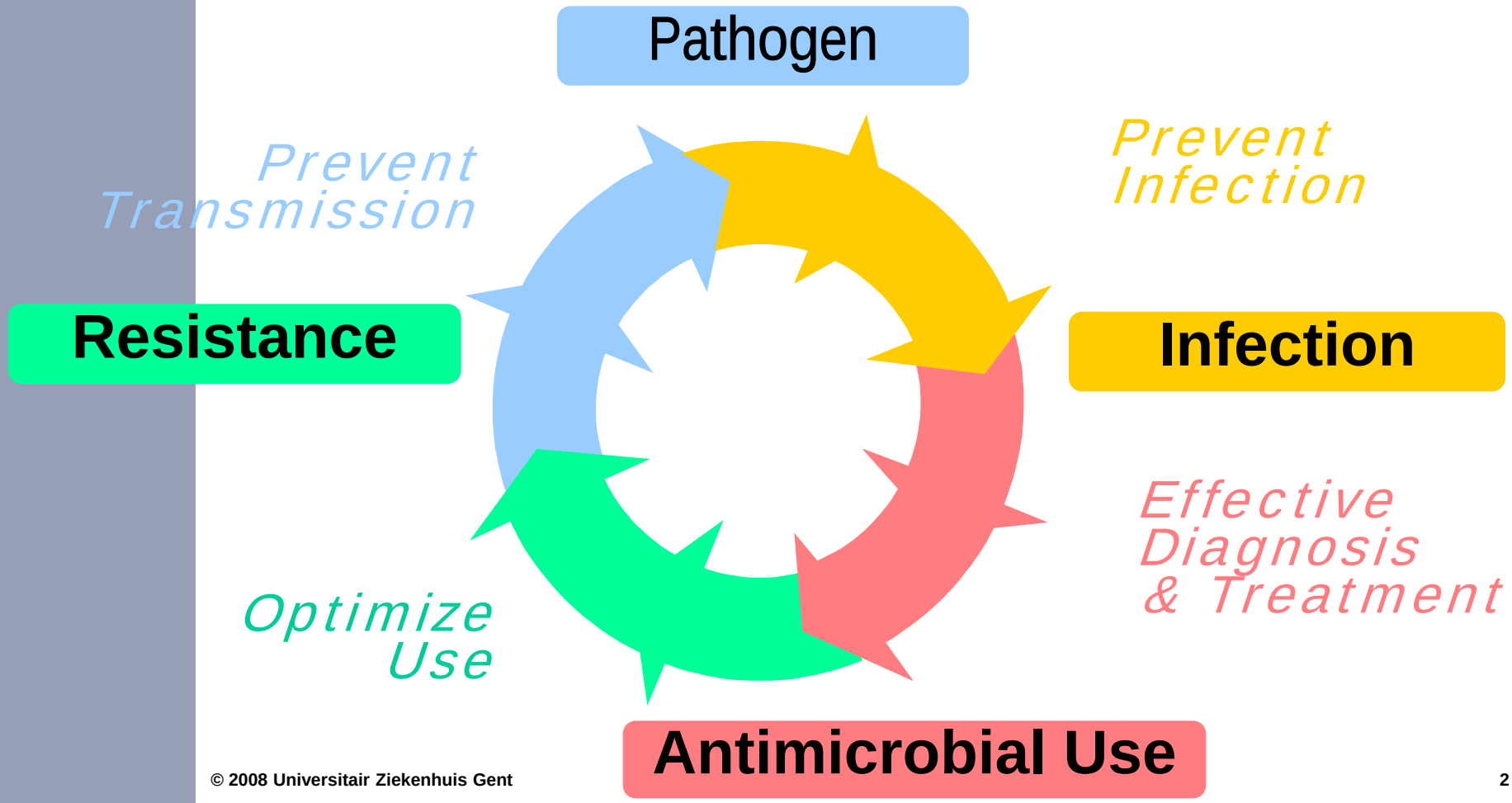
Preventie en behandeling van hemodialyse gerelateerde bacteriële infecties

Workshop

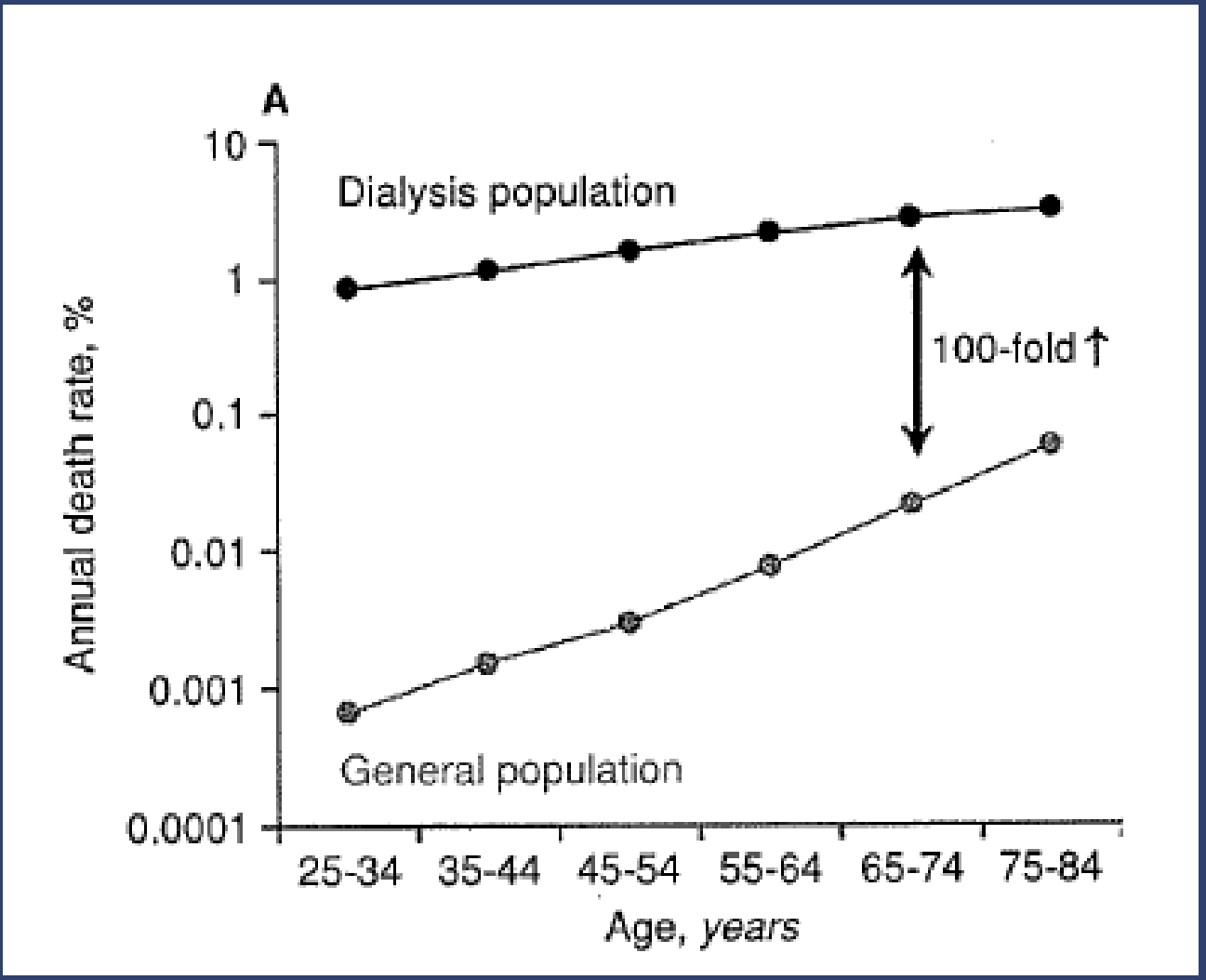
Prof. Dr. Dirk Vogelaers
Dienst algemene inwendige ziekten
UZ Gent
ORPADT symposium, Affligem, 21.5.2015

© 2008 Universitair Ziekenhuis Gent

Antimicrobial Resistance: Key Prevention Strategies



© 2008 Universitair Ziekenhuis Gent



© 2008 Universitair Ziekenhuis Gent

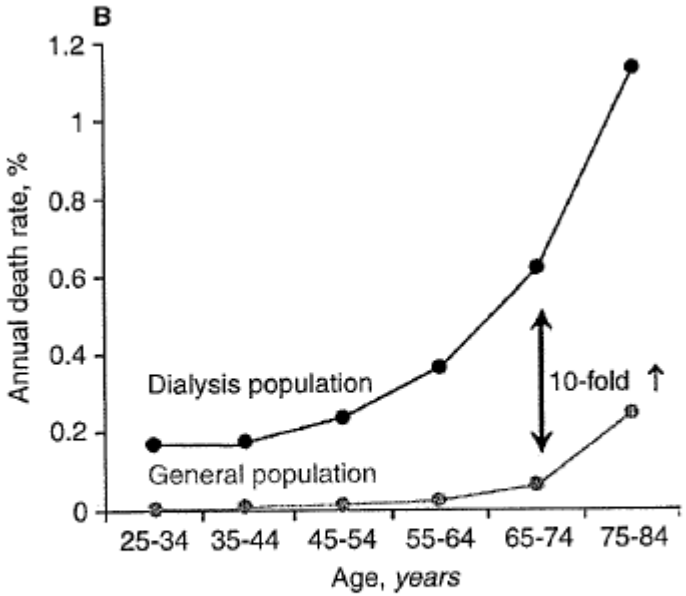
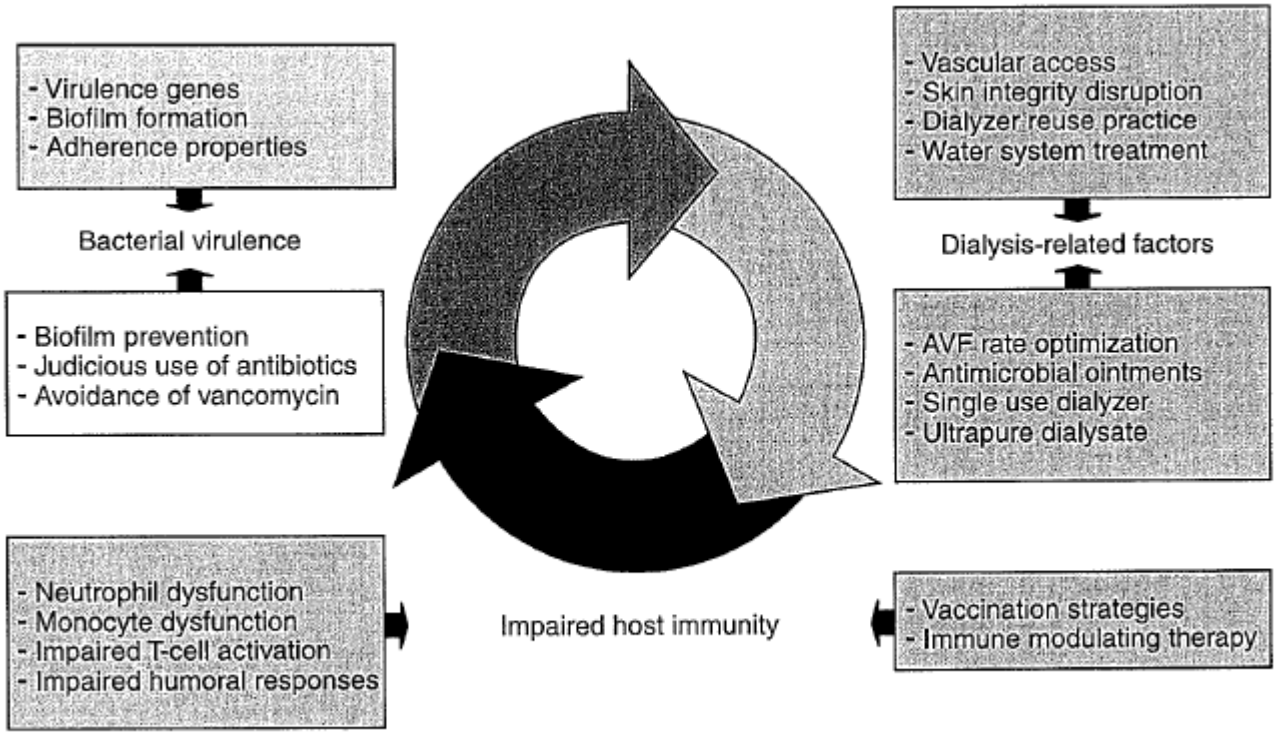


Fig. 1. Annual death rates due to sepsis (*A*) and pulmonary infections (*B*) among dialysis patients (black line) compared with the general population (gray line). The data are stratified by age and are shown on a logarithmic (A) or normal (B) scale. Reproduced with permission from [2, 3].

