Bacteraemia and Central Venous Catheter (CVC) related Infections

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CLINICAL MICROBIOLOGIST

Bacteraemia

- The Presence of microorganisms in the blood stream:

- **TRANSITORY : sporadic detection of circulating microorganisms (e.g. instrumental maneuvers).**

- **INTERMITTENT: due to the release in the circulation of bacteria from extravascular inflammatory sites (abscesses, peritonitis, arthritis etc.). Also related to the pathogenicity of some microorganisms (Salmonella typhi, Brucella melitensis e.g.)**

- **CONTINUOUS: due to an intravasal infectious process such as bacterial endocarditis, infection with catheters or cannulas etc.**

TRANSITORY BACTERAEMIA

- In normal subjects, micro-organisms are rapidly eliminated (± 45 min.) by the immune reaction (phagocytosis).

- In some cases, (anatomical anomalies, prostheses and particular microorganisms) it can be primum movens of persistent infectious processes (endocarditis).

INCIDENCE OF TRANSITORY BACTERAEMIA DURING MEDICAL PROCEDURES

PROCEDURES	% OF BACTERAEMIA
DENTAL	
TEETH EXTRACTION	18-85%
RESPIRATORY TRACT	
TONSILLECTOMY	28-38%
GASTROINTESTINAL TRACT	
ENDOSCOPY	8-12%

Evolution of bacteremia

MICROORGNISMS ENTER THE BODY

↓

TRANSITORY BACTERAEMIA

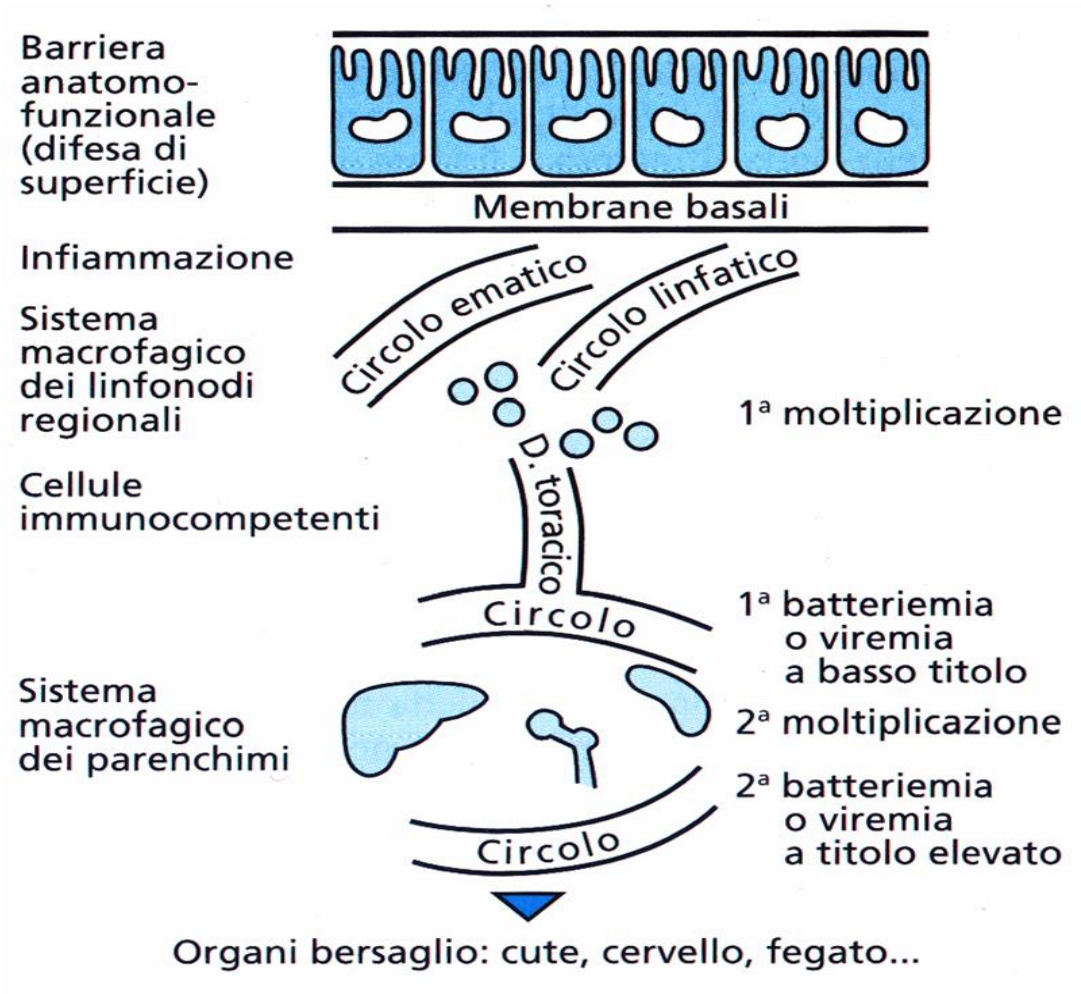
↓

ORGAN LOCATION

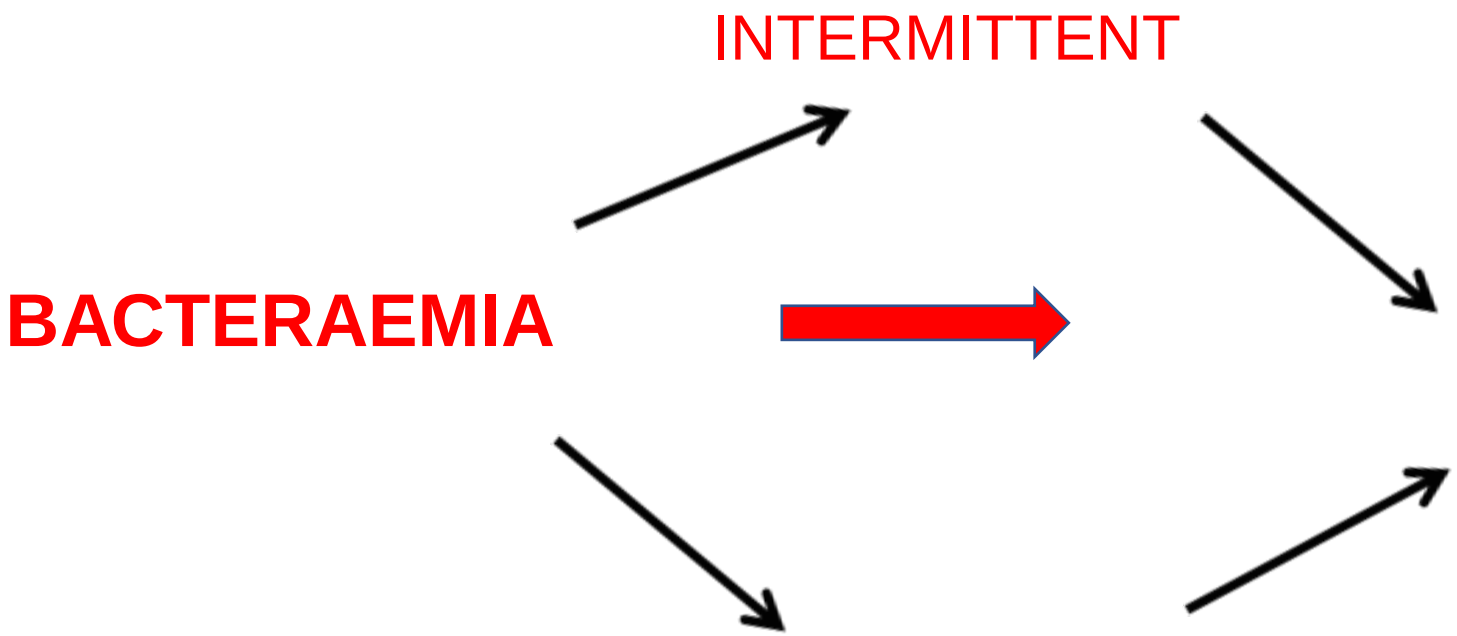
↓

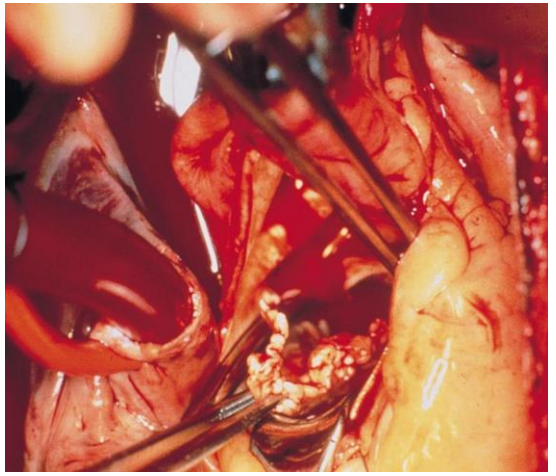
BACTERAEMIA

INTERMITTENT OR CONTINUE



From bacteremia to sepsis





Sepsis or septicemia is a clinical concept, not microbiological.

The progession of infection/sepsis in acute cases

infection

bacteraemia

LPS

sepsis

septic shock

SIRS

multiple organ failure (MOF/MODS)

DEATH

The microbiology laboratory in the diagnosis of bacteremia

The search for bacteria in the blood (Blood Culture) allows us to define:

- the etiology of either bacteremia or sepsis
- the most appropriate antimicrobial strategy
- the bacteraemic phase of an infectious process.

The diagnostic procedure has to be as fast and more accurate as possible.

Blood Culture

- The assessment of bacteremia must always be considered an urgent diagnosis.
- Since the beginning of a bacteremic phase sustained by gram negative bacteria the risk of a shift into a septicemic phase increases by about 10/15% every hour.
- Therefore, the faster is the appropriate therapy, the better is the clinical outcome.

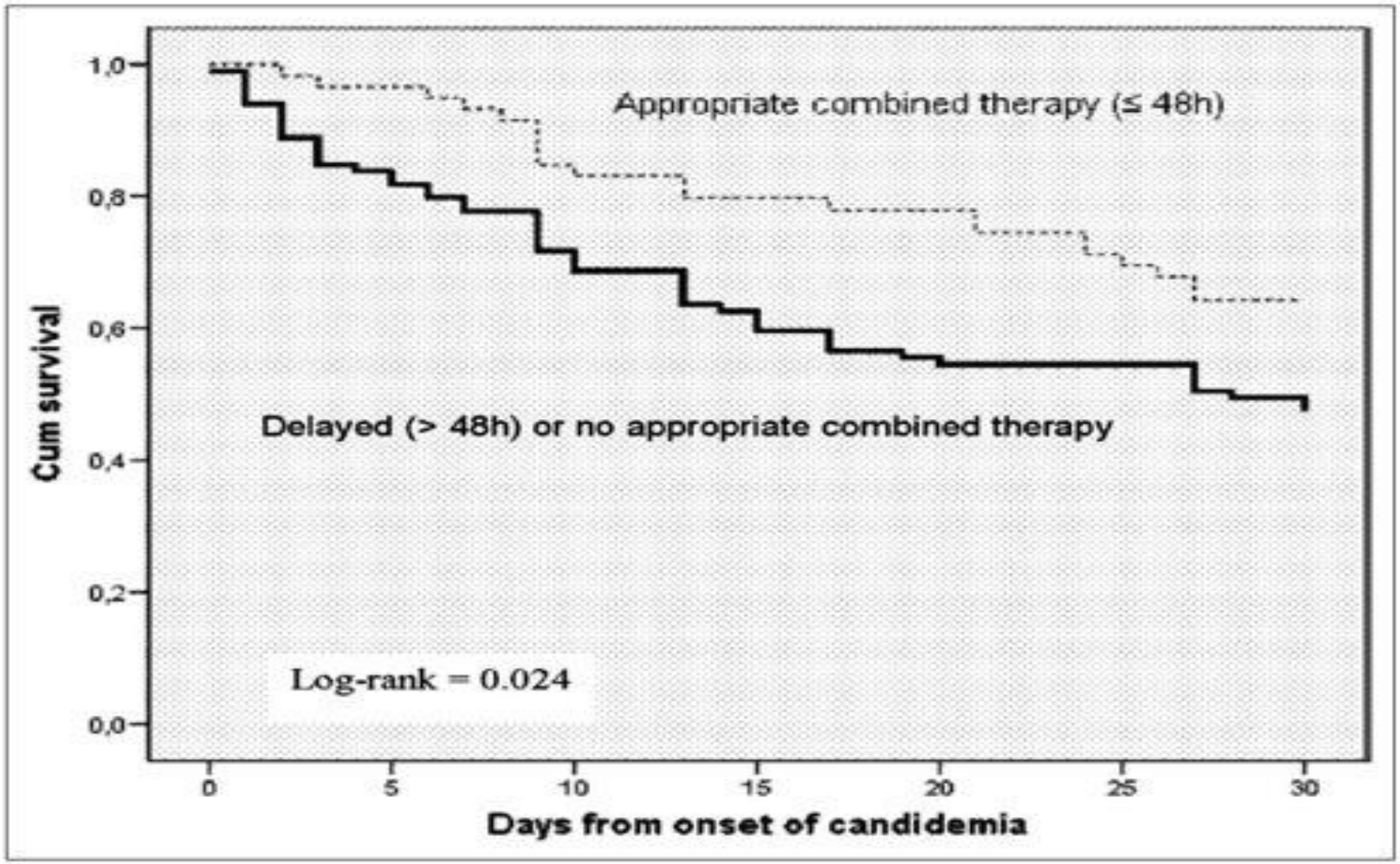


Figure 2. Kaplan-Meier 30-day survival curves according to appropriate combined therapy in the first 48 hr after candidemia diagnosis.

Blood Culture

- Blood is sterile.
- The presence of a germ may be due to for:
  - Pathogenic germ that overcomes defensive barriers (eg *Brucella*)
  - Opportunistic germ that is transported beyond defensive barriers (CVC, surgery)
  - Infectious episode (i.e. complicated UTI) that pours germs into the circulatory stream (bacteremia).
  - Alteration of epithelial and / or mucous barriers (K colon)
  - Contamination at the time of collection.