© 2008 Universitair Ziekenhuis Gent



, **Pathogenesis of bacteremia in hemodialysis patients.** Gray boxes contain common pathogenic factors, white boxes therapeutic strategies.

© 2008 Universitair Ziekenhuis Gent

Haemodialysis catheter related bacteremia/AV access infection: round table questions

- Incidence
- Benchmarking
- % MRSA: institution, unit, clinical indication
- % MRSE (CoNS)

© 2008 Universitair Ziekenhuis Gent

Incidence of bacteremia in hemodialysis patients

Source [reference]	Country	Year	*N*	Incidence of bacteremia per 100 patient-years	Bacteremia due to vascular access	% bacteremia due to gram-positive cocci
Dobkin et al.[13]	USA	1978	N/A	15	73%	70%[a]
Kessler et al.[8]	France	1993	1455	8.4	51%	69.80%
USRDS[1]	USA	1996	USRDS	7.6	48%	N/A
Marr et al.[9] [b]	USA	1998	445	14.4	89%	100%
Kaplowitz et al.[18]	USA	1988	71	8.4	27%	50%[c]
Hoen et al.[20]	France	1998	988	11.2	N/A	68%

N denotes number of hemodialysis patients during the study period. N/A denotes data not available.

[a] Rate applies if bacteremia is vascular access-related

[b] A study on *staphylococcal aureus* bacteremia

[c] Percent of combined bacteremic and nonbacteremic infections related to vascular access

Nassar, George M. & Ayus, Juan Carlos *Kidney International 2001* **60** (1), 1-13

Incidence of catheter-related bacteremia (CRB) in hemodialysis patients

Source [reference]	Country	Year	*N*	Incidence of CRB per 1000 catheter-days	% CRB due to gram-positive cocci
Moss et al.[28]	USA	1990	131	0.7	N/A
Marr et al.[29]	USA	1997	102	3.9	63%
Kairaitis and Gottlieb[21]	Australia	1999	105	6.5	100%
Beathard[30]	USA	1999	387	3.4	84.5%[b]
Saad[31]	USA	1999	101	5.5	67.4%[c]
Cuevas et al (abstract)[a]	Spain	1999	189	1.54	84%
Cuevas et al (abstract)	Spain	1999	45	1	84%

N denotes number of patients with hemodialysis catheters; N/A denotes data not available.

[a] A study on temporary dialysis catheters

[b] Includes 9.8% of cultures due to mixed gram-positive and gram-negative infections

[c] Includes 12.8% cultures with mixed gram-positive and gram-negative infections

Nassar, George M. & Ayus, Juan Carlos *Kidney International* **60** (1), 1-13

Incidence of bacteremia/ catheter-related infections

- **Rates of access-related bacteremia per 100 patient-months (CDC surveillance study)**
  - 0.25 for native fistulae
  - 0.53 for synthetic bridge grafts
  - 4.8 for tunneled cuffed catheters
  - 8.7 for non-cuffed catheters

(Tokars. Am J Infect Control 2002; 30:288-95)

© 2008 Universitair Ziekenhuis Gent

Tunneled dialysis catheters

- 2,0-5,5 episodes of bacteremia per 1000 catheter days

(Rocklin, Am J Kidney Dis 2001; 37: 557-63)

(Saad Am J Kidney Dis 1999; 37: 1114-1125)

→ translates into 22-100.000 cases of catheter-related bacteremia annually in US

- Significant associated morbidity and cost

© 2008 Universitair Ziekenhuis Gent

Catheter related bacteremia: outcome

- **Rapid defervescence following catheter removal the rule.**
- **Metastatic infection (osteomyelitis, IE) or septic thrombophlebitis to be considered with persisting fever (> 72 hrs) + recurrence of bacteremia**
  - TEE
  - duplex ultrasound , CT + contrast
- **Metastatic infection not uncommon:**
  - range of incidence reported in mainly retrospective studies
  - IE in 25 % of S. aureus bacteremia in association with IV catheter

(Fowler et al. CID 1999; 28: 106-14)

© 2008 Universitair Ziekenhuis Gent

Consequences of CR-BSI

- **94 pts with 102 episodes of CR-BSI**
  - major complications in 33 episodes (32 %)
    - septic shock (12 episodes)
    - sustained sepsis (12)
    - suppurative thrombophlebitis (7)
    - metastatic infection (5)
    - endocarditis (2)
  - highest risk for major complications with Candida, P. aeruginosa, S. aureus and polymicrobial CR-BSI
  - extra hospital cost assessed through revieuw of medical and billing records
    - 3.707 USD for all episodes
    - 6.064 USD for S. aureus CR-BSI

(Arnow et al. CID 1993; 16: 778-84)

© 2008 Universitair Ziekenhuis Gent

Clinical impact of MRSA bacteremia

- **3.700 USD extra cost attributable to resistance**

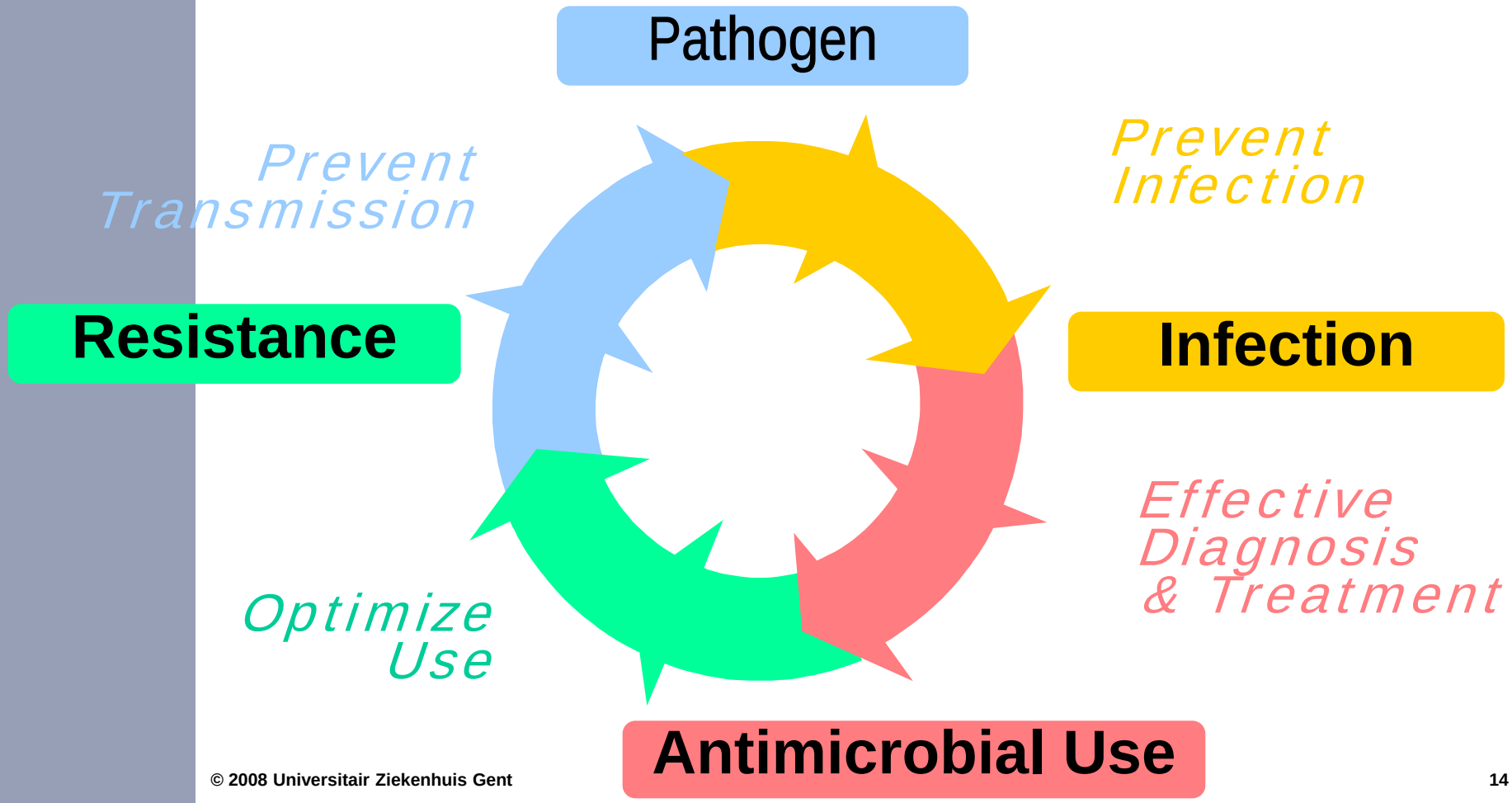
  (Rubin. Emerg Infect Dis 1999;5:9-17)

- **Data from 31 studies of *S. aureus* bacteremia pooled between 1980-2000:**
  - mortality ↑ with MRSA bacteremia: OR 1.93 (95 % CI 1.54-2.42) (p<0.001 vs MSSA)

  (Cosgrove. CID 2003:36(1):53-9)

© 2008 Universitair Ziekenhuis Gent

Antimicrobial Resistance: Key Prevention Strategies



© 2008 Universitair Ziekenhuis Gent

Table 5. General Infection-Control Measures for Patient Contacts in the Dialysis Unit

- Wash hands or use an alcohol-based hand rub after touching one patient and before going to the next patient or to a clean area.
- Wear disposable nonsterile gloves when it is anticipated that hands may contact blood, body fluids, or contaminated items. The CDC recommends use of gloves for all contact with hemodialysis patients and equipment.
- Remove gloves and perform hand hygiene after patient contacts.
- Consider any medication or equipment taken to the dialysis station to be potentially contaminated. Discard or disinfect such items before they are used on another patient.
- Wipe all surfaces at the dialysis station, including control panel and knobs on dialysis machines, with a disinfectant between patients.
- For patients at increased risk for transmitting VRE or MRSA, with infected skin wounds, or with fecal incontinence or diarrhea, consider:
  - Use of nonsterile gloves and a separate gown for staff members treating the patient, to be removed when finished with care
  - Dialyzing patient at a station with as few adjacent stations as possible.

© 2008 Universitair Ziekenhuis Gent

Summary of Recommendations: Guidelines for the Prevention of Intravascular Catheter-related Infections

Naomi P. O'Grady,[1] Mary Alexander,[2] Lillian A. Burns,[3] E. Patchen Dellinger,[4] Jeffrey Garland,[5] Stephen O. Heard,[6] Pamela A. Lipsett,[7] Henry Masur,[1] Leonard A. Mermel,[8] Michele L. Pearson,[9] Issam I. Raad,[10] Adrienne G. Randolph,[11] Mark E. Rupp,[12] Sanjay Saint,[13] and the Healthcare Infection Control Practices Advisory Committee (HICPAC) (Appendix 1)

Clinical Infectious Diseases 2011;52(9):1087–1099

- Education, training, staffing
- Selection of catheters and sites
- Hand hygiene and aseptic technique
- Sterile barrier precautions
- Patient cleansing and skin preparation
- Catheter site dressing regimens
- Antimicrobial/antiseptic impregnated catheters
- Systemic antibiotic prophylaxis
- Antibiotic/antiseptic ointments
- Antibiotic lock prophylaxis
- anticoagulants

© 2008 Universitair Ziekenhuis Gent

Table 1. Recommendations for the Prevention of Hemodialysis Catheter Infection

Use sterile technique (cap, mask, sterile gown, large sterile drapes, and gloves) for catheter insertion.
Limit use of femoral vein catheters to 5 days.
Limit use of noncuffed central venous catheters to 3 to 4 weeks.
Use the catheter solely for hemodialysis unless there is no alternative.
Restrict catheter manipulation and dressing changes to trained personnel.
Examine exit site for infection at each hemodialysis treatment.
Consider soaking caps or blood catheter connectors in povidone-iodine for 3 to 5 minutes and allow to dry before separation.
Keep catheter lumens sterile: maintain aseptic technique when accessing the catheter.
Do not leave the catheter lumen open to air.
Replace catheter-site dressing at each dialysis treatment or if damp, loose, or soiled.
Disinfect skin before catheter insertion and dressing changes. Use a 2% chlorhexidine-based preparation (preferred), tincture of iodine, an iodophor, or 70% alcohol.
Consider having patients wear surgical masks when the catheter cap is removed and the bloodstream is accessed and for dressing changes.
Ensure that catheter-site care is compatible with the catheter material.
Have dialysis health care workers wear gloves and surgical masks or face shields when removing the catheter cap and accessing the bloodstream and for dressing changes.
Consider the use of nasal mupirocin for documented carriers of *S aureus* in patients with previous catheter-related bacteremia if ongoing catheter-based hemodialysis is necessary.

© 2008 Universitair Ziekenhuis Gent

Table 2. Recommendations for the Prevention of AV Fistula and Graft Infection

Wash the area to be punctured with antibacterial soap or scrub (eg, 2% chlorhexidine) and treat the area with tincture of chlorhexidine, 70% alcohol, or povidone-iodine before cannulation (NOTE: Alcohol should be applied in a rubbing motion for 1 minute immediately before cannulation. Povidone-iodine should be applied for 2 to 3 minutes and allowed to dry before cannulation.)
Use clean gloves for access puncture, with new gloves used for each patient. Gloves should be changed if contaminated.
Ensure that dialysis personnel receive adequate training and follow recommended access-puncture techniques.

© 2008 Universitair Ziekenhuis Gent

Meta-analysis: Antibiotics for Prophylaxis against Hemodialysis Catheter–Related Infections

Matthew T. James, MD; Joslyn Conley, MSc, MD; Marcello Tonelli, MD, SM; Braden J. Manns, MD, MSc; Jennifer MacRae, MD, MSc; and Brenda R. Hemmelgarn, PhD, MD, for the Alberta Kidney Disease Network

Background: Catheter-related infections cause morbidity and mortality in patients undergoing hemodialysis.

Purpose: To examine whether topical or intraluminal antibiotics reduce catheter-related bloodstream infection compared with no antibiotic therapy in adults undergoing hemodialysis.

Data Sources: Electronic databases, trial registries, bibliographies, and conference proceedings up to October 2007, with no language restrictions.

Study Selection: Two reviewers independently selected randomized, controlled trials using topical or intraluminal antibiotics for prophylaxis of infection in adults with catheters who are undergoing hemodialysis.

Data Extraction: Two independent reviewers assessed studies for inclusion, quality, and extracted data.

Data Synthesis: Fixed-effects models were used to estimate pooled rate ratios for outcomes. Topical antibiotics reduced the rate of bacteremia (rate ratio, 0.22 [95% CI, 0.12 to 0.40]; 0.10 vs. 0.45 case of bacteremia per 100 catheter-days), exit-site infection (rate ratio, 0.17 [CI, 0.08 to 0.38]; 0.06 vs. 0.41 case of infection per 100 catheter-days), need for catheter removal, and hospitalization for infection. Intraluminal antibiotics reduced the rate of bacteremia (rate ratio, 0.32 [CI, 0.22 to 0.47]; 0.12 vs. 0.32 case of bacteremia per 100 catheter-days) and need for catheter removal. Intraluminal antibiotics did not significantly reduce the rate of exit-site infection, and no hospitalization data were available for these agents.

Limitations: The evidence base included only 16 trials, and most had less than 6 months of follow-up. Only one third of studies were blinded. Publication bias was evident.

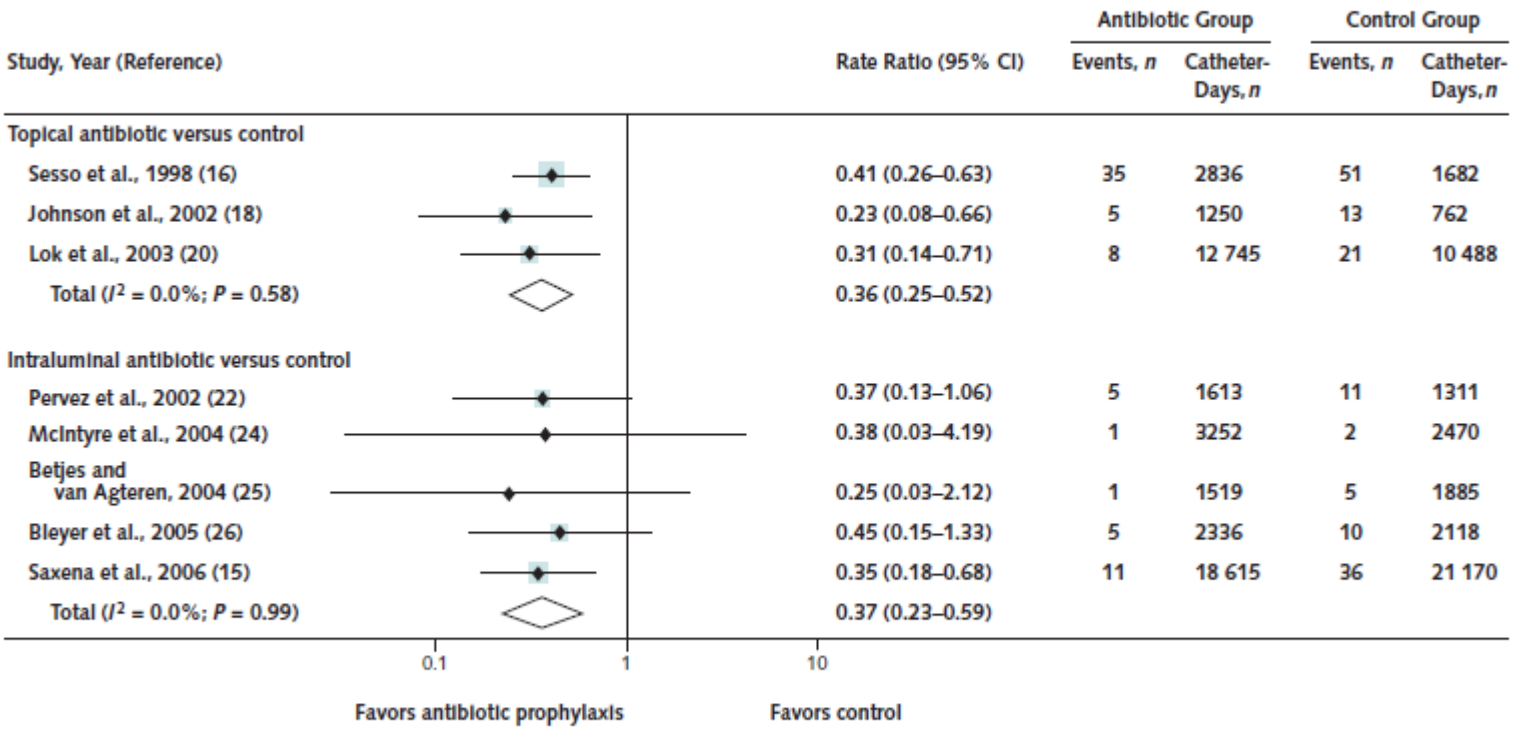
Conclusion: Both topical and intraluminal antibiotics reduced the rate of bacteremia as well as the need for catheter removal secondary to complications. Whether these strategies will lead to antimicrobial resistance and loss of efficacy over longer periods remains unclear.

Ann Intern Med. 2008;148:596-605. www.annals.org

For author affiliations, see end of text.

© 2008 Universitair Ziekenhuis Gent

Figure 3. **Forest plot of studies comparing the effect of topical or intraluminal antibiotics versus no antibiotics on the rate of catheter removal due to complication in hemodialysis patients.**



Solid diamonds represent point estimates, lines represent 95% CIs, and shaded boxes represent the percentage of weight contributed by each study. Open diamonds represent pooled results and are centered on the pooled point estimate, with length representing the pooled 95% CI.

© 2008 Universitair Ziekenhuis Gent

Screening and treatment for *Staphylococcus aureus* in patients undergoing hemodialysis: a systematic review and meta-analysis

Cibele Grothe[1*], Mônica Taminato[1], Angélica Belasco[1], Ricardo Sesso[2] and Dulce Barbosa[1]

Abstract

Background: This study was performed to evaluate the effectiveness of surveillance for screening and treatment of patients with chronic kidney disease undergoing hemodialysis and colonized by *Staphylococcus aureus*.

Methods: A systematic review and meta-analysis were performed. The literature search involved the following databases: the Cochrane Controlled Trials Register, Embase, LILACS, CINAHL, SciELO, and PubMed/Medline. The descriptors were "*Staphylococcus aureus*", "MRSA", "MSSA", "treatment", "decolonization", "nasal carrier", "colonization", "chronic kidney disease", "dialysis", and "haemodialysis" or "hemodialysis". Five randomized controlled trials that exhibited agreement among reviewers as shown by a kappa value of >0.80 were included in the study; methodological quality was evaluated using the STROBE statement. Patients who received various treatments (various treatments group) or topical mupirocin (mupirocin group) were compared with those who received either no treatment or placebo (control group). The outcomes were skin infection at the central venous catheter insertion site and bacteremia.

Results: In total, 2374 patients were included in the analysis, 626 (26.4%) of whom were nasal carriers of *S. aureus*. The probability of *S. aureus* infection at the catheter site for hemodialysis was 87% lower in the mupirocin group than in the control group (odds ratio [OR], 0.13; 95% confidence interval [CI], 0.05–0.34; $p < 0.001$). The risk of bacteremia was 82% lower in the mupirocin group than in the control group (OR, 0.18; 95% CI, 0.08–0.42; $p < 0.001$). No statistically significant difference in bacteremia was observed between the various treatments group (excluding mupirocin) and the control group (OR, 0.77; 95% CI, 0.51–1.15; $p = 0.20$).