When to perform a blood culture

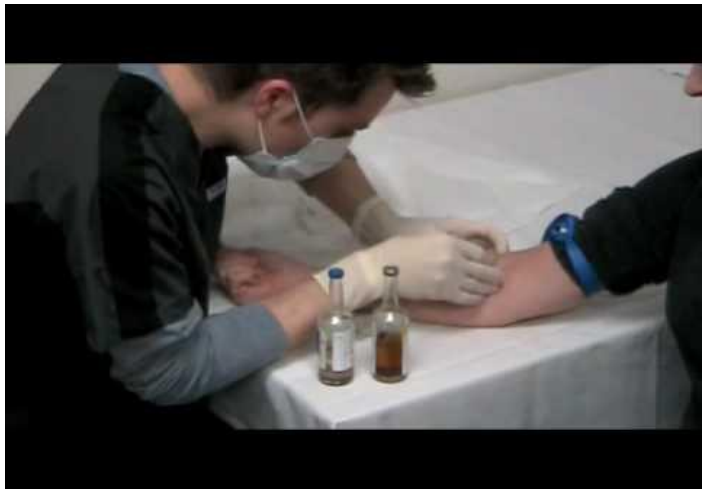
- In all the clinical conditions in which the detection of microorganisms in the blood assumes clinical significance.

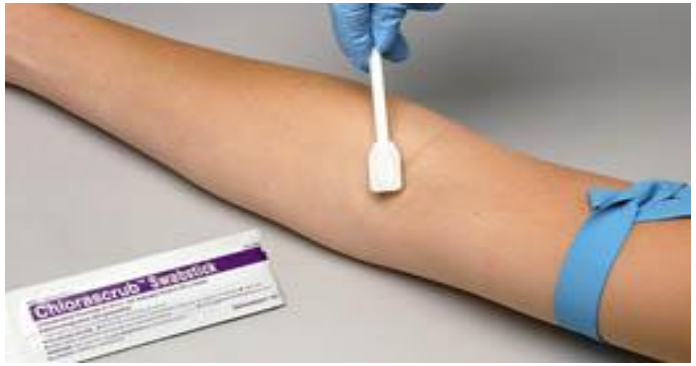
Blood sampling for the culture. Critical points

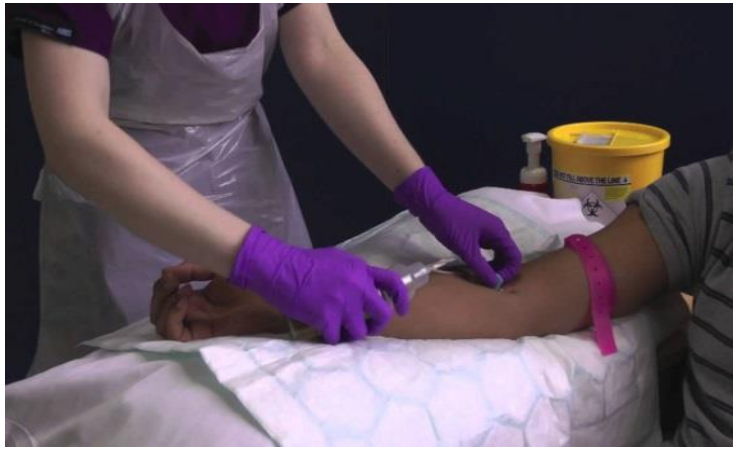
- Disinfection.
- Anatomical sites for sampling.
- Time for collection and number of samples.
- Volume of blood to be drawn.

Disinfection.

- Palpate the vein before sampling.
- Disinfect the area with iodized disinfectants or with 0.05% chlorhexidine alcohol solution (avoid the use of denatured alcohol) and allow to dry.
- Take the sample (don't palpate again!)







Anatomical sites of sampling.

- Venous puncture in different locations during the various sampling times.
- Avoid collection from venous and / or arterial indwelling catheters wherever possible, unless catheter sepsis is suspected.
- In this case, always perform sampling (s) from a peripheral vein.

Sampling times and numbers

- Before antibiotic therapy.
- If possible before the feverish rise (shiver).
- Upward feverish
- Draw three to five successive samples within a short time (15-30 minutes).

Volume of blood to be drawn

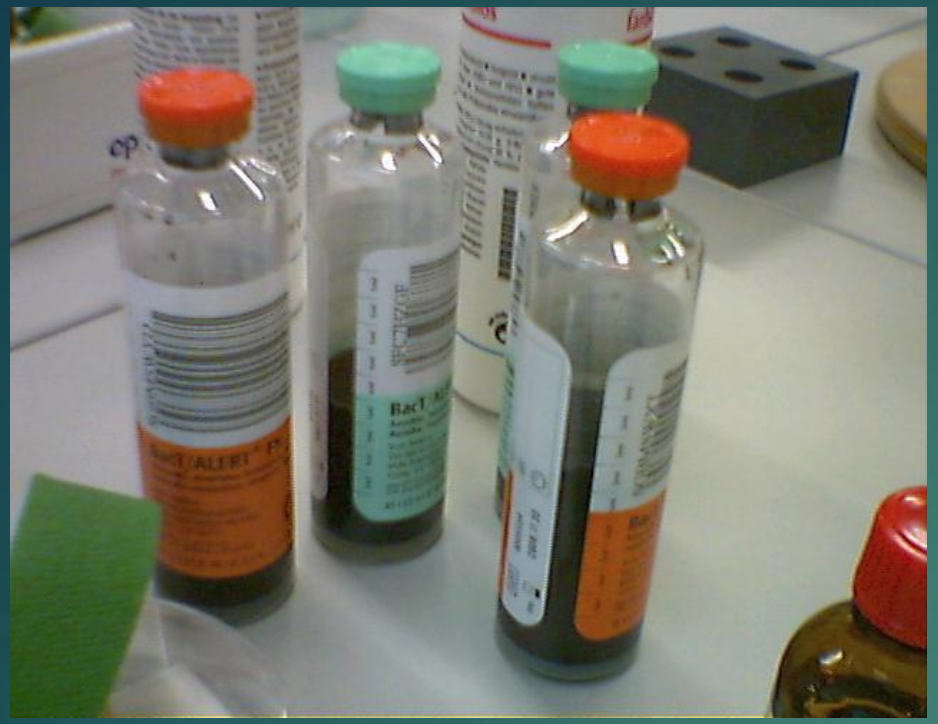
- There is a direct relationship between the volume of cultured blood and the probability of obtaining positive cultures.

- 5 to 10 mL for adults and 1-5 mL for children, for each sample.

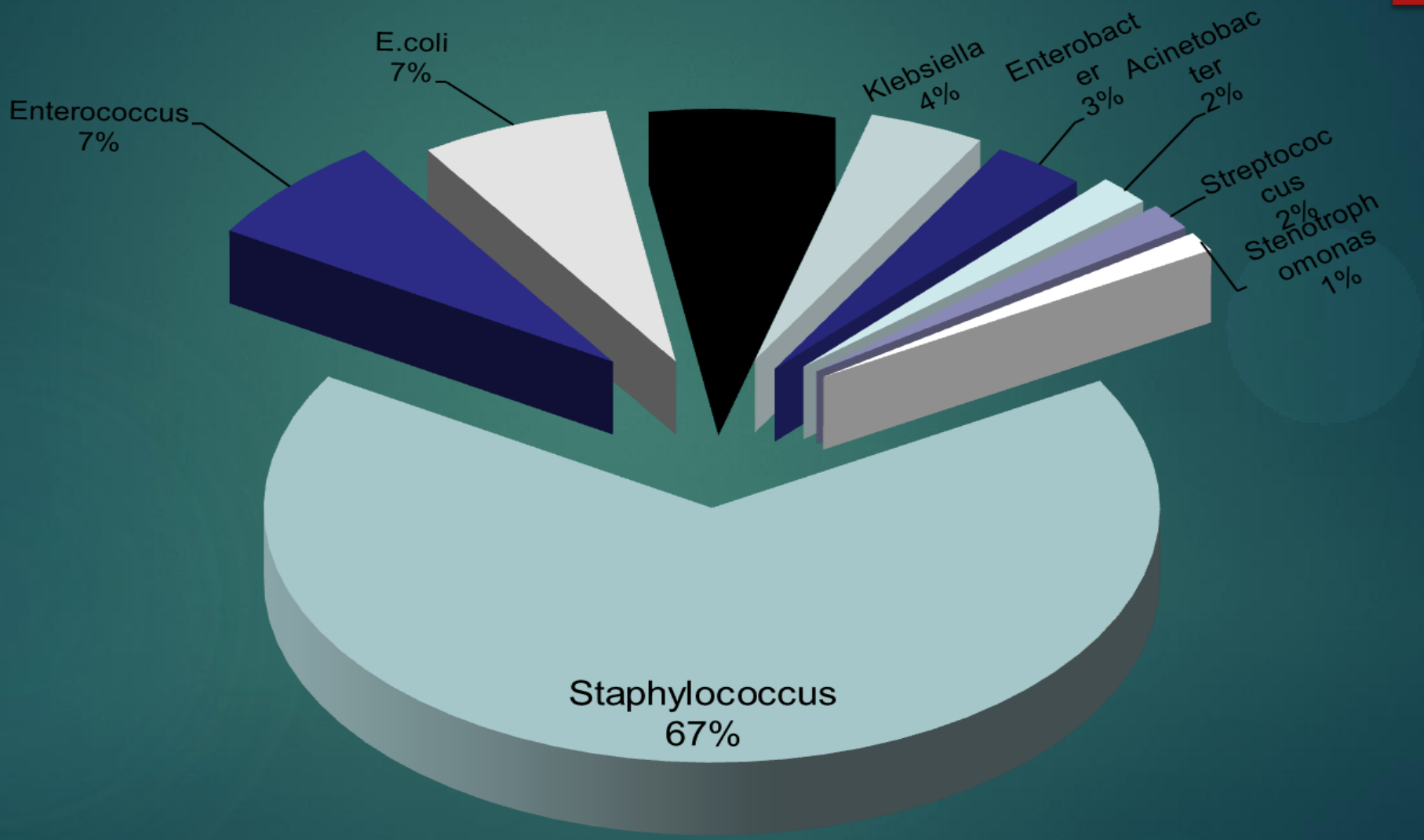
Volume of blood to be drawn

- For the set of samples taken, a total volume of at least 40 mL is recommended (consider the search for anaerobes).

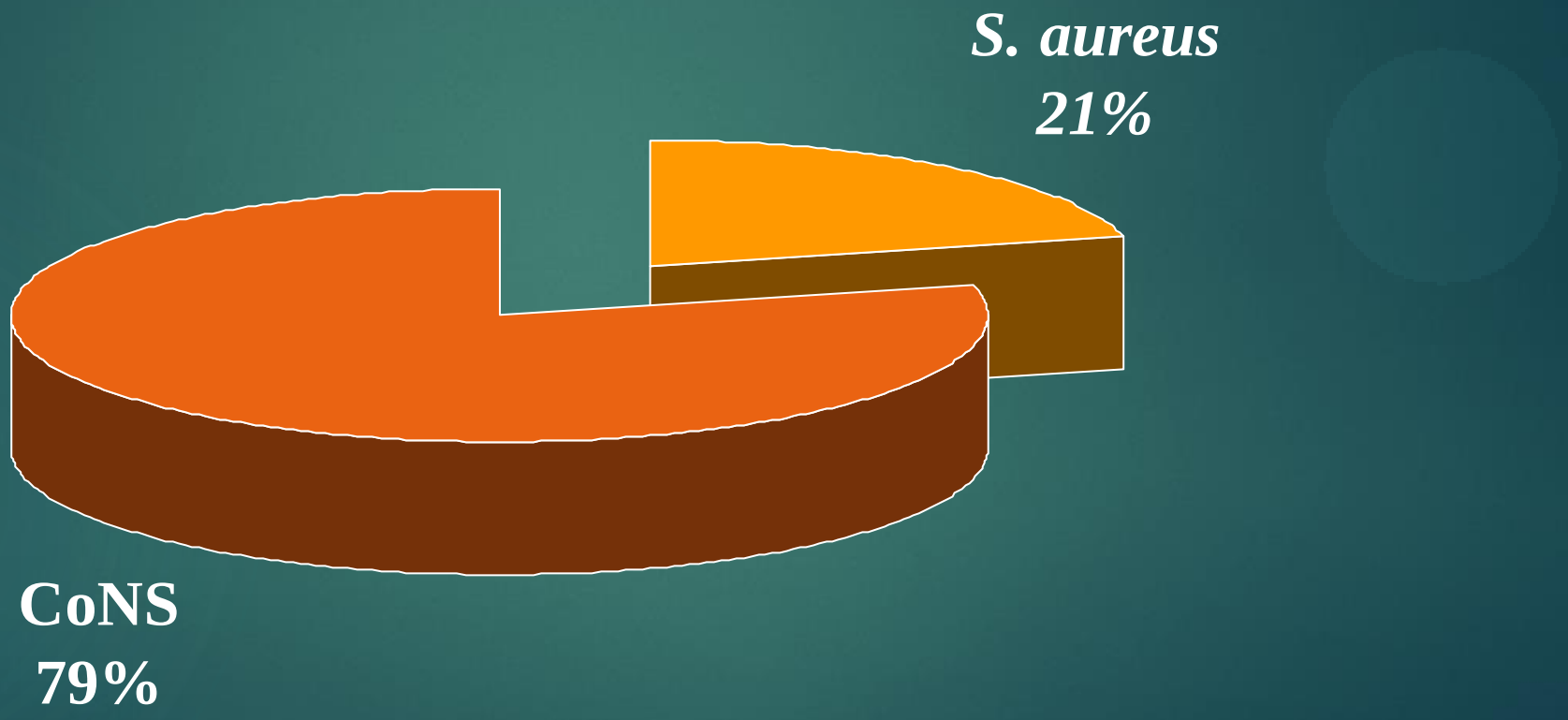
- The three / six samples should be considered as a single sample in reporting and clinical interpretation.