Conclusions: Twenty-six percent of patients undergoing hemodialysis were nasal carriers of *S. aureus*. Of all treatments evaluated, topical mupirocin was the most effective therapy for the reduction of *S. aureus* catheter site infection and bacteremia in patients undergoing chronic hemodialysis.

Keywords: *Staphylococcus aureus*, Colonization, Infection, Hemodialysis, Treatment

© 2008 Universitair Ziekenhuis Gent

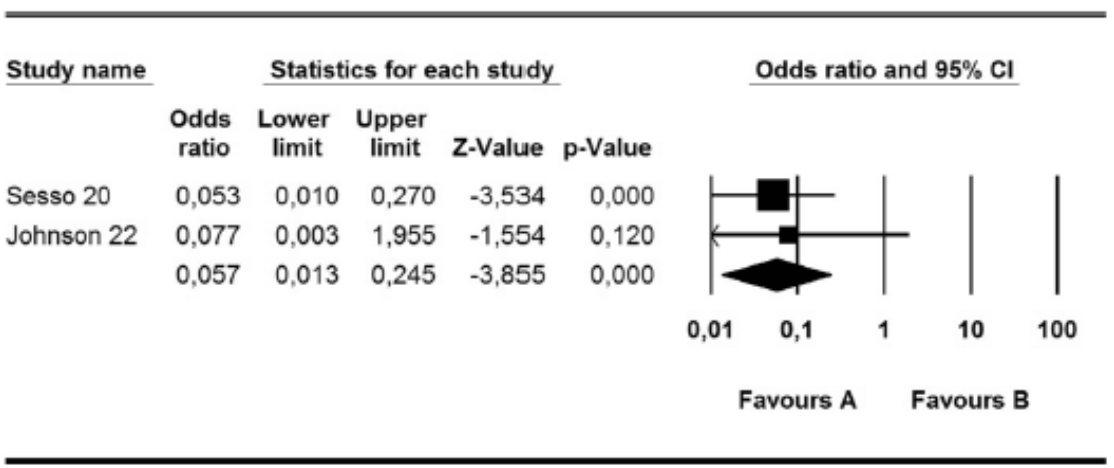


Figure 2 Meta-analysis of mupirocin versus control: eradication of *S. aureus* nasal colonization in hemodialysis patients.

© 2008 Universitair Ziekenhuis Gent

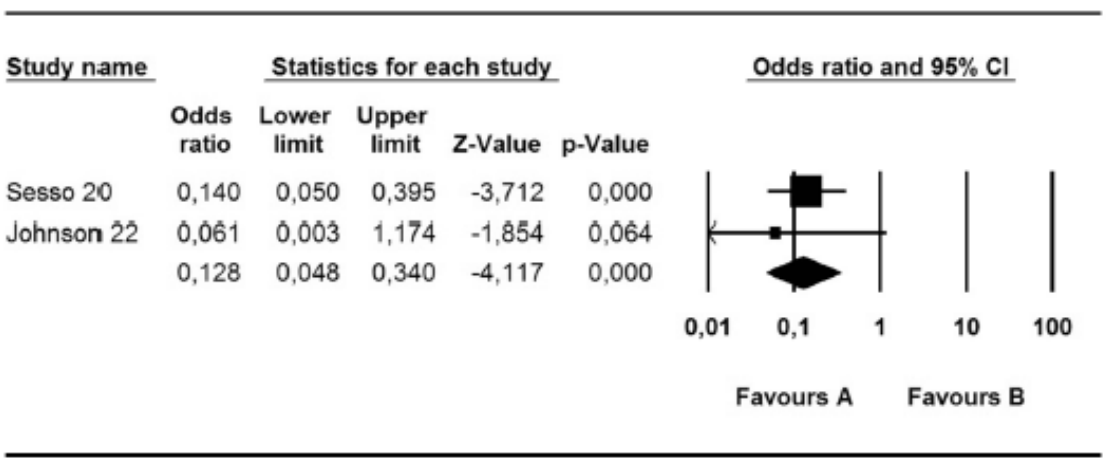


Figure 3 Meta-analysis of mupirocin versus control: *S. aureus* skin infection at catheter insertion site.

© 2008 Universitair Ziekenhuis Gent

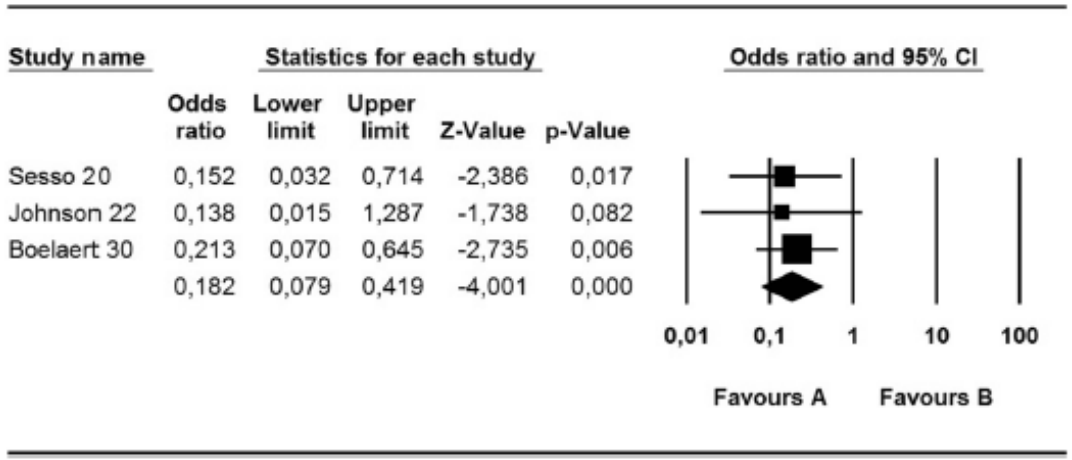


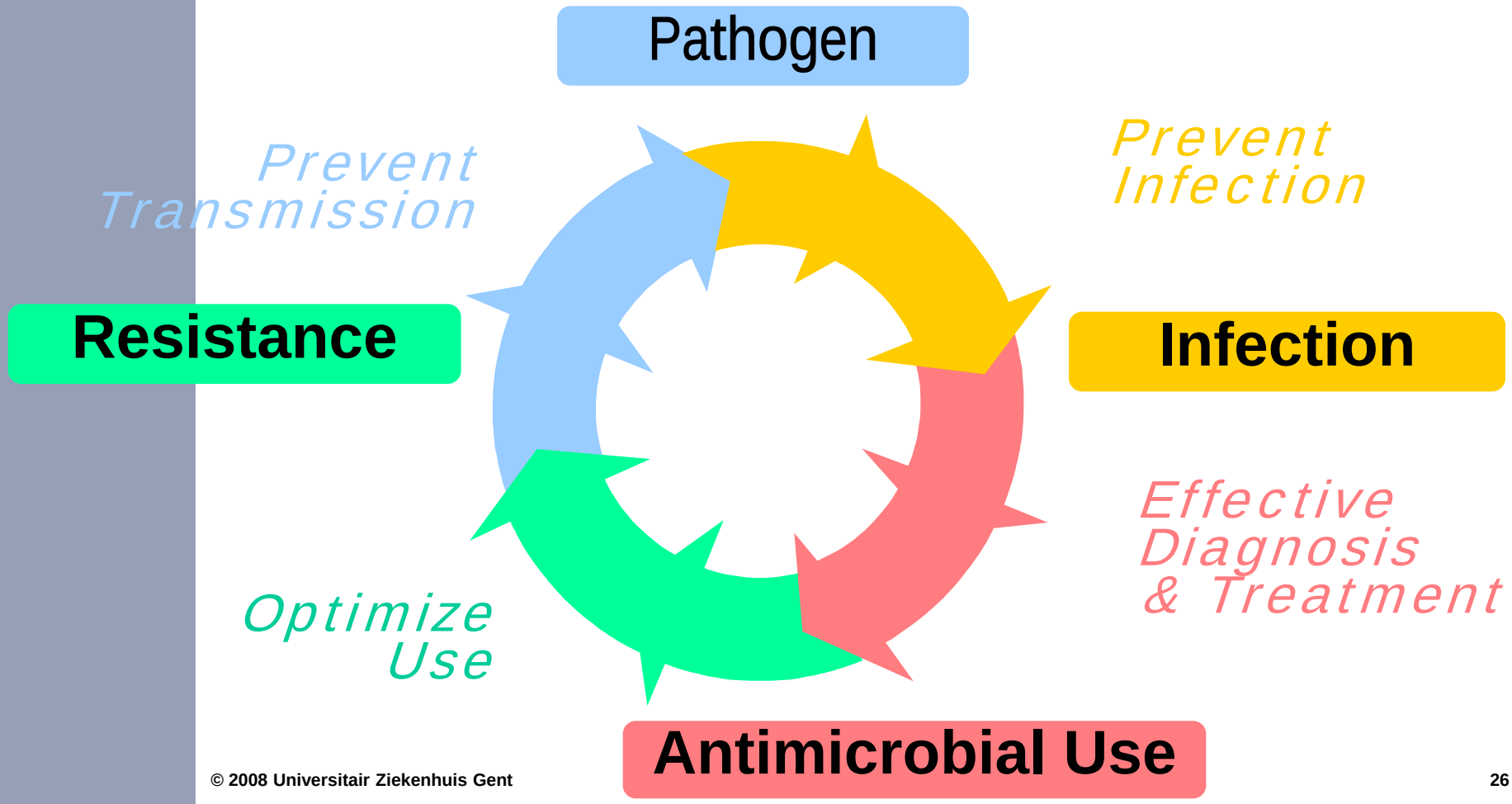
Figure 4 Meta-analysis of mupirocin versus control: risk of *S. aureus* bacteremia.

© 2008 Universitair Ziekenhuis Gent

- **Protocolair werken**
- **Bundle approach**
- **Use of checklists**

© 2008 Universitair Ziekenhuis Gent

Antimicrobial Resistance: Key Prevention Strategies



© 2008 Universitair Ziekenhuis Gent

Clinical case history 1

- 65 y old woman; 3 weeks dialysis through non-cuffed temporary dialysis catheter.
- 3 days of spiking fever with chills + general malaise.

© 2008 Universitair Ziekenhuis Gent

Clinical case history 1

- 65 y old woman; 3 weeks dialysis through non-cuffed temporary dialysis catheter.
- 3 days of spiking fever with chills + general malaise.
- Blood cultures: number?
- Empirical antimicrobials?

© 2008 Universitair Ziekenhuis Gent

Empiric choice: result of a systematic reflection

- **Clinical diagnosis + modifying circumstances**
  - Cholangitis
  - Community-acquired vs nosocomial
  - Biliary tract stent
- **Frequency distribution of pathogens + knowledge about susceptibility**
  - Local epidemiologic data (unit- and population-specific)
  - Regional data from regular surveys (in reference labs)(S pneumoniae in CAP, anaerobes in intra-abdominal infection)
- **Basis of GCP (good clinical practice), as reflected in antimicrobial guides (e.g Belgian Sanford guide on antimicrobial therapy)**

© 2008 Universitair Ziekenhuis Gent

Clinical case history 1

- **65 y old woman; 3 weeks dialysis through non-cuffed temporary dialysis catheter.**
- **3 days of spiking fever with chills + general malaise.**
- **Blood cultures:**
  - To be obtained before inititiation of empiric antimicrobials
  - 2 to 3 as opposed to 1 (increases likelihood of identifying pathogen + discrimination of CoNS as true pathogen or contaminant)
  - At least one peripheral blood culture, even in pts with limited venous sites or with considerations of preservation of future AV access sites.
- **Empirical antimicrobials:**
  - Vancomycin
  - Linezolid as short term alternative until cultures are known.

© 2008 Universitair Ziekenhuis Gent

Clinical case history 1

- **Blood cultures grow…..**
  - S aureus (MSSA)
  - S aureus (MRSA)
  - Coagulase negative staphylococci (CoNS), methicillin-sensitive
  - Methicillin-resistant CoNS (MRSE)
  - Candida albicans
  - Candida non-albicans
  - Gram negative bacilli

© 2008 Universitair Ziekenhuis Gent

Case 2 (variant)

- MSSA bacteremia treated with flucloxacillin 4 x 500 mg for 14 days
- TEE after 2 weeks of therapy positive for vegetations

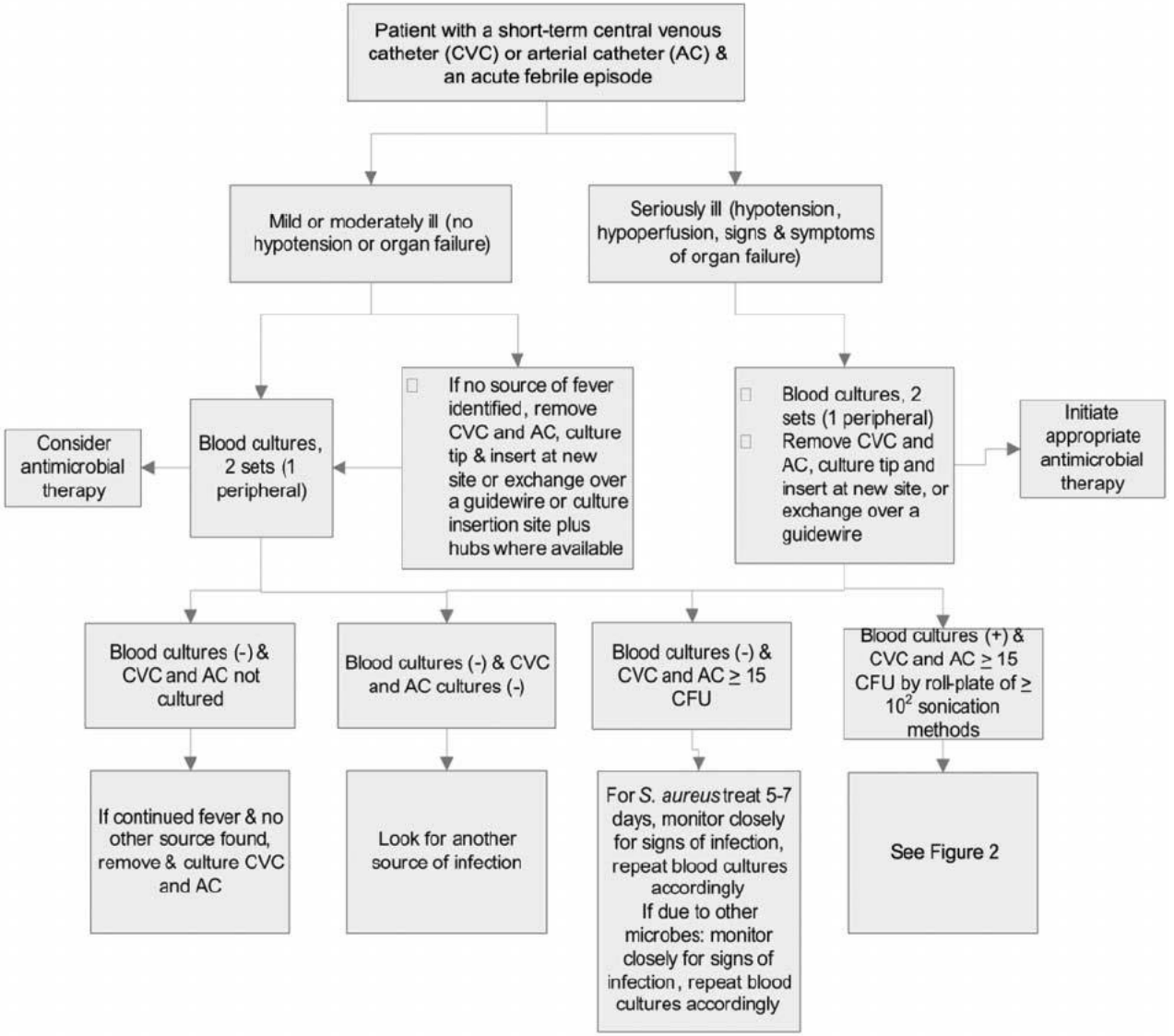
© 2008 Universitair Ziekenhuis Gent

Key reference

Mermel et al. Guidelines for the diagnosis and management of intravascular catheter-related infections: 2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 49: 1-45

© 2008 Universitair Ziekenhuis Gent

Methods for the diagnosis of acute fever for a patient suspected of having short-term CVC infection or arterial catheter infection

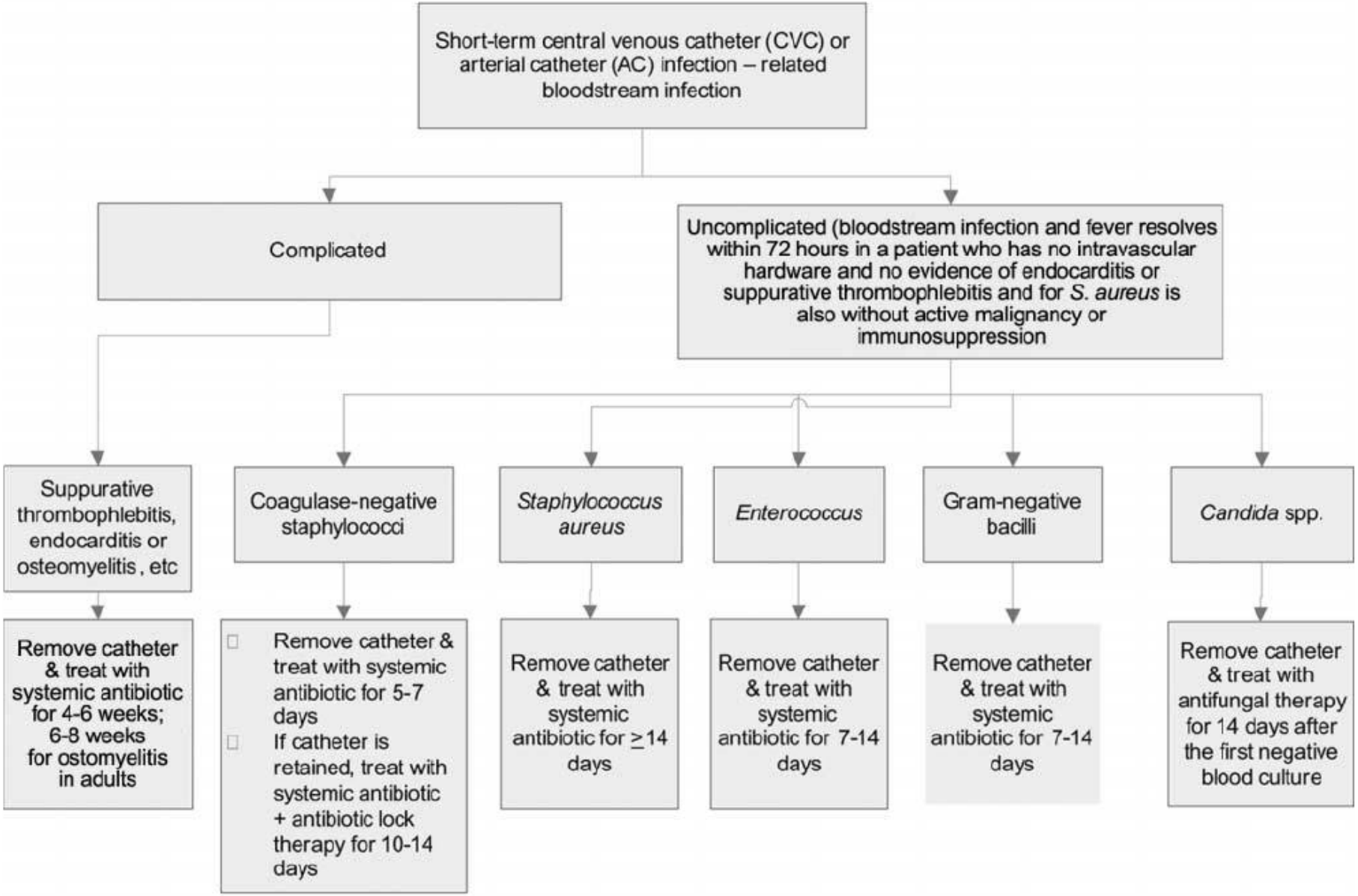


© 2008 Universitair

Approach to the management of patients with short-term CVC-related or arterial catheter-related bloodstream infection