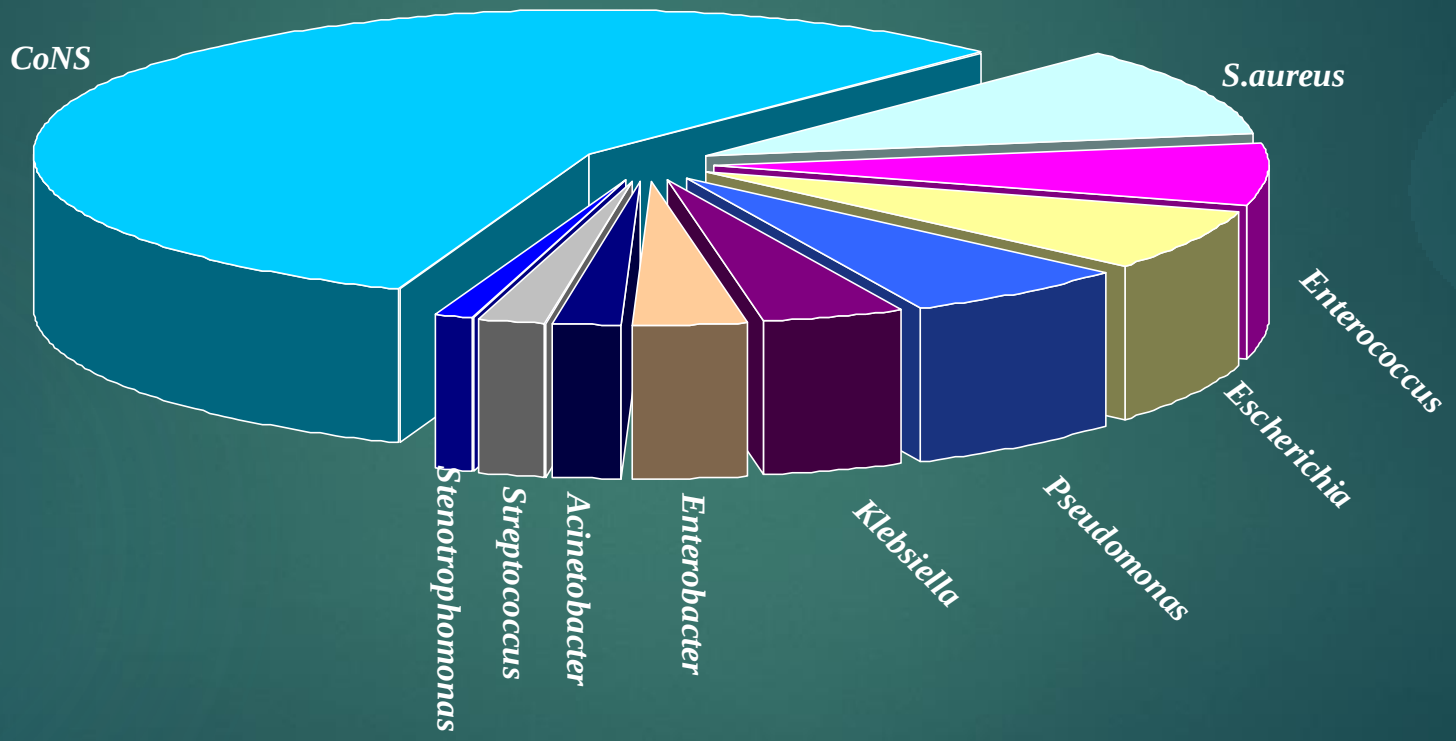
Bacterial isolates from blood



Staphylococci isolated from the blood.



Bacterial isolates from blood



Clinical dilemma

- Isolation of coagulase negative staphylococci from blood samples: bacteremia or contamination?

QUESTION

- Are there differential criteria for attributing clinical significance to"commensal" germs isolated from positive blood cultures?

ANSWER

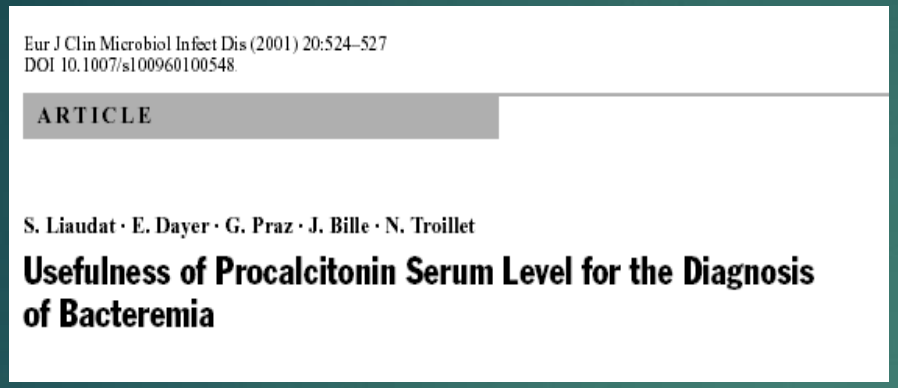
- NO…. or better …..
- ……there is no single criterion with sufficient specificity.

Time to positivity

- In the case of CoNS, culture positivity is observed more rapidly in significant bacteraemia than in contamination (23.6 vs 29.2 h, J Med Microbiol 2004, 53: 67-72).

- Parameter not correctly assessable in all laboratories.

Procalcitonin

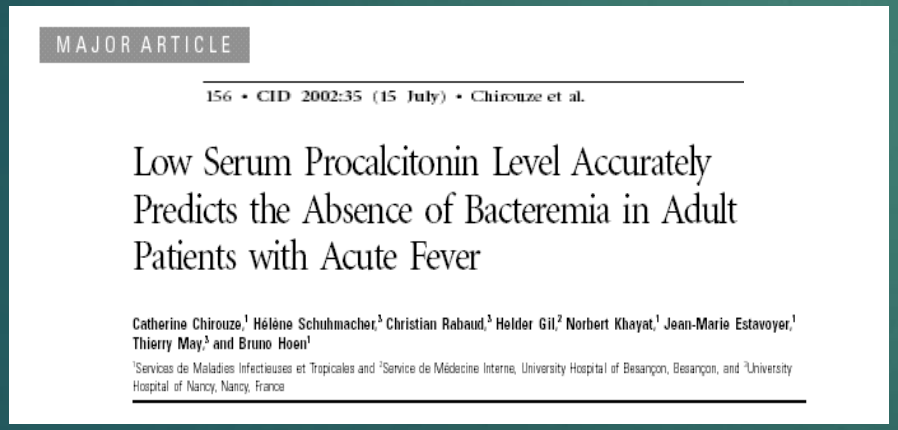


Eur J Clin Microbiol Infect Dis (2001) 20:524–527
DOI 10.1007/s100960100548

ARTICLE

S. Liaudat · E. Dayer · G. Praz · J. Bille · N. Troillet

Usefulness of Procalcitonin Serum Level for the Diagnosis of Bacteremia



MAJOR ARTICLE

Low Serum Procalcitonin Level Accurately Predicts the Absence of Bacteremia in Adult Patients with Acute Fever

Catherine Chirouze,[1] Hélène Schuhmacher,[3] Christian Rabaud,[3] Helder Gil,[2] Norbert Khayat,[1] Jean-Marie Estavoyer,[1] Thierry May,[3] and Bruno Hoen[1]

[1]Services de Maladies Infectieuses et Tropicales and [2]Service de Médecine Interne, University Hospital of Besançon, Besançon, and [3]University Hospital of Nancy, Nancy, France

- Values> 0.5 ng / mL correlate with significant bacteremia.
- Values <0.4 ng / mL exclude the diagnosis of bacteremia.
- Not valid for candidemia.

Other criteria

- Clinical parameters (CDC definition for primary BSI).
- Molecular features (pattern PFGE).
- Species of the microorganism (es. *S.haemolyticus)*.
- Meticillin/oxacillin resistance .
- Presence of a central venous catheter (CVC).

Interpretation of the blood culture set

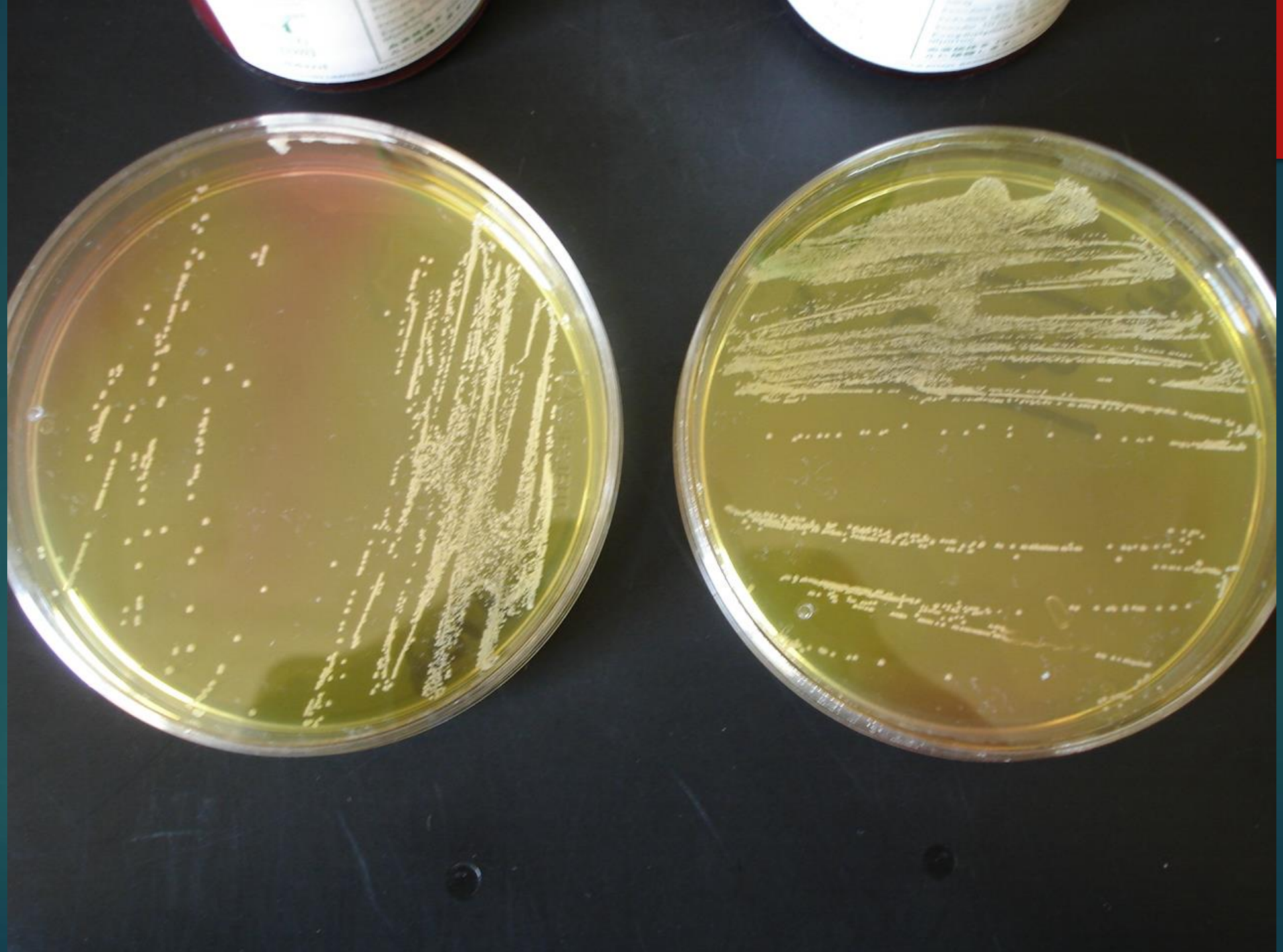
- Positivity for a pathogen (e.g. *S.aureus)* from one or more bottles
- Positivity for a commensal (e.g. *S. epidermidis)* from 1 bottle out of 3.
- Positivity for *S. epidermidis* from 2 or 3 bottles out of 3.

Frequency of positive blood cultures in infections

Endocarditis, endovascular infections	85-95 %
Bacterial pneumonia	15-60 %
Pyelonephritis	30-50 %
Bacterial meningitis	50-80 %
Osteomyelitis	40-60 %
Abdominal abscesses	variable
Fever of unknown origin (FUO)	variable

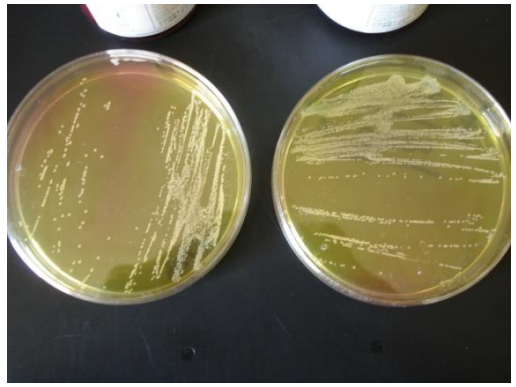

ARN804SH
NRGTGDBH


E' ASSOLUTAMENTE
VIETATO L'USO DELLE
SIRINGHE PER LA LAVO-
RAZIONE DELLE EMOCOLTU-
RE BACTEC
GAMMA STERILIZED



Positivity of blood culture

Cultivation of broth cultures on solid media to get isolated colonies



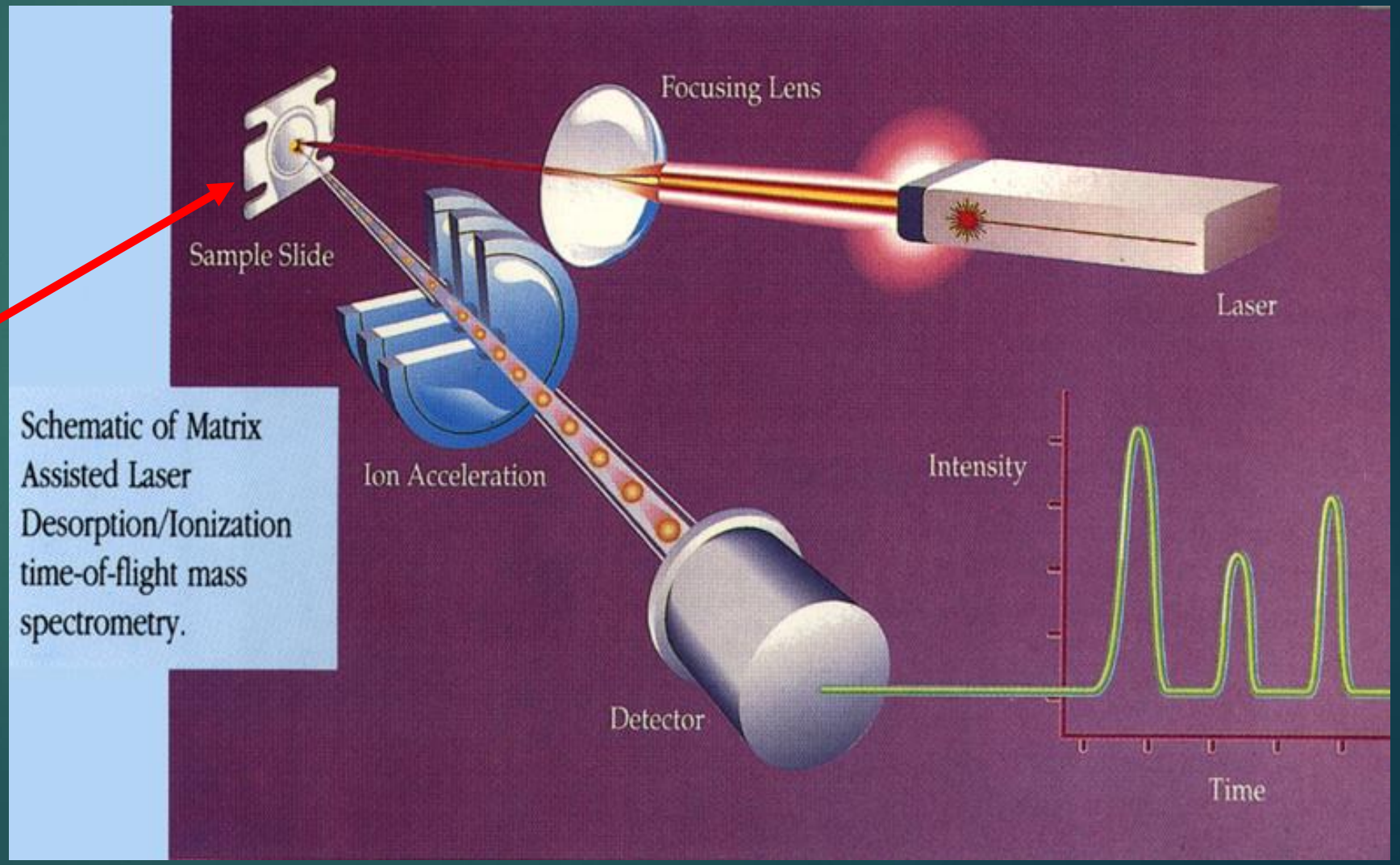
Identification and antimicrobial susceptibility test (AST).

Before being reported negative, a blood culture must be incubated at least 5 days.

Rapid AST directly from blood culture bottles (EUCAST guidelines)

- EUCAST has recently published recommendations for short incubation (4, 6 and 8 hours) AST directly from positive blood culture bottles
- Shortened incubation - 4, 6 and 8 hours with breakpoints adapted to each incubation time.
- Breakpoints for each species and each reading time.
- Identity of species must be known prior to interpretation of AST results.

MALDI TOF



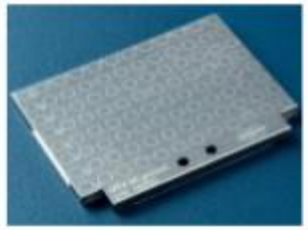
Schematic of Matrix Assisted Laser Desorption/Ionization time-of-flight mass spectrometry.

Sampling

Incubation of blood culture bottles

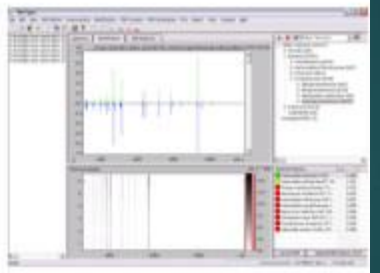
WHEN POSITIVE

Preparation of a bacterial pellet



Deposition of bacterial pellet on MALDI microplate

Acquisition of the proteic profile



Comparison with a database

OPEN ACCESS Freely available online

PLoS one

Direct Identification of Bacteria in Positive Blood Culture Bottles by Matrix-Assisted Laser Desorption Ionisation Time-of-Flight Mass Spectrometry

Bernard La Scola*, Didier Raoult

Pôle des Maladies Infectieuses, Assistance Publique-Hôpitaux de Marseille and URMITE UMR CNRS-IRD 6236, IFR48, Faculté de Médecine, Université de la Méditerranée, Marseille, France

Identification is quick; bacterial identification is obtained on the day the bacterial colonies grow on subculture and thus the result is obtained approximately one day earlier than with the conventional procedure. As positive blood cultures represent a suspension of

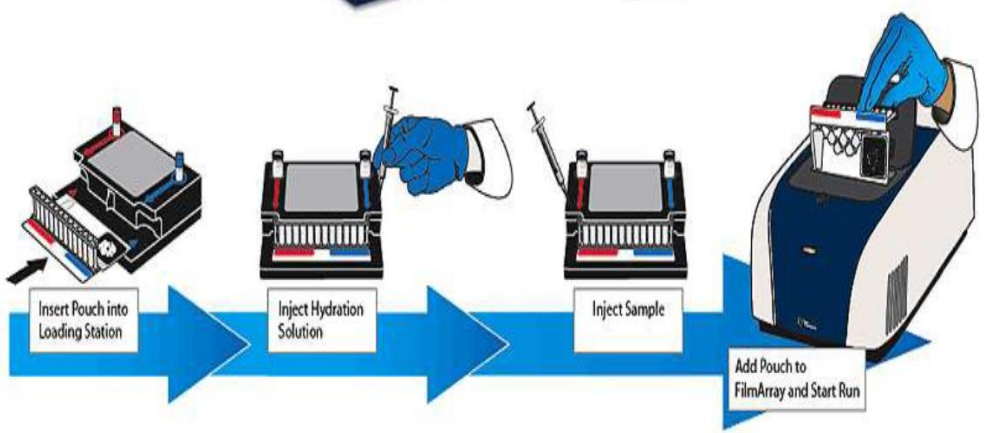
Conclusions/Significance: MALDI-TOF MS is an efficient method for direct routine identification of bacterial isolates in blood culture, with the exception of polymicrobial samples and viridans streptococci. It may replace routine identification performed on colonies, provided improvement for the specificity of blood culture broths growing viridans streptococci is obtained in the near future.

Rapid AST directly from blood culture bottles (EUCAST guidelines)

The method is currently validated for the following species.

- *Escherichia coli*
- *Klebsiella pneumoniae*
- *Pseudomonas aeruginosa*
- *Staphylococcus aureus*
- *Streptococcus pneumoniae*
- *Enterococcus faecalis* and *Enterococcus faecium*
- *Acinetobacter baumannii*

FilmArray



Gram + :

- *S. aureus*
- *S. pyogenes*
- *S. agalactiae*
- *S. pneumoniae*
- *Coagulase Neg. Staph.*
- *Enterococcus spp.*
- *Streptococcus spp*
- *L. monocytogenes*

Funghi:

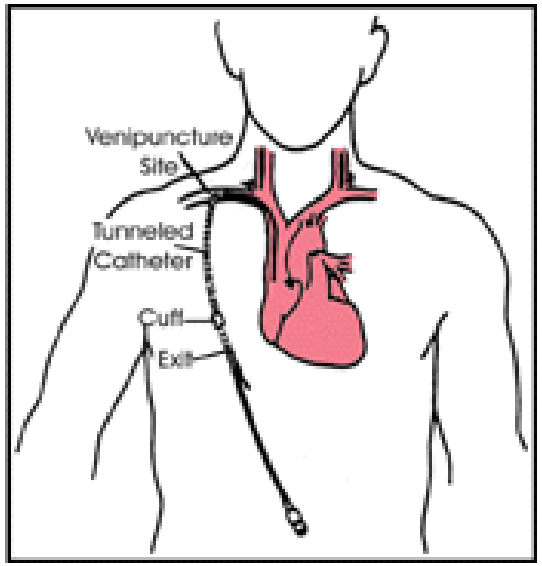
- *C. albicans/dubliniensis*
- *C. parapsiolosis/tropicalis*
- *C. glabrata*
- *C. krusei*

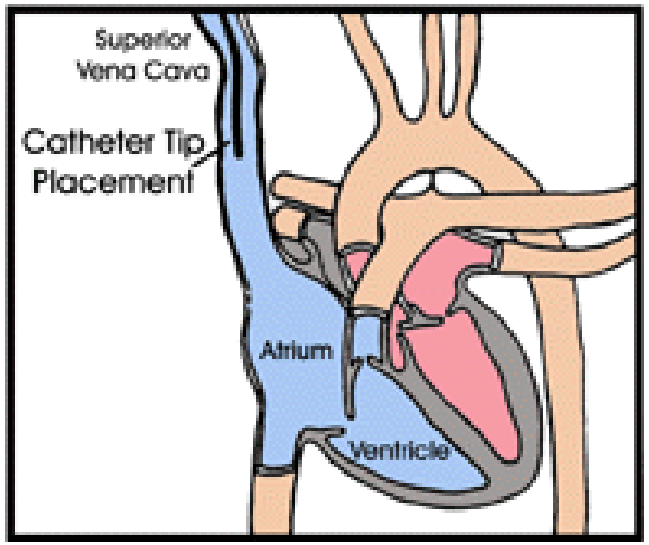
Gram - :

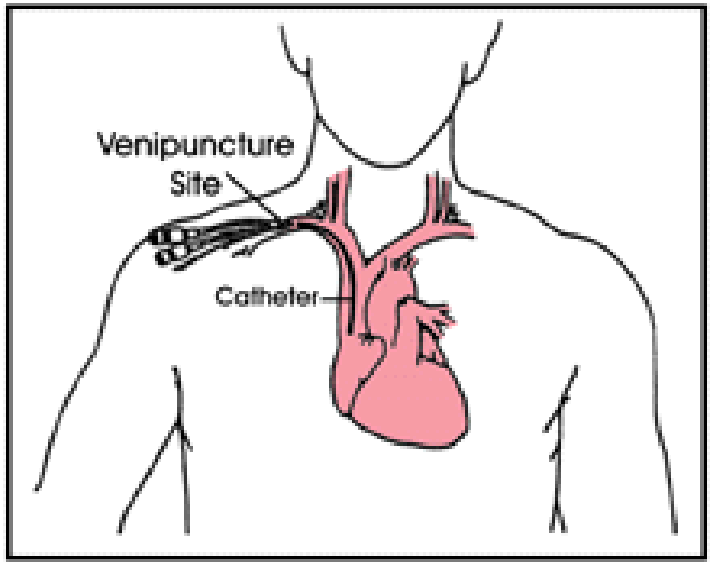
- *H. influenzae*
- *N. meningitidis*
- *P. aeruginosa*
- *E. coli*
- *A. Spp*
- *A. baumannii*
- *E. Cloacae*
- Enteric spp. Pan
- *K. pneumoniae*
- *K. oxytoca*
- *S. marcescens*

Resistenze:

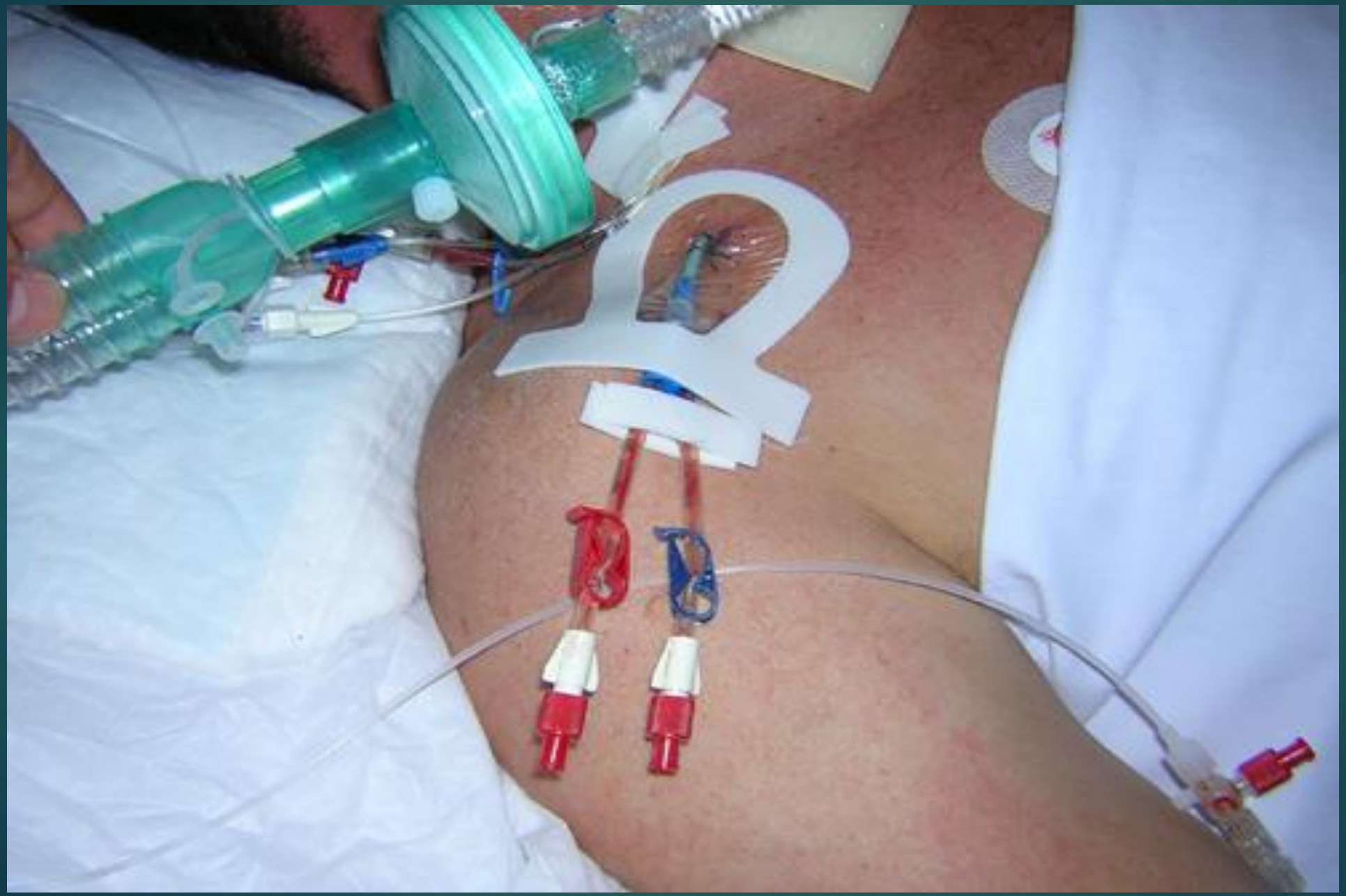
- mecA
- Van A/B
- KPC

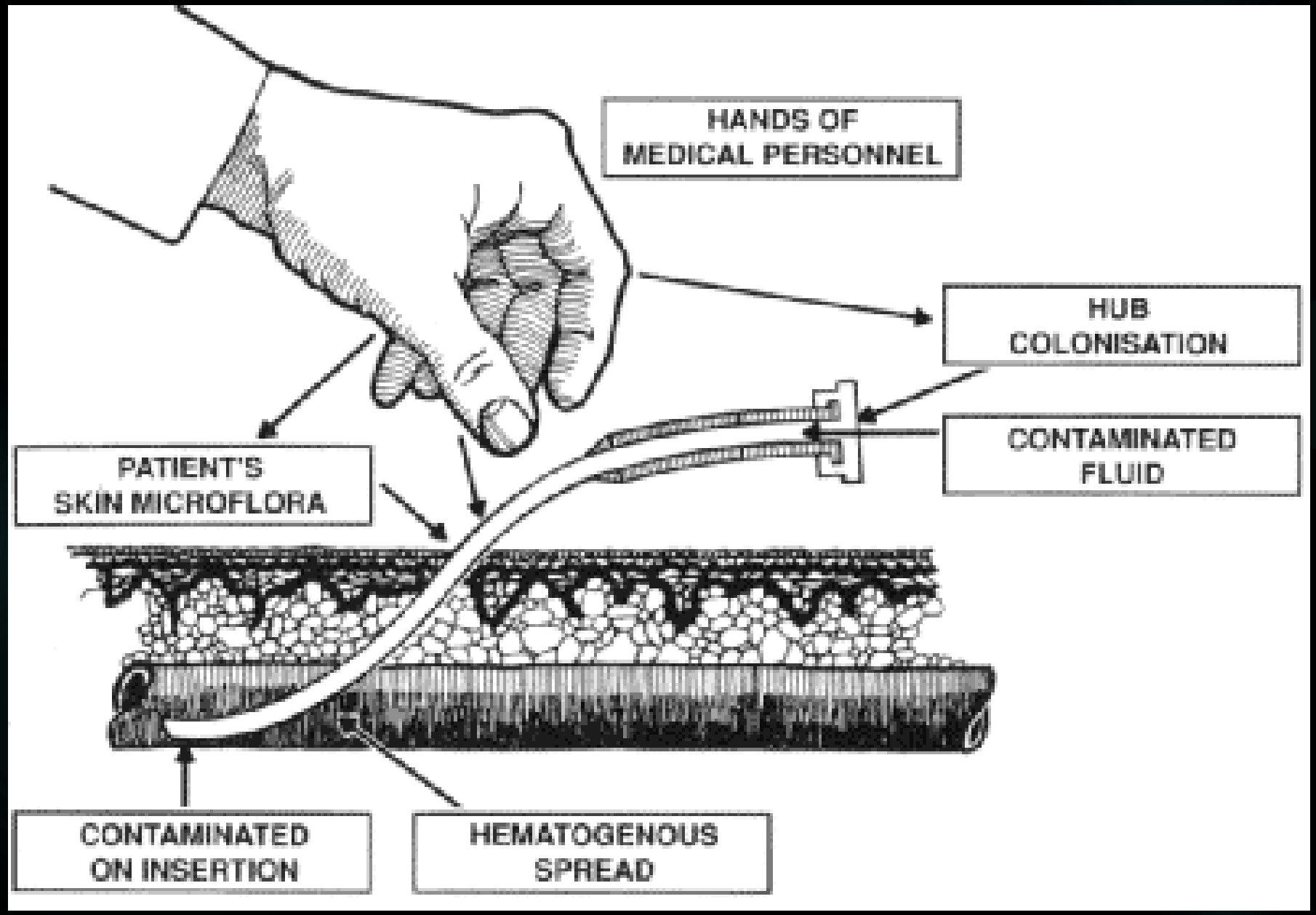






Central venous catheters (CVC)




HANDS OF
MEDICAL PERSONNEL
HUB
COLONISATION
CONTAMINATED
FLUID
PATIENT'S
SKIN MICROFLORA
CONTAMINATED
ON INSERTION
HEMATOGENOUS
SPREAD

CVC colonization

- Fast (within 24h).
- May depend on host factors (platelets, plasma, tissue proteins)
- The extent and location depends on the duration of catheterization.
  - < 10 days: microbial biofilm on the outer surface
  - > 10 days: microbial biofilm on the inner surface
- It may depend on the contamination of the administered fluid.
  - In the case of gram negative contamination, fluid may not be cloudy (< 10^7 CFU/mL)
- **CVC removal may be required.**

CVC colonization

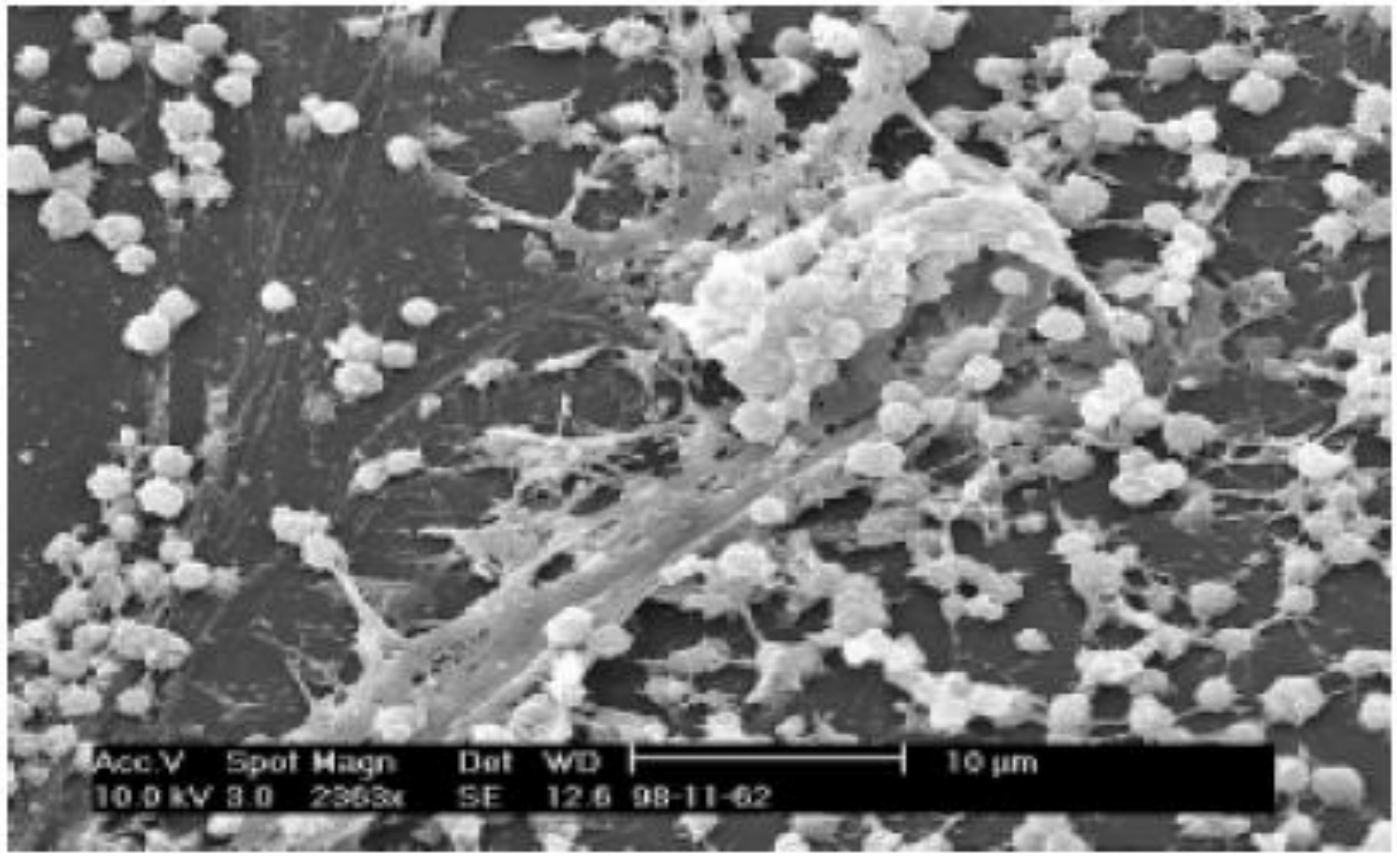
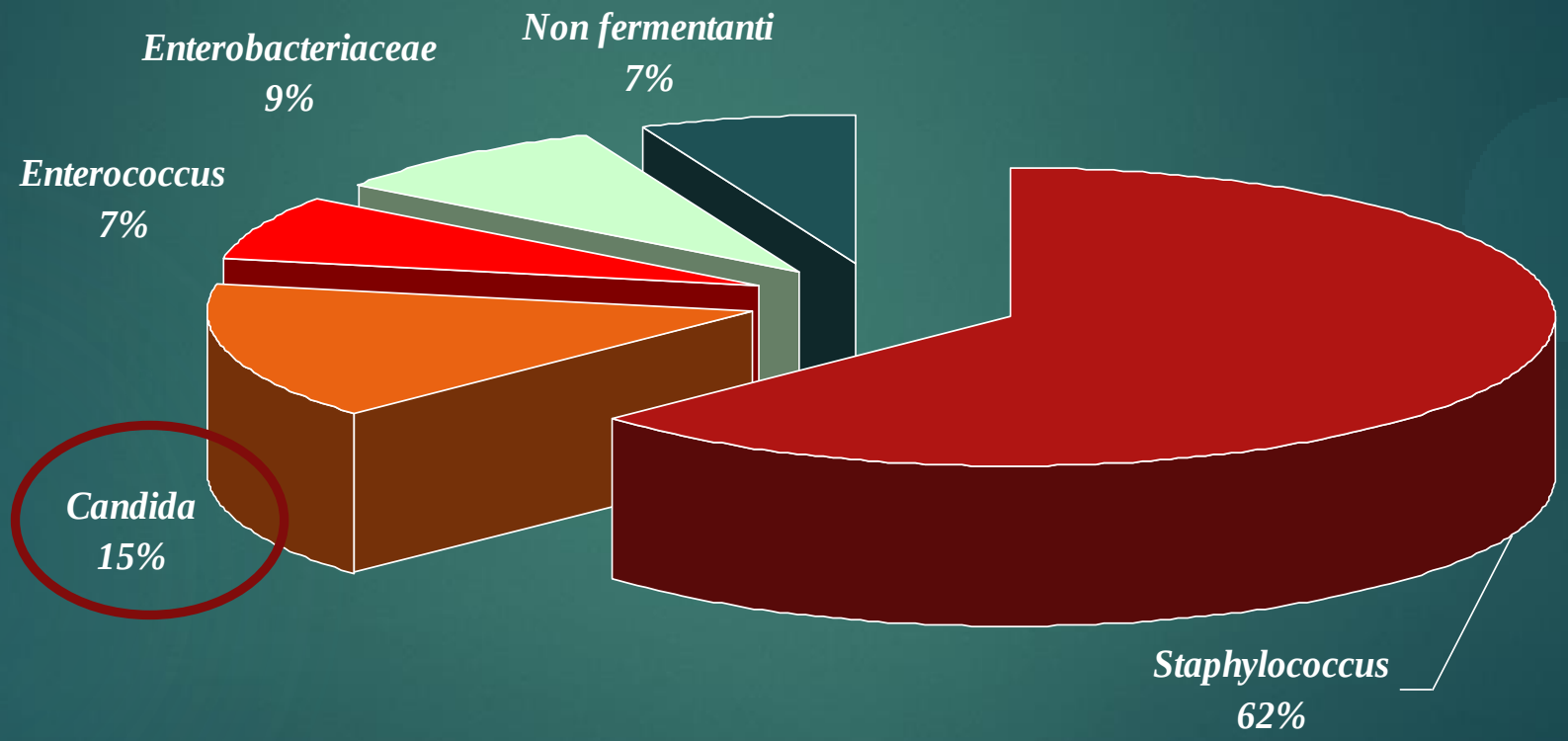
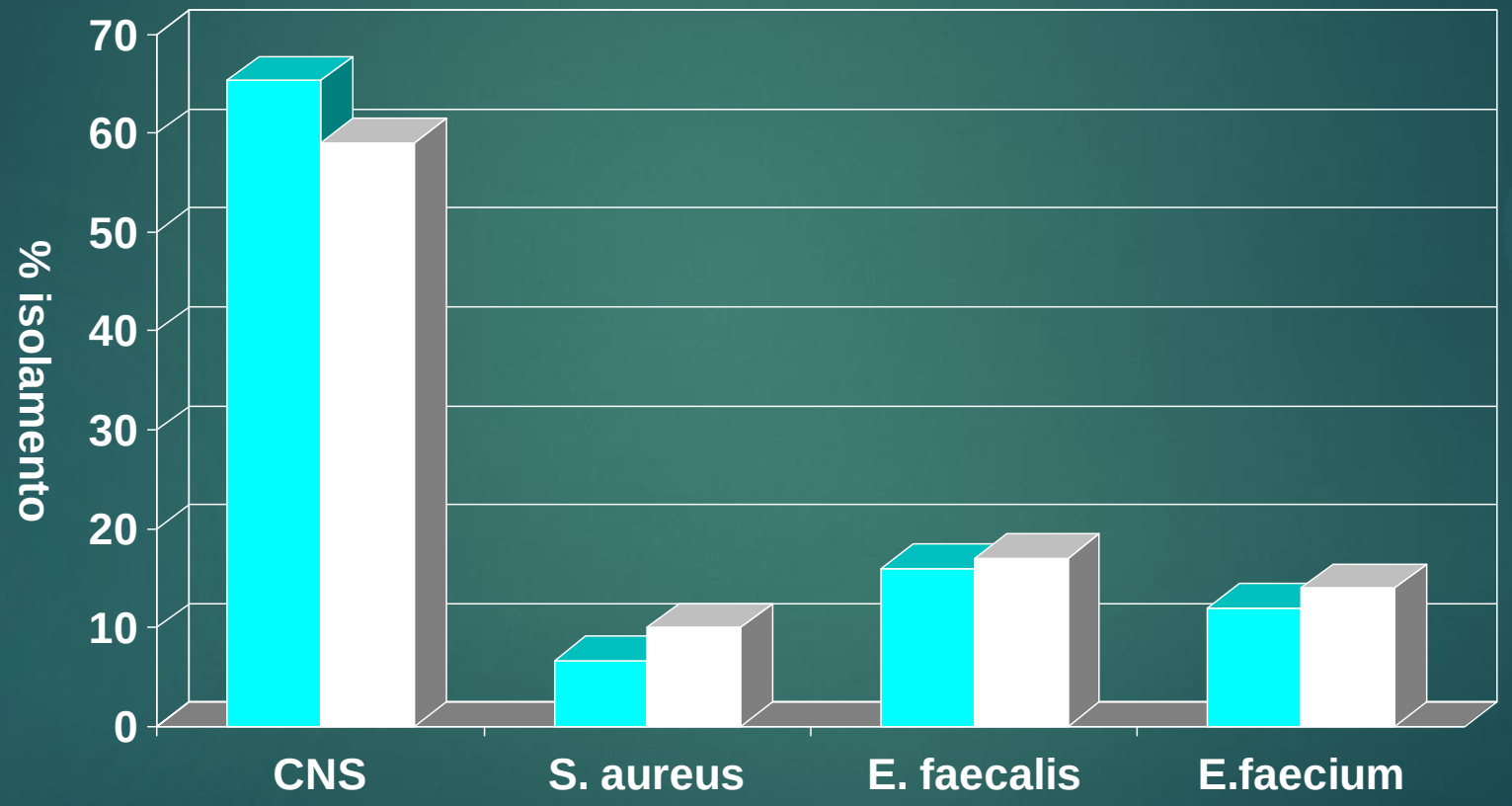