Universitair Ziekenhuis Gent

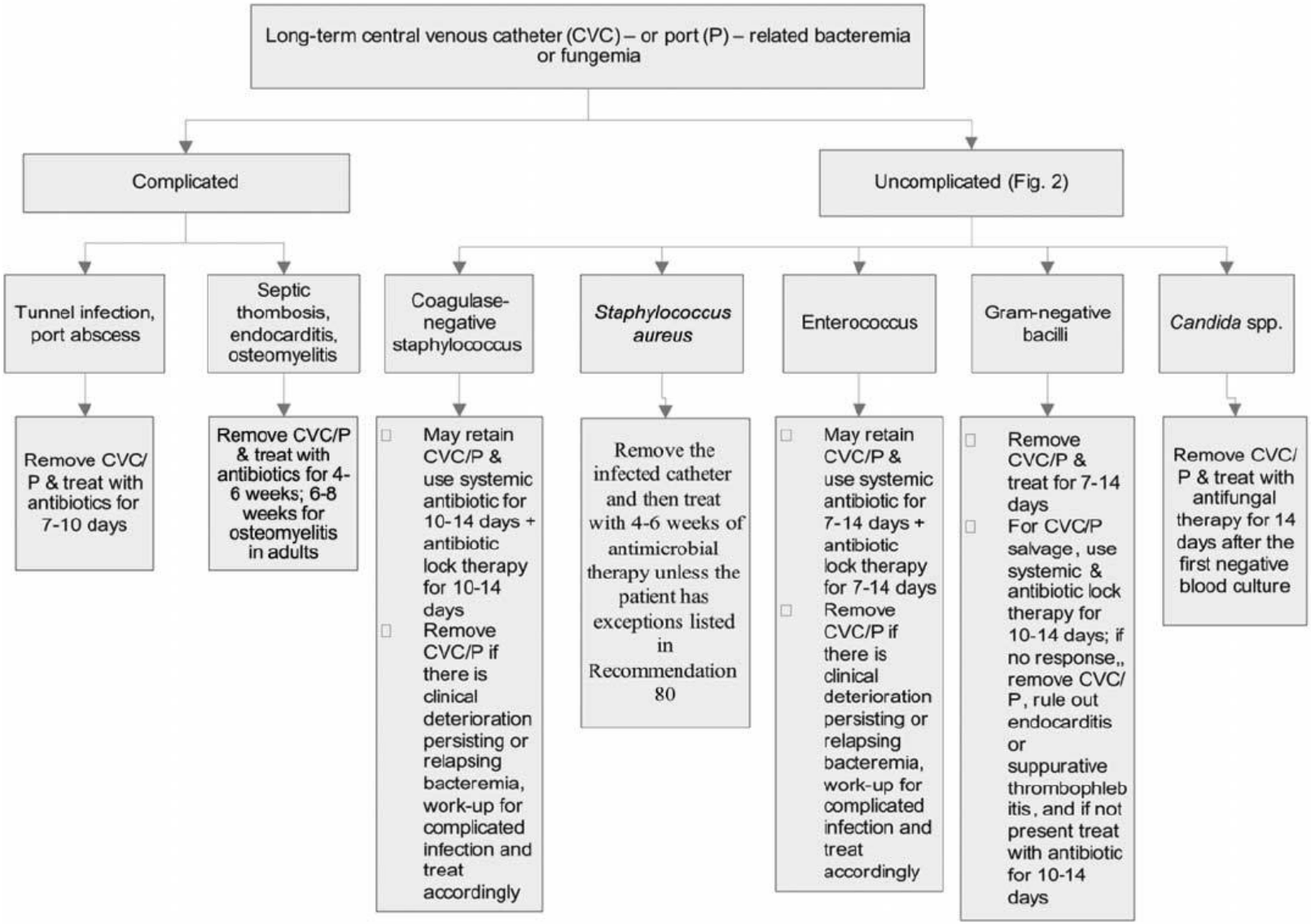
UNIVERSITEIT GENT



Approach to the treatment of a patient with a long-term CVC or a port (P)-related bloodstream infection

Universitair Ziekenhuis Gent

UNIVERSITEIT GENT



β-lactams vs glycopeptides

- ↑ left-sided complications (46 % with vanco (n=39) vs 22 % with β-lactams (n=45)) and higher mortality (33.5 % with vanco vs 8.9 %) in S. aureus (MSSA) endocarditis

  (Lodize ICAAC 2002)
- More persistent bacteremia in hemodialysis pts with MSSA bacteremia
- Higher recurrence rate in S aureus osteomyelitis treated with GP (28 % with PRSP and ceftriaxone vs 53 % with vanco) (CI 0.99-7.2) on limited no. of pts (n= 56 with PRSP, n = 32 with CTX and n=9 with vanco)

© 2008 Universitair Ziekenhuis Gent

What are the unique aspects of managing patients receiving hemodialysis through catheters for whom catheter-related infection is suspected or proven?

© 2008 Universitair Ziekenhuis Gent

Peripheral blood samples should be obtained for culture from vessels that are not intended for future use in creating a dialysis fistula (e.g., hand veins)	A-III
When a peripheral blood sample cannot be obtained, blood samples may be drawn during hemodialysis from bloodlines connected to the CVC	B-II
In patients with suspected CRBSI for whom blood cultures have been obtained and for whom antibiotic therapy has been initiated, antibiotic therapy can be discontinued if both sets of blood cultures have negative results and no other source of infection is identified	B-II

© 2008 Universitair Ziekenhuis Gent

When a peripheral blood sample cannot be obtained, no other catheter is in place from which to obtain an additional blood sample, there is no drainage from the insertion site available for culture, and there is no clinical evidence for an alternate source of infection, then positive results of culture performed on a blood sample obtained from a catheter should lead to continuation of antimicrobial therapy for possible CRBSI in a symptomatic hemodialysis patient	B-II
The infected catheter should always be removed for patients with hemodialysis CRBSI due to *S. aureus*, *Pseudomonas* species, or *Candida* species and a temporary (nontunneled catheter) should be inserted into another anatomical site	A-II

© 2008 Universitair Ziekenhuis Gent

If absolutely no alternative sites are available for catheter insertion, then exchange the infected catheter over a guidewire	B-II
When a hemodialysis catheter is removed for CRBSI, a long-term hemodialysis catheter can be placed once blood cultures with negative results are obtained	B-III
For hemodialysis CRBSI due to other pathogens (e.g., gram-negative bacilli other than *Pseudomonas* species or coagulase-negative staphylococci), a patient can initiate empirical intravenous antibiotic therapy without immediate catheter removal. If the symptoms persist or if there is evidence of a metastatic infection, the catheter should be removed	B-II

© 2008 Universitair Ziekenhuis Gent

If the symptoms that prompted initiation of antibiotic therapy (fever, chills, hemodynamic instability, or altered mental status) resolve within 2–3 days and there is no metastatic infection, then the infected catheter can be exchanged over a guidewire for a new, long-term hemodialysis catheter	B-II
Alternatively, for patients for whom catheter removal is not indicated (i.e., those with resolution of symptoms and bacteremia within 2–3 days after initiation of systemic antibiotics and an absence of metastatic infection), the catheter can be retained, and an antibiotic lock can be used as adjunctive therapy after each dialysis session for 10–14 days	B-II

© 2008 Universitair Ziekenhuis Gent

Empirical antibiotic therapy should include vancomycin and coverage for gram-negative bacilli, based on the local antibiogram (e.g., third-generation cephalosporin, carbapenem, or β-lactam/β-lactamase combination)	A-II
Patients who receive empirical vancomycin and who are found to have CRBSI due to methicillin-susceptible *S. aureus* should be switched to cefazolin	A-II
For cefazolin, use a dosage of 20 mg/kg (actual body weight), rounded to the nearest 500-mg increment, after dialysis	A-II

© 2008 Universitair Ziekenhuis Gent

A 4–6-week antibiotic course should be administered if there is persistent bacteremia or fungemia (i.e., >72 h in duration) after hemodialysis catheter removal or for patients with endocarditis or suppurative thrombophlebitis, and 6–8 weeks of therapy should be administered for the treatment of osteomyelitis in adults (figures 3 and 4)	B-II
Patients receiving dialysis who have CRBSI due to vancomycin-resistant enterococci can be treated with either daptomycin (6 mg/kg after each dialysis session) or oral linezolid (600 mg every 12 h)	B-II
It is not necessary to confirm negative culture results before guidewire exchange of a catheter for a patient with hemodialysis-related CRBSI if the patient is asymptomatic	B-III

© 2008 Universitair Ziekenhuis Gent

Surveillance blood cultures should be obtained 1 week after completion of an antibiotic course for CRBSI if the catheter has been retained	B-III
If the blood cultures have positive results, the catheter should be removed and a new, long-term dialysis catheter should be placed after additional blood cultures are obtained that have negative results	B-III

© 2008 Universitair Ziekenhuis Gent

Antibiotic lock is indicated for patients with CRBSI involving long-term catheters with no signs of exit site or tunnel infection for whom catheter salvage is the goal	B-II
For CRBSI, antibiotic lock should not be used alone; instead, it should be used in conjunction with systemic antimicrobial therapy, with both regimens administered for 7–14 days	B-II

© 2008 Universitair Ziekenhuis Gent

Dwell times for antibiotic lock solutions should generally not exceed 48 h before reinstallation of lock solution; preferably, reinstallation should take place every 24 h for ambulatory patients with femoral catheters (B-II). However, for patients who are undergoing hemodialysis, the lock solution can be renewed after every dialysis session	B-II
However, for patients who are undergoing hemodialysis the lock solution can be renewed after every dialysis session.	B-II

© 2008 Universitair Ziekenhuis Gent

Catheter removal is recommended for CRBSI due to *S. aureus* and *Candida* species, instead of treatment with antibiotic lock and catheter retention, unless there are unusual extenuating circumstances (e.g., no alternative catheter insertion site)	A-II
For patients with multiple positive catheter-drawn blood cultures that grow coagulase-negative staphylococci or gram-negative bacilli and concurrent negative peripheral blood cultures, antibiotic lock therapy can be given without systemic therapy for 10–14 days	B-III

© 2008 Universitair Ziekenhuis Gent

For vancomycin, the concentration should be at least 1000 times higher than the MIC (e.g., 5 mg/mL) of the microorganism involved	B-II
At this time, there are insufficient data to recommend an ethanol lock for the treatment of CRBSI	C-III

© 2008 Universitair Ziekenhuis Gent

Clinical case 2

- **52 y male; 2 yr haemodialysis synthetic bridge graft (Goretex); 3 days spiking fever with chills + regional inflammation over fistula.**

© 2008 Universitair Ziekenhuis Gent

Clinical case 2

- 52 y male; 2 yr haemodialysis synthetic bridge graft (Goretex); 3 days spiking fever with chills + regional inflammation over fistula + pustular lesion.
- Hospitalisation + empiric vancomycin.
- Day 2: discharge of some pus + positive blood culture for S aureus (MSSA).

© 2008 Universitair Ziekenhuis Gent

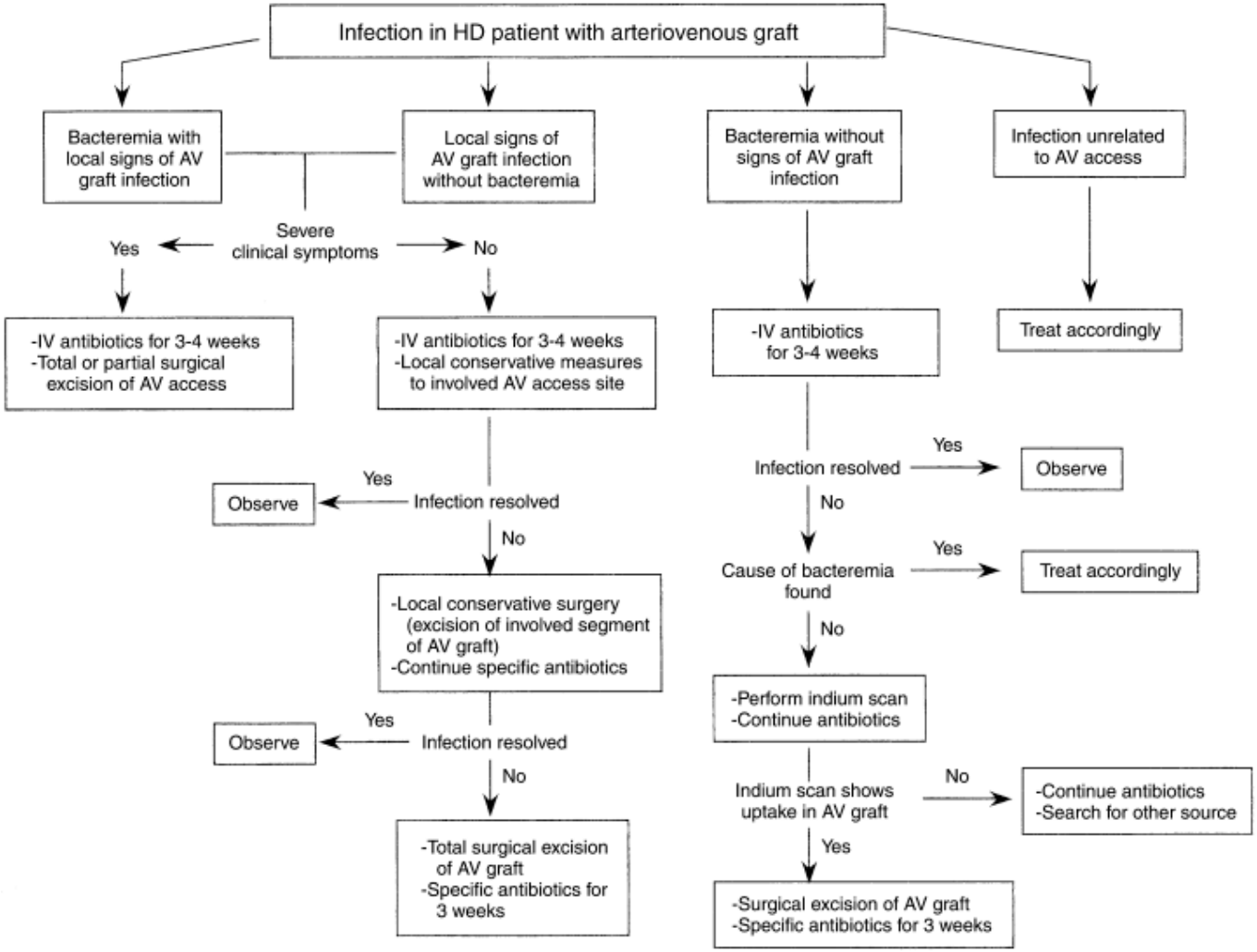
Infections of AV access

- **Only a minority of pts dialysed through native AV fistula (lowest risk modality).**
- **Initial postoperative 30 day PTFE graft infection rate 6 %**

  (Zibari. Am J Kidney Dis 1997; 30:343-8)
- **Overt infection (pain, irritation, tenderness, redness, serous or purulent discharge and skin breakdown)**

  with or without bacteremia.
- **Surgery warranted in:**
  - Abscess formation in immediate graft proximity
  - Purulent drainage from infection that dissects onto graft material
  - Infected aneurysmal dilatations of graft
- **Silent AV graft infection (explains high rates of recurrent bacteremia if gone undetected).**
- **Infection of old clotted AV grafts.**

© 2008 Universitair Ziekenhuis Gent



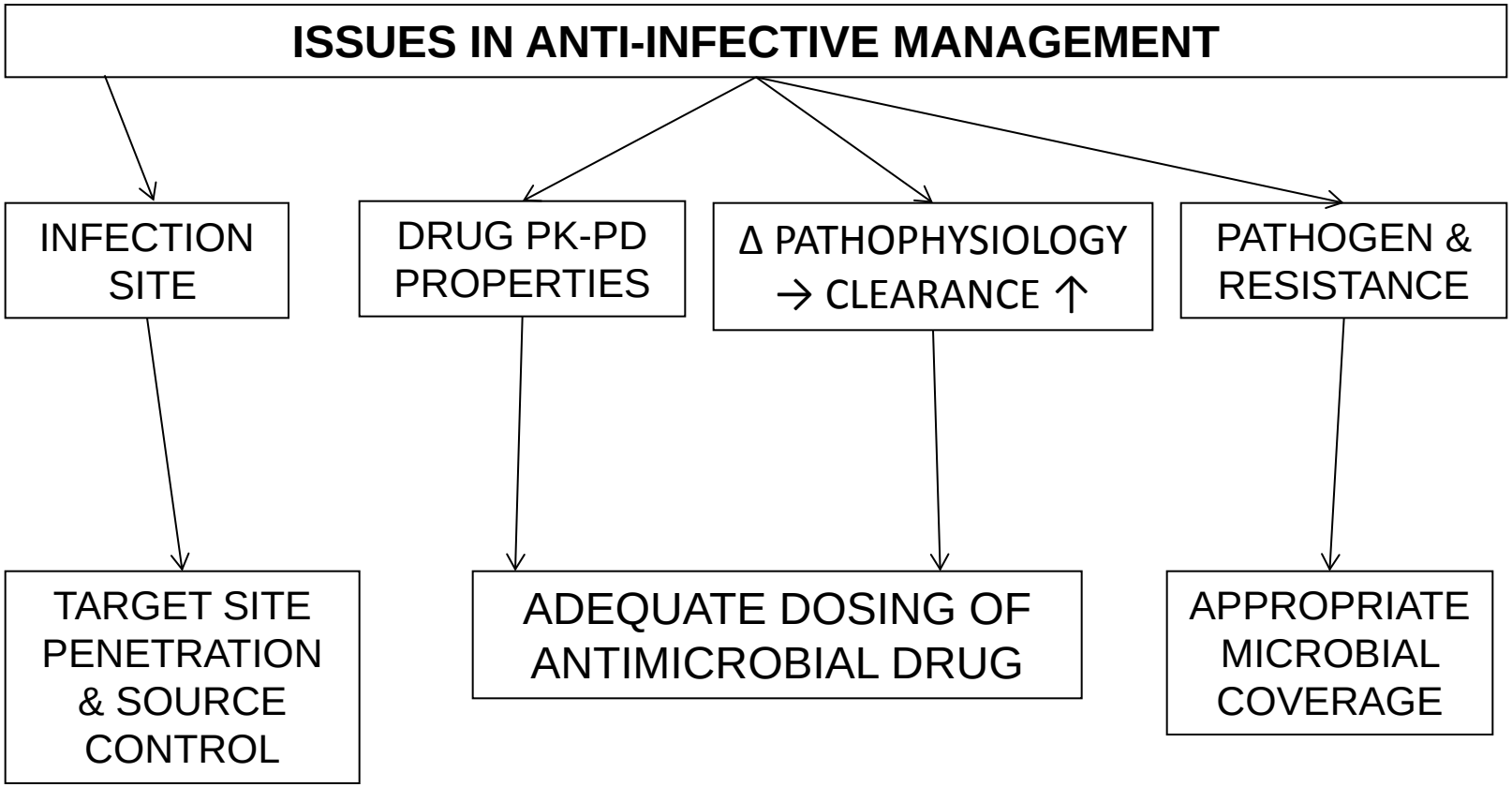
© 2008 Universitair Ziekenhuis Gent

Nassar & Ayus *Kidney International* 2001; **60** (1), 1-13

Key references.

- Nassar, Ayus. Infectious complications of the hemodialysis access. Kidney Int 2001; 60:1-13
- Berns. Infection with antimicrobial-resistant microorganisms in dialysis patients. Sem in Dialysis 2003; 16:30-7
- Mermel et al. Guidelines for the diagnosis and management of intravascular catheter-related infections:2009 update by the Infectious Diseases Society of America. Clin Infect Dis 2009; 49: 1-45
- Berns, Tokars. Preventing bacterial infections and antimicrobial resistance in dialysis pts. Am J Kidney Dis 2002; 40: 886-98

© 2008 Universitair Ziekenhuis Gent



© 2008 Universitair Ziekenhuis Gent

How to Optimize Antimicrobial Therapy : the 4Ds Strategy

Drug — Choose the most appropriate antibiotic(s) for early empiric therapy

Dose — Use the antibiotic(s) with the correct dose and correct dosing schedule

De-escalate — Adapt the antimicrobial treatment when culture results and susceptibilities are available

Duration — Use the shortest course of antibiotic therapy that is clinically indicated

Case 1

- Renal Tx for SLE nephritis
- Suspected rejection: corticosteroid bolus
- ESRD clearance < 10 ml/min with residual diuresis 200 ml/day
- Reinitiation of HD thrice weekly

- Fever with lymphadenopathies in neck region

- Biopsy: M avium intracellulare infection

- Regimen: clarithromycin + ethambutol + amikacin

© 2008 Universitair Ziekenhuis Gent

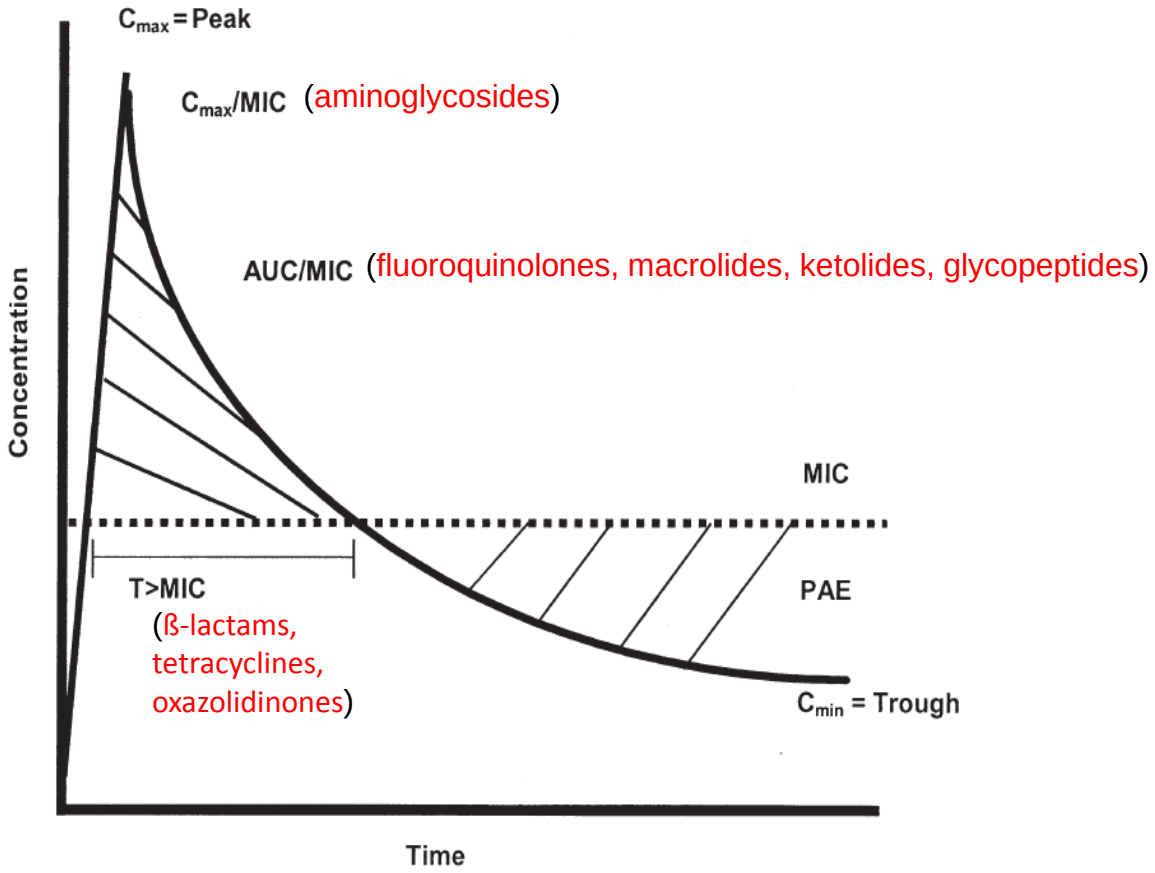


Figure 1 Pharmacodynamic parameters found to be important in describing the efficacy of different antibiotics. AUC = area under the concentration–time curve; C_{max} = maximum concentration; C_{min} = minimum concentration; MIC = minimum inhibitory concentration; PAE = postantibiotic effect; T = time.

Rybak MJ Am J Med 2006;119:S37.