Figure 1. Scanning electron micrograph of a *Staphylococcus* biofilm on the inner surface of a needleless connector.
Photograph by Janice Carr, Centers for Disease Control and Prevention, Atlanta, GA USA.

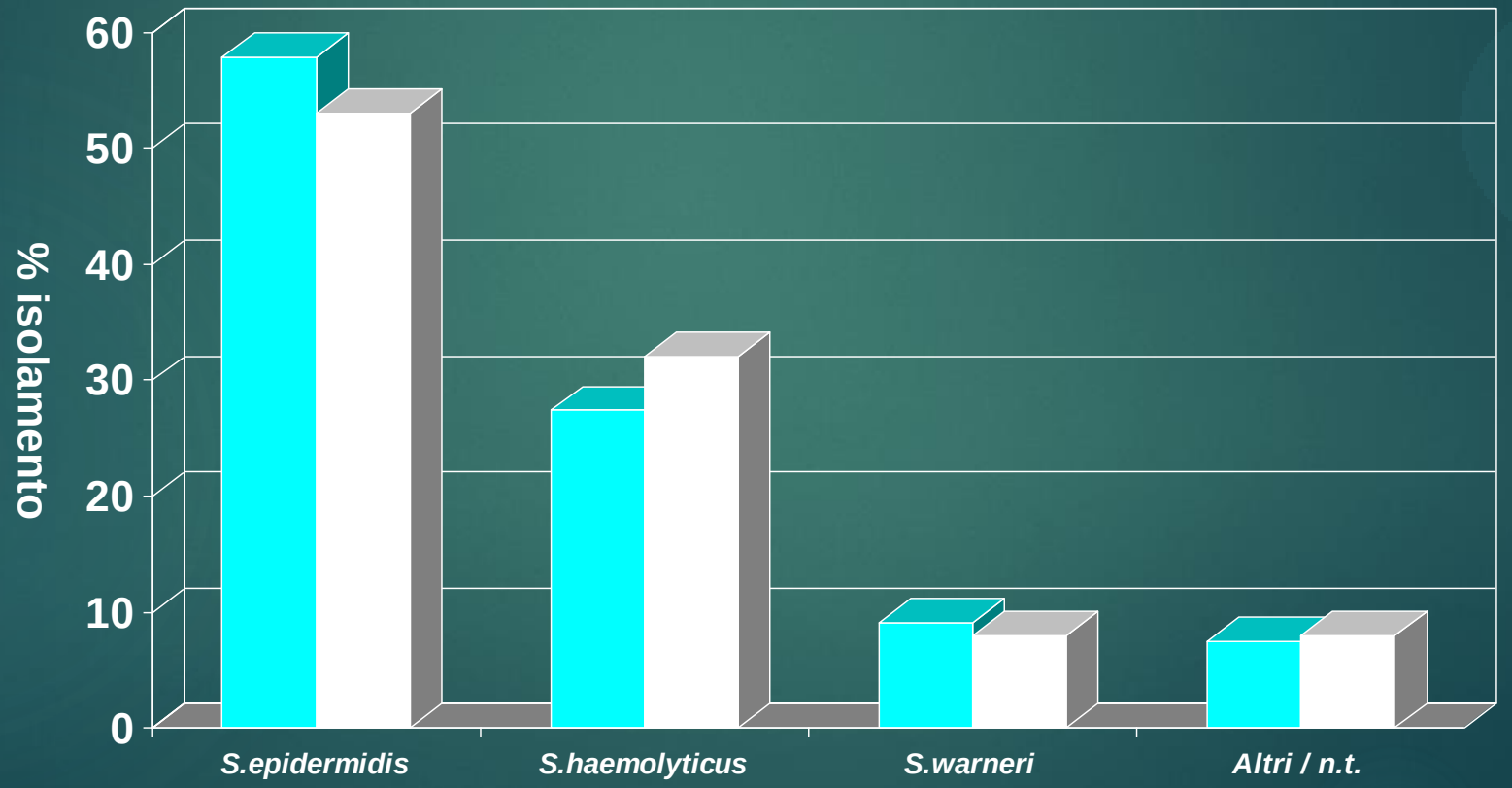
CVC: implicated microorganisms.



Gram positive



Coagulase-negative Staphylococci

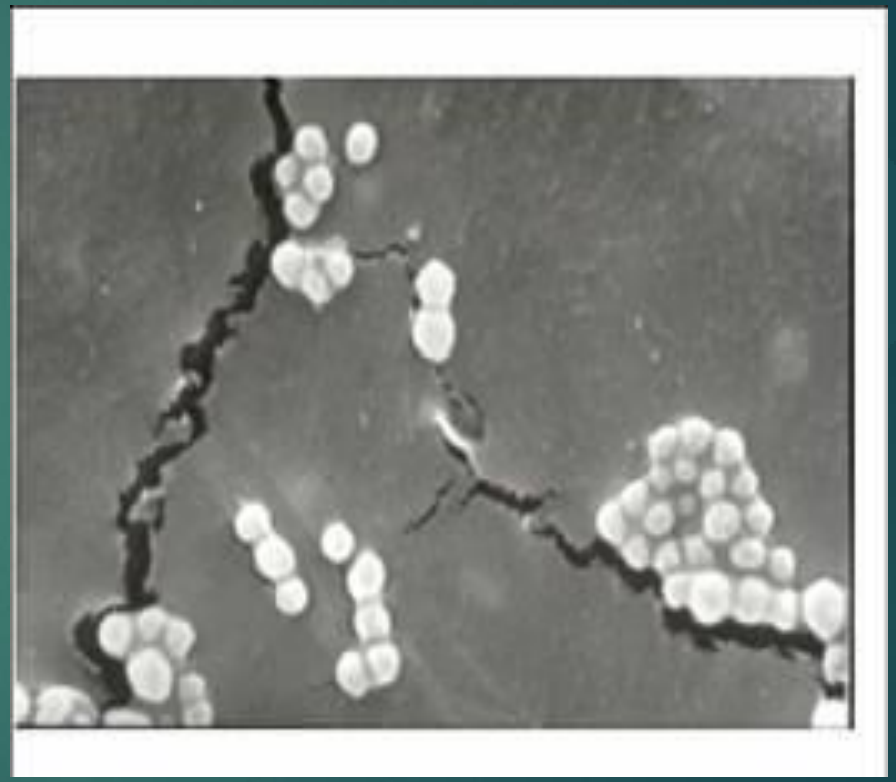


Staphylococci

- Coagulase positive Staphylococci : *S.aureus*
- Coagulase negative Staphylococci : 38 species
  - *S.epidermidis*
  - *S.haemolyticus*
  - *S.warneri*
  - *S.hominis*

Coagulase negative Staphylococci

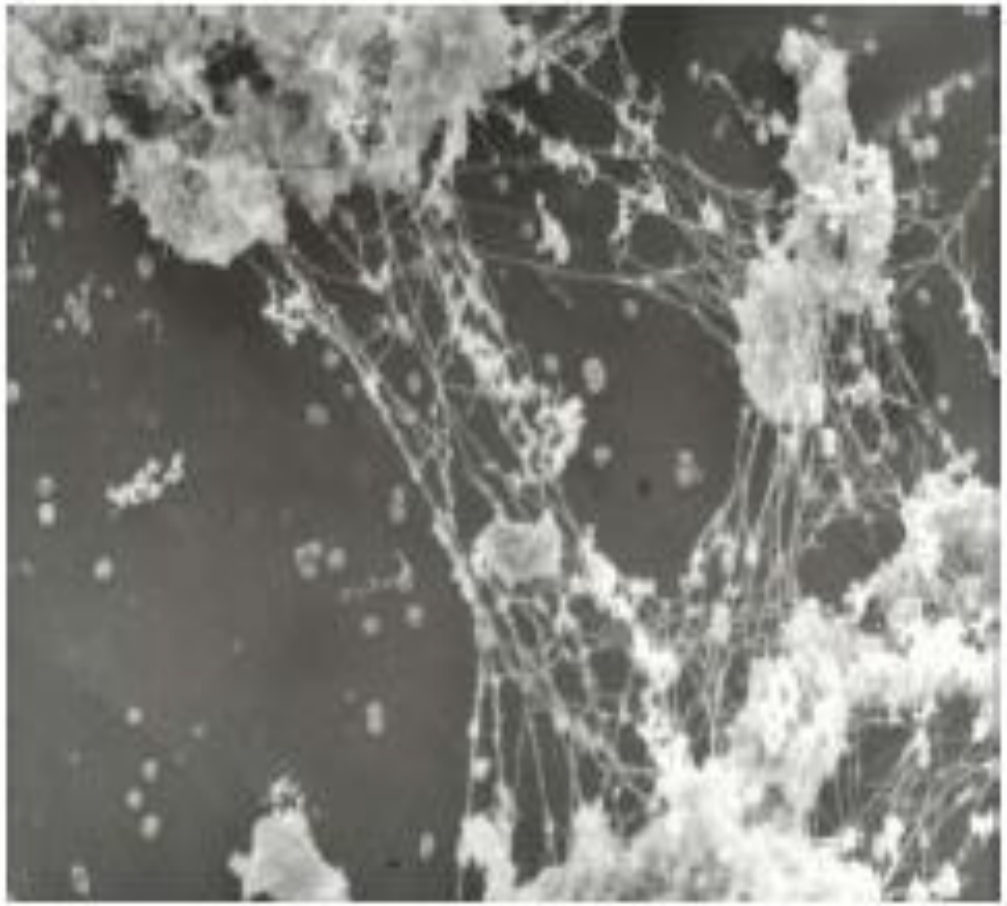
- Opportunistic bacteria can become dangerous pathogens in the presence of foreign bodies.
- Frequently associated with biomaterials, they have a high ability to colonize polymeric materials.



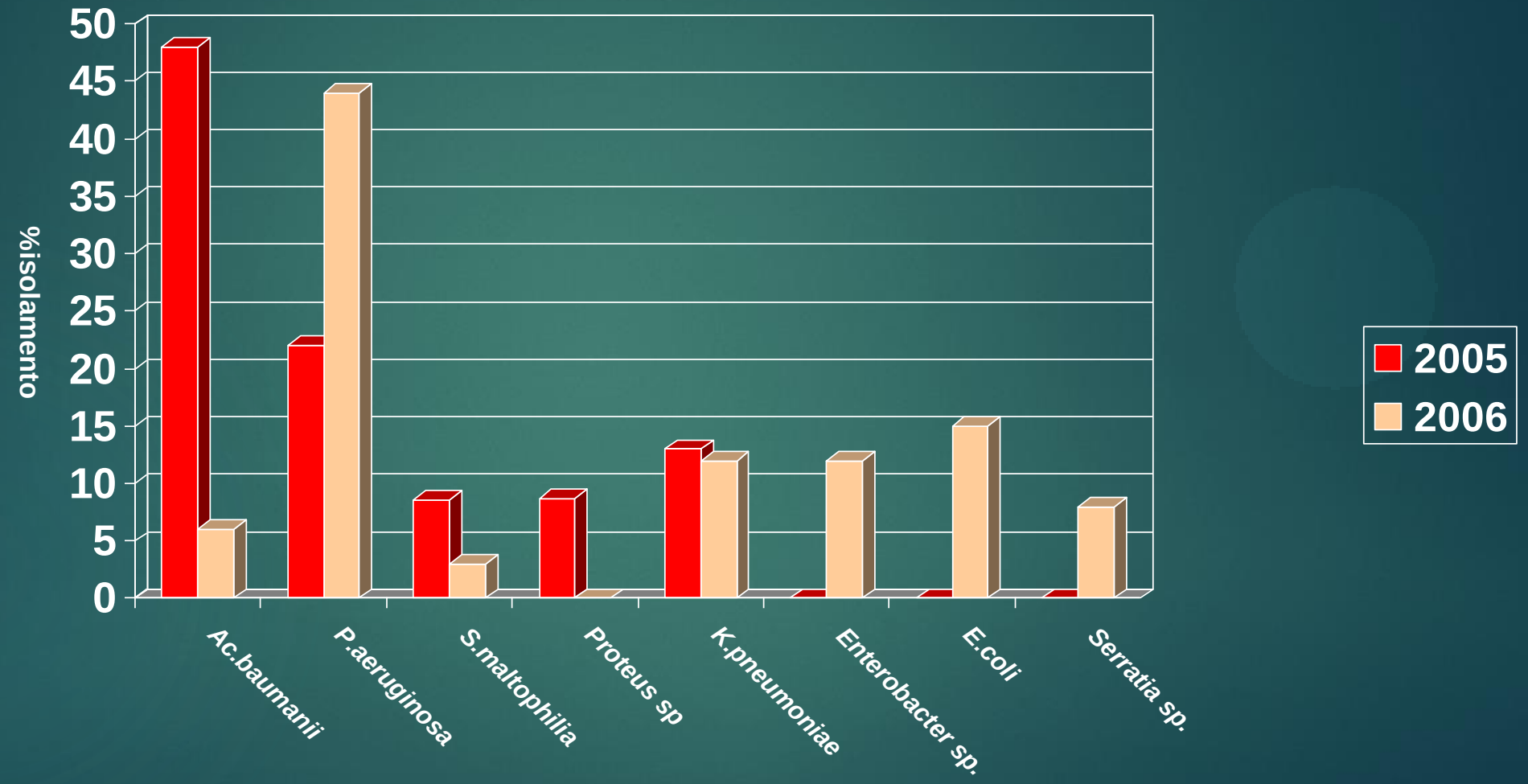
CVC colonized by S.epidermidis

Coagulase negative Staphylococci

- They produce an extracellular substance of a glycoprotein nature (slime).
- Slime producers have a high adhesive capacity to polymeric materials.

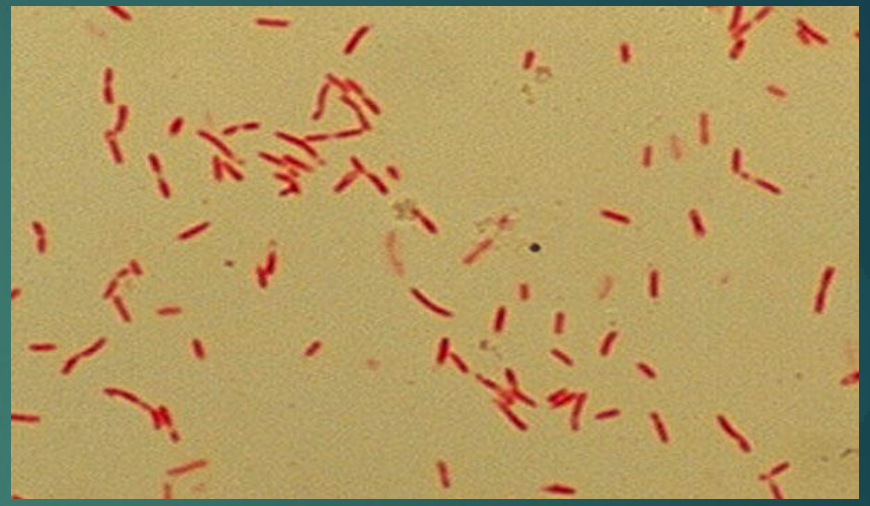


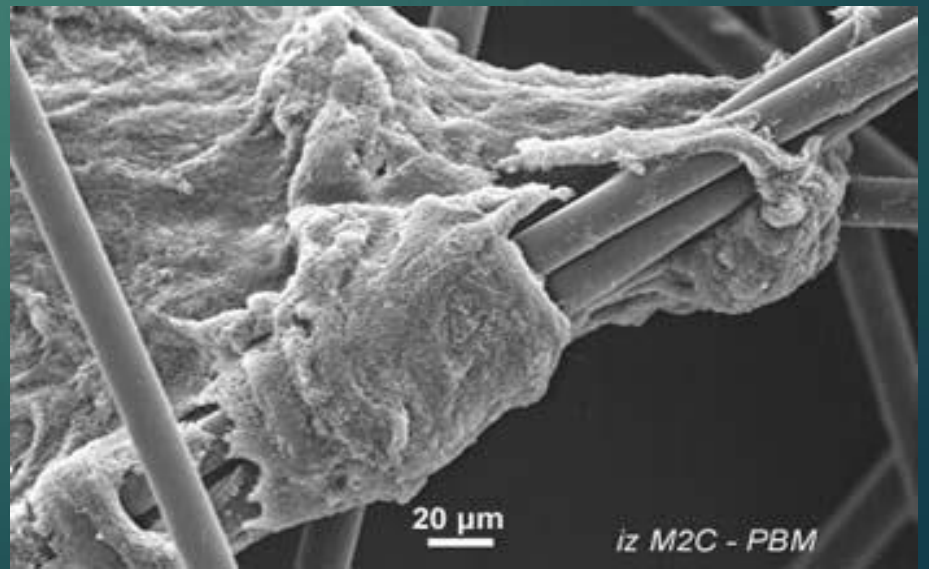
Gram negative

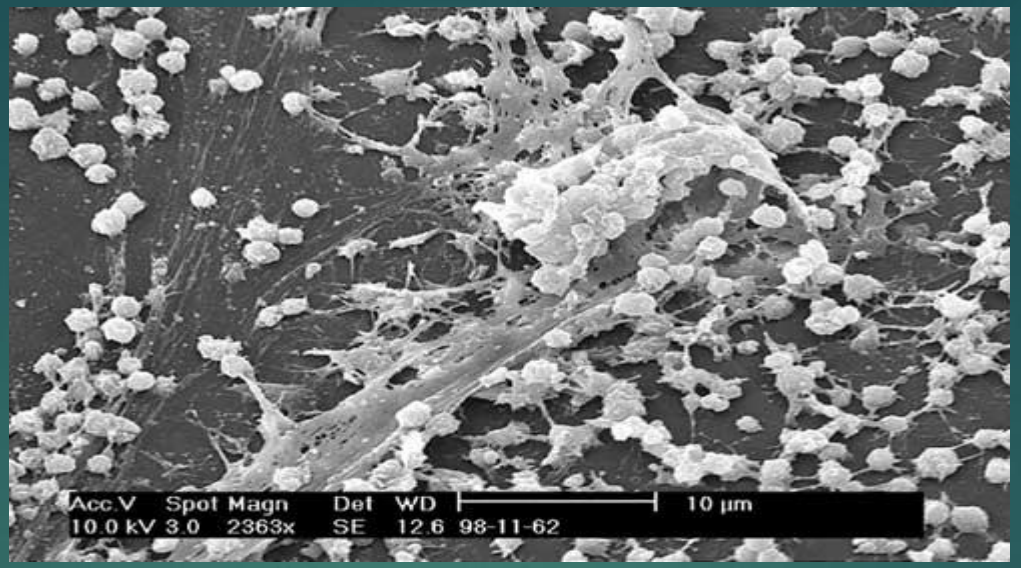


Pseudomonas aeruginosa

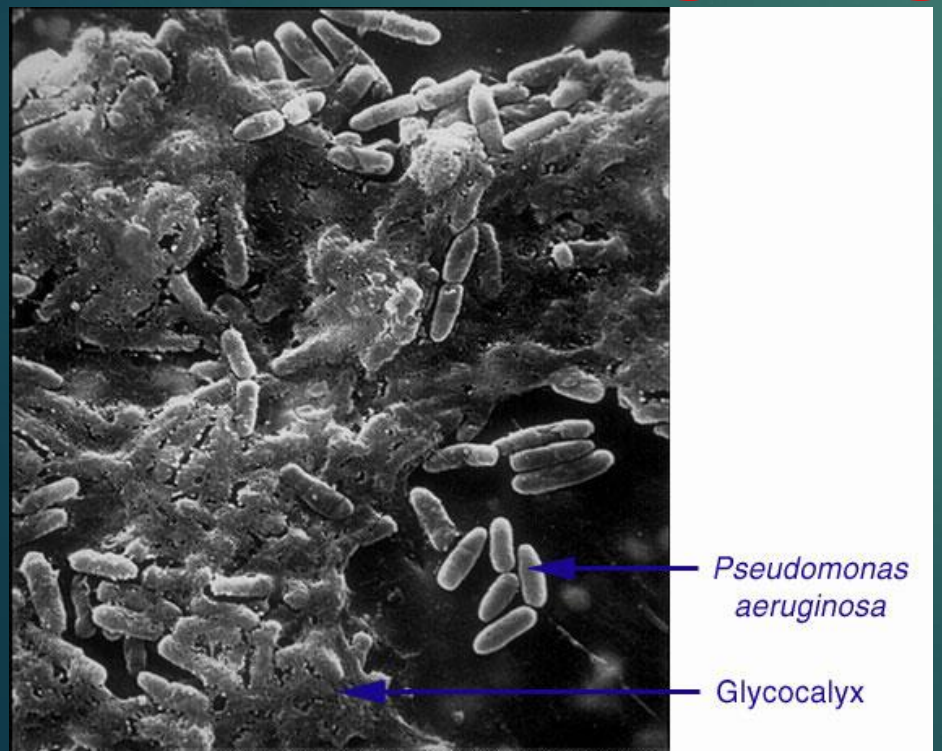
- G- ubiquitous and opportunist
- It grows on multiple substrates (disinfectants)
- Glycocalyx is one of the main pathogenic factors:
  - Cell wall polysaccharide.
  - It favors adhesion to even inorganic substrates.
  - Increases resistance to phagocytosis.
  - It hinders the penetration of antibiotics.

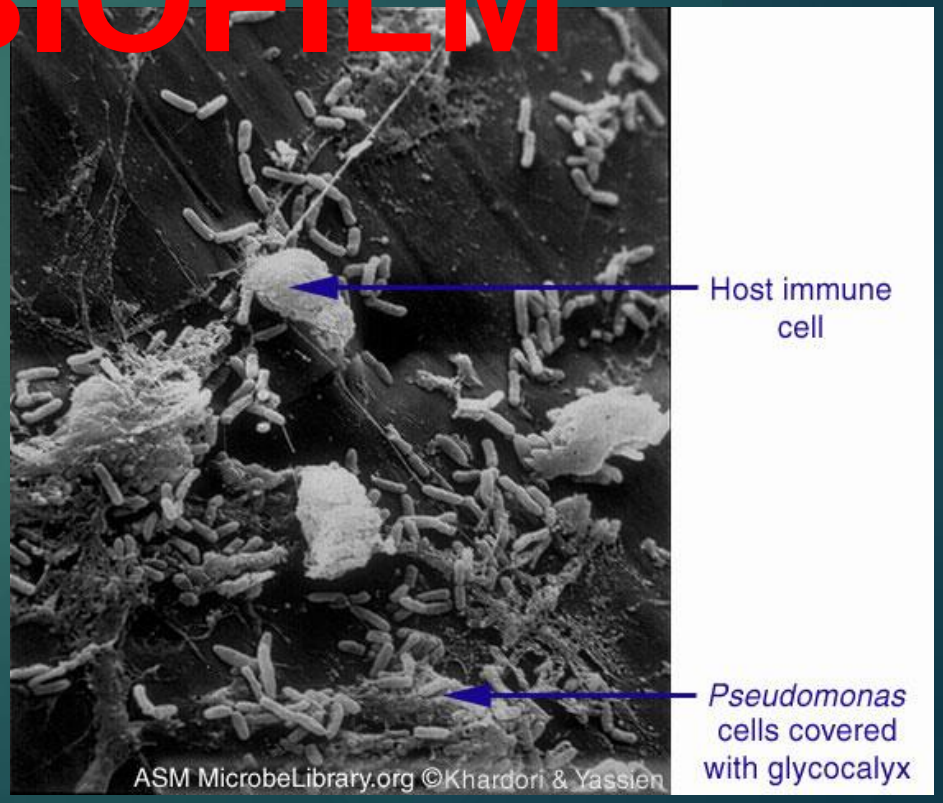






MICROBIAL BIOFILM





Microbial biofilm

- Composed of microbes irreversibly adhered to organic and inorganic surfaces and immersed in an extracellular polysaccharide matrix (EPS) produced by themselves.
- EPS production takes place in 12 - 48h.
- The EPS matrix can appear as a thin layer or more frequently in multiple layers.
- In biofilm the largest volume is occupied by the matrix.