© 2008 Universitair Ziekenhuis Gent

ANTIBACTERIAL	DOSAGE BASED ON ESTIMATED CREATININE CLEARANCE					SUPPLEMENT FOR ADULTS ON HEMODIALYSIS	DOSAGE IN ADULTS ON CRRT[1]	DOSAGE IN ADULTS ON CAPD[1]
	≥ 90 ML/MIN	89 → 60 ML/MIN	59 → 30 ML/MIN	29 → 15 ML/MIN	< 15 ML/MIN (ESRD[1])			
AMINOGLYCOSIDES								
- Maintenance dosage is mainly guided by peak and trough serum levels, therapeutic drug monitoring recommended (see table 5F).								
- Whenever possible, use of aminoglycosides in patients with severe renal insufficiency should be avoided.								
- Dosage has to be based on adjusted weight [ideal body weight + 0.4 x (actual weight – ideal body weight)].								
Amikacin iv UD[1].	15-20 mg/kg/day div q8-24h	15-20 mg/kg/day div q8-24h	15-20 mg/kg q48h	15-20 mg/kg q72h	15-20 mg/kg q96h	15-20 mg/kg 1 to 2 hour(s) before dialysis	15-20 mg/kg q48h	
Gentamicin iv UD[1].	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg q48h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg 1 to 2 hour(s) before dialysis	4.5-7.5 mg/kg q48h	
Paromomycin po.	250-500 mg q6-12h	250-500 mg q6-12h	250-500 mg q6-12h	250-500 mg q6-12h	250-500 mg q6-12h	None[3].	250-500 mg q6-12h	250-500 mg q6-12h
Spectinomycin im.	2-4 gm (single dose)	2-4 gm (single dose)	2-4 gm (single dose)	2-4 gm (single dose)	2-4 gm (single dose)	Not applicable.	2-4 gm (single dose)	2-4 gm (single dose)
Streptomycin[2] im.	7.5 mg/kg q12h	7.5 mg/kg q24h	7.5 mg/kg q24-48h	7.5 mg/kg q48-72h	7.5 mg/kg q72h	7.5 mg/kg after dialysis	7.5 mg/kg q24h	
Tobramycin iv UD[1].	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg q48h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg 1 to 2 hour(s) before dialysis	4.5-7.5 mg/kg q48h	
BETALACTAMS: CEPHALOSPORINS								
Cefadroxil po.	1 gm q12h	1 gm q12h	1 gm q12h	1 gm q24h	500 mg q24h	500 mg to 1 gm after dialysis		500 mg q24h
Cefalexin po.	250-500 mg q6h	250-500 mg q6h	250-500 mg q6h	250-500 mg q12h	250-500 mg q24h	250-500 mg after dialysis		250-500 mg q24h
Cefazolin iv UD[1].	1-2 gm q8h	1-2 gm q8h	1-2 gm q8h	1 gm q12h	1-2 gm q24-48h	1 gm after dialysis	1-2 gm q8h	500 mg q12h
Cefazolin iv HD[1].	2 gm q6h	2 gm q6h	2 gm q6h	2 gm q12-24h	2 gm q24h	2 gm after dialysis	2 gm q6h	1 gm q12h
Cefepime iv.	2 gm q8h	2 gm q8h	2 gm q12h	1 gm q12h	1 gm q24h	1 gm after dialysis	2 gm q12h	1 gm q24h
Cefotaxime iv UD[1].	1 gm q6h	1 gm q6h	1 gm q8-12h	1 gm q12h	1 gm q24h	1 gm after dialysis	1 gm q8-12h	1 gm q24h
Ceftazidime iv.	2 gm q8h	2 gm q8h	2 gm q12h	2 gm q24h	2 gm q48h	1 gm after dialysis	2 gm q12h	2 gm q48h
Ceftriaxone iv UD[1].	1-2 gm q24h	1-2 gm q24h	1-2 gm q24h	1-2 gm q24h	1-2 gm q24h	1-2 gm after dialysis	1-2 gm q24h	1-2 gm q24h
Cettriaxone iv HD[1].	2 gm q12h	2 gm q12h	2 gm q12h	2 gm q12h	2 gm q12h	2 gm after dialysis	2 gm q12h	2 gm q12h
Cefuroxime iv UD[1].	750 mg q8h	750 mg q8h	750 mg q8h	750 mg q12h	750 mg q24h	750 mg after dialysis	750 mg q8h	750 mg q12h
Cefuroxime iv UD[1].	1.5 gm q8h	1.5 gm q8h	1.5 gm q8-12h	1.5 gm q12h	1.5 gm q24h	1.5 gm after dialysis	1.5 gm q8h	1.5 gm q12h
Cefur. axetil po UD[1].	500 mg q12h	500 mg q12h	500 mg q12h	500 mg q12h	500 mg q24h	500 mg after dialysis	500 mg q12h	500 mg q24h
Cefur. axetil po UD[1].	500 mg q8h	500 mg q8h	500 mg q8h	500 mg q12h	500 mg q24h	500 mg after dialysis	500 mg q8h	500 mg q24h

© 2008 Universitair Ziekenhuis Gent

ANTIBACTERIAL	DOSAGE BASED ON ESTIMATED CREATININE CLEARANCE					SUPPLEMENT FOR ADULTS ON HEMODIALYSIS	DOSAGE IN ADULTS ON CRRT[1]	DOSAGE IN ADULTS ON CAPD[1]
	≥ 90 ML/MIN	89 → 60 ML/MIN	59 → 30 ML/MIN	29 → 15 ML/MIN	< 15 ML/MIN (ESRD[1])			
AMINOGLYCOSIDES								
- Maintenance dosage is mainly guided by peak and trough serum levels, therapeutic drug monitoring recommended (see table 5F).								
- Whenever possible, use of aminoglycosides in patients with severe renal insufficiency should be avoided.								
- Dosage has to be based on adjusted weight [ideal body weight + 0.4 x (actual weight – ideal body weight)].								
Amikacin iv UD[1].	15-20 mg/kg/day div q8-24h	15-20 mg/kg/day div q8-24h	15-20 mg/kg q48h	15-20 mg/kg q72h	15-20 mg/kg q96h	15-20 mg/kg 1 to 2 hour(s) before dialysis	15-20 mg/kg q48h	
Gentamicin iv UD[1].	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg q48h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg 1 to 2 hour(s) before dialysis	4.5-7.5 mg/kg q48h	
Paromomycin po.	250-500 mg q6-12h	250-500 mg q6-12h	250-500 mg q6-12h	250-500 mg q6-12h	250-500 mg q6-12h	None[3].	250-500 mg q6-12h	250-500 mg q6-12h
Spectinomycin im.	2-4 gm (single dose)	2-4 gm (single dose)	2-4 gm (single dose)	2-4 gm (single dose)	2-4 gm (single dose)	Not applicable.	2-4 gm (single dose)	2-4 gm (single dose)
Streptomycin[2] im.	7.5 mg/kg q12h	7.5 mg/kg q24h	7.5 mg/kg q24-48h	7.5 mg/kg q48-72h	7.5 mg/kg q72h	7.5 mg/kg after dialysis	7.5 mg/kg q24h	
Tobramycin iv UD[1].	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg/day div q8-24h	4.5-7.5 mg/kg q48h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg q72h	4.5-7.5 mg/kg 1 to 2 hour(s) before dialysis	4.5-7.5 mg/kg q48h	
BETALACTAMS: CEPHALOSPORINS								
Cefadroxil po.	1 gm q12h	1 gm q12h	1 gm q12h	1 gm q24h	500 mg q24h	500 mg to 1 gm after dialysis		500 mg q24h
Cefalexin po.	250-500 mg q6h	250-500 mg q6h	250-500 mg q6h	250-500 mg q12h	250-500 mg q24h	250-500 mg after dialysis		250-500 mg q24h
Cefazolin iv UD[1].	1-2 gm q8h	1-2 gm q8h	1-2 gm q8h	1 gm q12h	1-2 gm q24-48h	1 gm after dialysis	1-2 gm q8h	500 mg q12h
Cefazolin iv HD[1].	2 gm q6h	2 gm q6h	2 gm q6h	2 gm q12-24h	2 gm q24h	2 gm after dialysis	2 gm q6h	1 gm q12h
Cefepime iv.	2 gm q8h	2 gm q8h	2 gm q12h	1 gm q12h	1 gm q24h	1 gm after dialysis	2 gm q12h	1 gm q24h
Cefotaxime iv UD[1].	1 gm q6h	1 gm q6h	1 gm q8-12h	1 gm q12h	1 gm q24h	1 gm after dialysis	1 gm q8-12h	1 gm q24h
Ceftazidime iv.	2 gm q8h	2 gm q8h	2 gm q12h	2 gm q24h	2 gm q48h	1 gm after dialysis	2 gm q12h	2 gm q48h
Ceftriaxone iv UD[1].	1-2 gm q24h	1-2 gm q24h	1-2 gm q24h	1-2 gm q24h	1-2 gm q24h	1-2 gm after dialysis	1-2 gm q24h	1-2 gm q24h
Cettriaxone iv HD[1].	2 gm q12h	2 gm q12h	2 gm q12h	2 gm q12h	2 gm q12h	2 gm after dialysis	2 gm q12h	2 gm q12h
Cefuroxime iv UD[1].	750 mg q8h	750 mg q8h	750 mg q8h	750 mg q12h	750 mg q24h	750 mg after dialysis	750 mg q8h	750 mg q12h
Cefuroxime iv UD[1].	1.5 gm q8h	1.5 gm q8h	1.5 gm q8-12h	1.5 gm q12h	1.5 gm q24h	1.5 gm after dialysis	1.5 gm q8h	1.5 gm q12h
Cefur. axetil po UD[1].	500 mg q12h	500 mg q12h	500 mg q12h	500 mg q12h	500 mg q24h	500 mg after dialysis	500 mg q12h	500 mg q24h
Cefur. axetil po UD[1].	500 mg q8h	500 mg q8h	500 mg q8h	500 mg q12h	500 mg q24h	500 mg after dialysis	500 mg q8h	500 mg q24h

© 2008 Universitair Ziekenhuis Gent

Table 6. Catheter lock solutions for prophylaxis against CRB[a]

Reference	Type of Lock Solution	Rate of CRB (per 1000 catheter-days)	
		Control	Intervention
Dogra *et al.*, 2002 (114)	Gentamicin	4.2	0.3
McIntyre *et al.*, 2004 (167)	Gentamicin	4.0	0.3
Kim *et al.*, 2006 (166)	Gentamicin/cefazolin	3.1	0.4
Nori *et al.*, 2006 (168)	Gentamicin	3.1	0
	Minocycline		0.4
Saxena *et al.*, 2006 (169)	Cefotaxime	3.6	1.7
Allon, 2003 (170)	Taurolidine	5.6	0.6
Betjes and van Agteren, 2004 (171)	Taurolidine	2.1	0
Weijmer *et al.*, 2005 (115)	30% citrate	4.1	1.1

[a]CRB, catheter-related bacteremia.

Allon M, Clin J Am Soc Nephrol 2007;2:786

© 2008 Universitair Ziekenhuis Gent

Case 3

- Diabetic nephropathy with ESRD (CrCl < 10 ml/min) undergoing elective surgery (e.g limb revascularisation
- Antimicrobial prophylaxis?
- Choices?
- Dosing?

© 2008 Universitair Ziekenhuis Gent

First dose always a loading dose without consideration of renal function

- **1-2 g of cefazolin**
- **20-30 mg/kg of vancomycin**
- **= filling the Vd**

- **Dose adaptation of subsequent maintenance dosing**
  - In PD
  - In systemic treatment
    - Calculation schedules taking into account elimination characteristics (renal + extrarenal clearance)
    - Significant in CVVH, hemodiafiltration,….: adapted/individualised dosing using predictive formulas and corrections with TDM

© 2008 Universitair Ziekenhuis Gent