Biofilms and Device-Associated Infections

Rodney M. Donlan

Centers for Disease Control and Prevention Atlanta, Georgia, USA

Emerging Infect Dis 2001, 7: 277-81

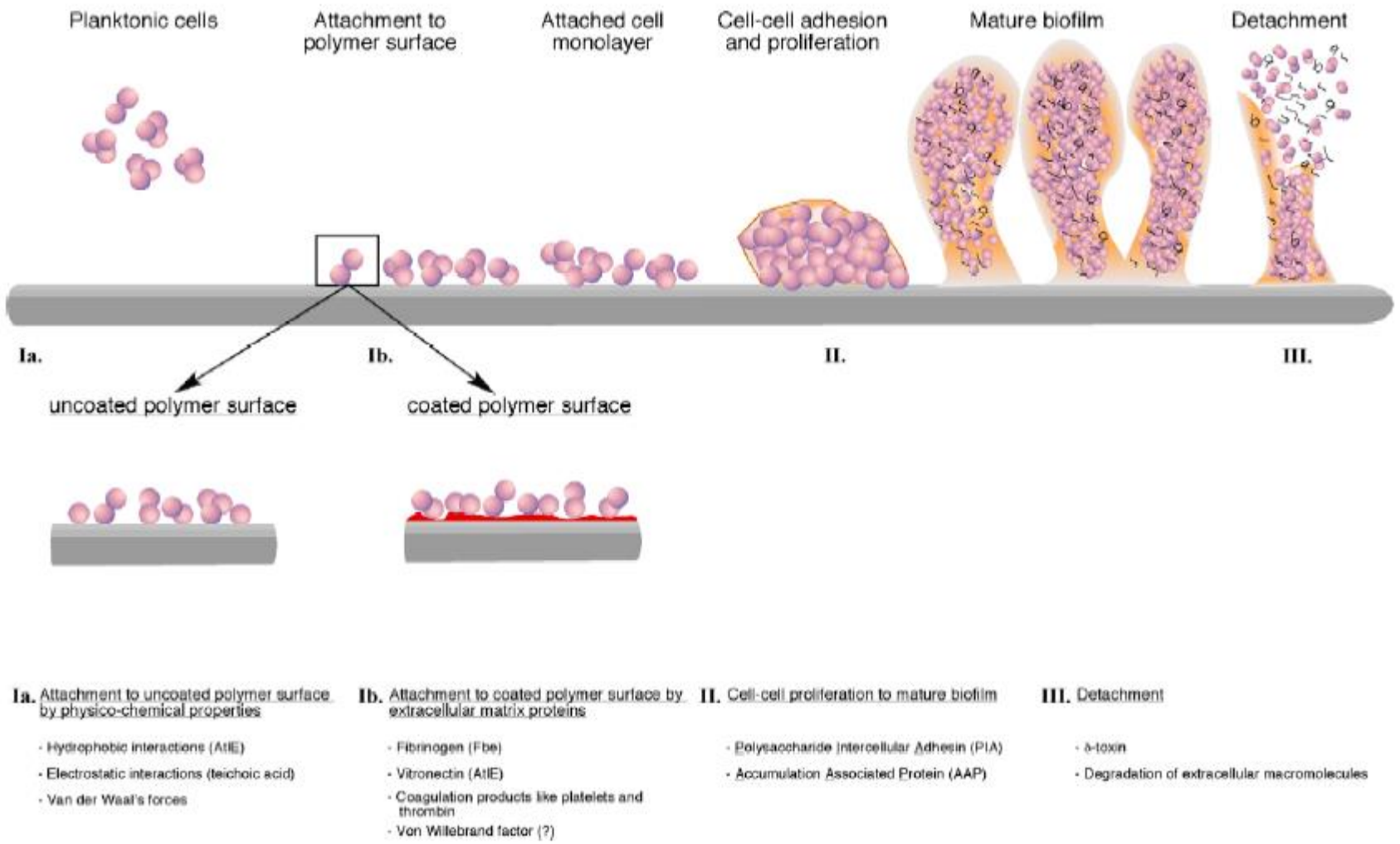


Fig. 1. Model of *S. epidermidis* biofilm formation and involved factors. Fbe, fibrinogen binding protein; AtlE, *S. epidermidis* autolysin.

Antibiotic resistance in biofilm

- There is no definitive evidence of bacterial resistance mechanisms in biofilm.
- Biofilm can represent a physical barrier to the penetration of antibiotics.
- Traditional mechanisms do not appear to be involved in bacterial resistance in the biofilm.

Nuno Cerca[1], Silvia Martins[1], Filipe Cerca[1], Kimberly K. Jefferson[2], Gerald B. Pier[2],
Rosário Oliveira[1] and Joana Azeredo[1]*

Journal of Antimicrobial Chemotherapy (2005) **56**, 331–336

Antibiotic resistance in biofilm

- The bacteria in the biofilm tolerate higher antibiotic concentrations than the planktonic form.
- The resistance of the bacterial phenotypes present in the biofilm is up to 1000 times higher than that of planktonic bacteria.

Nuno Cerca[1], Silvia Martins[1], Filipe Cerca[1], Kimberly K. Jefferson[2], Gerald B. Pier[2],
Rosário Oliveira[1] and Joana Azeredo[1]*

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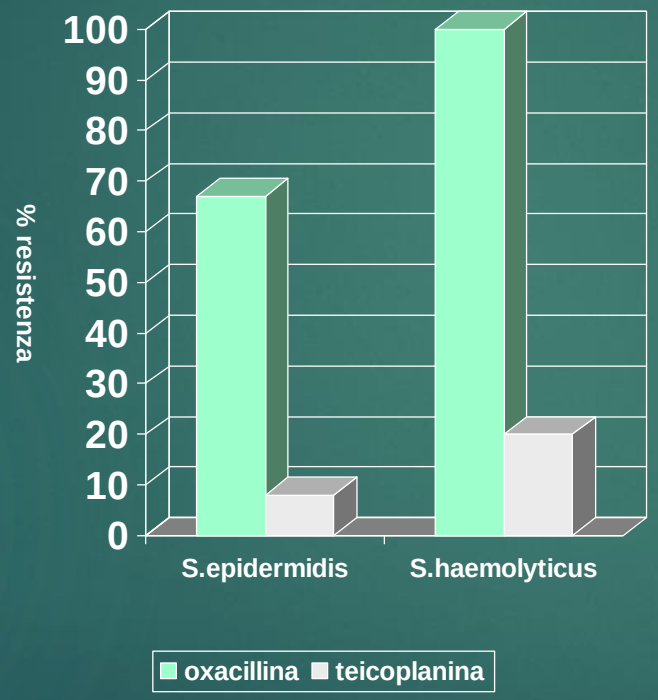
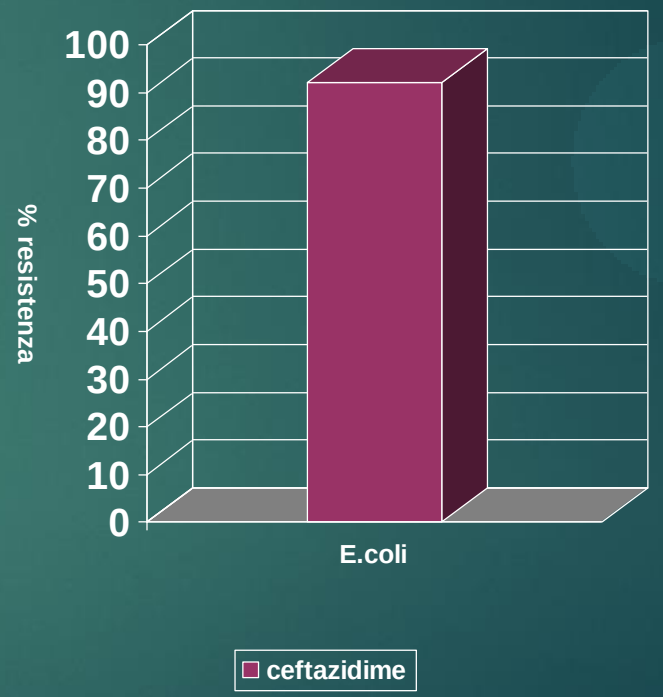
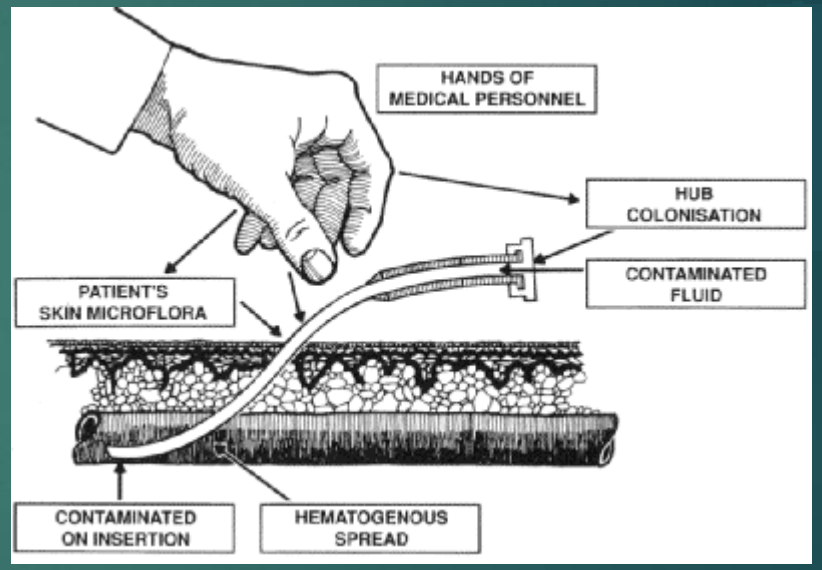
CVC ICU antimicrobial resistance





CVC : what to send to the laboratory?

- Segments of about 5 cm of the tip, the intermediate section, the tunnel and the emerging section, in a sterile container.
- Do not add conservation liquids or culture medium.
- When? As soon as possible (within 15 minutes).
- Also send blood cultures together with the segments.



CVC : what to send to the laboratory?

- Perform a set of blood cultures taken from both the catheter and a peripheral venous accesses.
- Before catheter removal.
- Without interrupting any flow of liquids.

MICROBIOLOGICAL DIAGNOSIS

There is no "gold standard"

MICROBIOLOGICAL DIAGNOSIS: Qualitative methods

Culture of the catheter segments in broth

Advantages

- High sensitivity
- Ease of execution
- Sterility of culture procedures

Disadvantages

False positives

Highlighted any microbial development

MICROBIOLOGICAL DIAGNOSIS: Quantitative methods

- Maki (semi-quantitative): rolling of the segment on solid media .
  - Colonization if < 15 CFU/segment.
  - CVC-related sepsis if > 15 CFU/segment.

MICROBIOLOGICAL DIAGNOSIS: Qualitative methods

- Cleri : vigorous stirring (vortex) in liquid (1 mL of sterile broth)
  - Colonization if <1000 CFU/ segment.
  - CVC-related sepsis if > 1000 CFU/ segment.
- Sherertz: segment sonication in liquid (1 mL of sterile broth)
  - Colonization if <100 CFU/ segment.
  - CVC-related sepsis if > 100 CFU/ segment.

MICROBIOLOGICAL DIAGNOSIS: Qualitative methods

- PRO
  - Possibility of "immediate" clinical correlation in case of positivity.

- CONS
  - Low clinical correlation if the isolates are those of the skin flora.

Bacteremia or sepsis related to C V C: criteria.

1. Positive catheter culture.
2. Positive blood cultures.
3. Isolation of the **same microorganism** from CVC and blood cultures.

J Clin Pathol 1999;52:165–172

Diagnosis of central venous catheter related sepsis—a critical look inside

B M Dobbins, P Kite, M H Wilcox

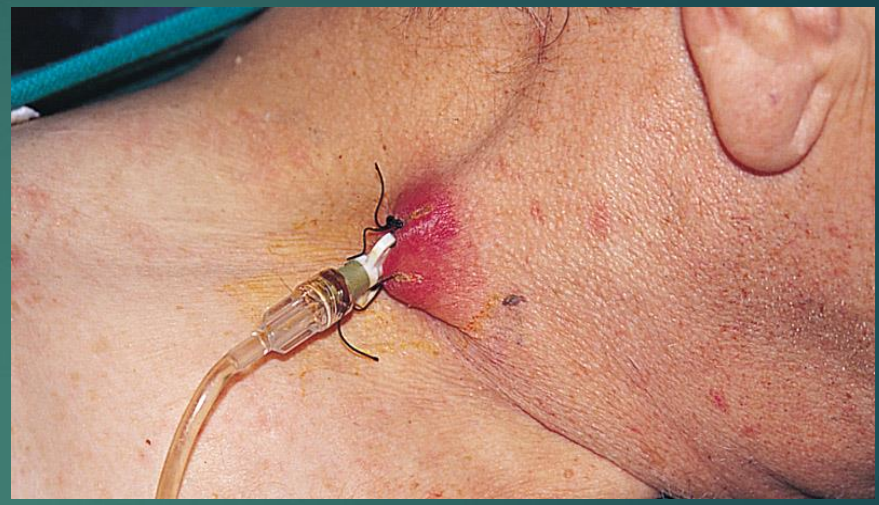
High predictive value when:

- Blood culture taken from the catheter is positive at least 2 hours before the culture of blood drawn from a peripheral vein.

Blot F. *et al.* Lancet 1999; 25:1071-7

CVC: local infection

- Swab in the presence of signs of infection at the insertion site



- Collection of the secretion along the tunnel or in correspondence of the bag in the tunneled catheters.