Microbiological diagnosis of infective endocarditis; what is new?

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Objectives

- Lab Diagnostic Approach
- Lab & clinical Challenges
  - Changing microbiology
  - Culture –ve IE
  - Special IE patients:S.aureus, Fungal, CIED
- Recommended Lab Work- Up
- Improved lab diagnosis
  - Increase the yield of blood culture
  - Serological and molecular methods

Lab Diagnostic Approach

- The criterion standard test for diagnosing infective endocarditis (IE) is the documentation of a continuous bacteremia (>30 min in duration) based on blood culture results.
- Never draw only 1 set of blood cultures; 1 is worse than none.
- The corner stone for diagnosis & AST is multiple positive blood cultures
- Other lab methods improve diagnosis: serology & molecular techniques

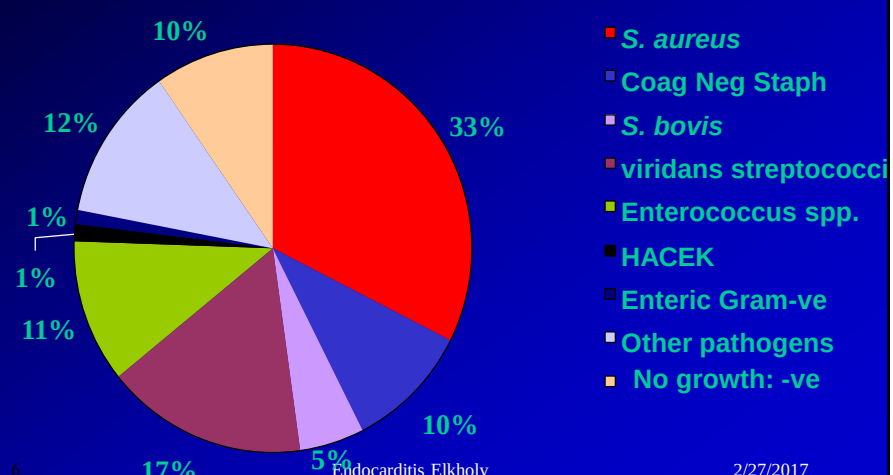
Challenges in interpreting Blood Culture Results

- False negative: BC may be negative despite a supportive clinical evaluation.
- False positive: contamination
- Positive BC in presence of sepsis difficult to interpret.
- BC may yield a bacterium rarely associated with IE

The significance of positive blood culture results correlates with the following:

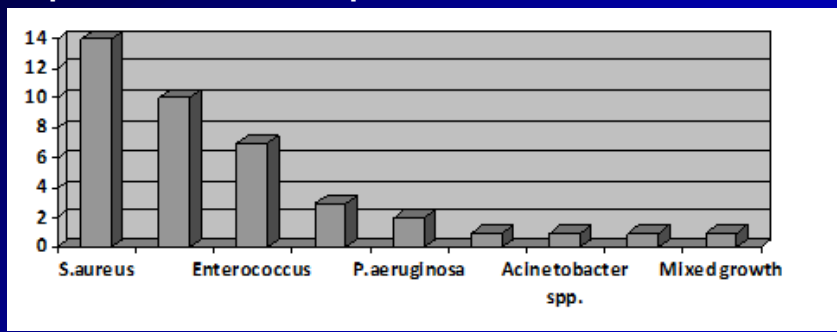
- The type of organism
- The clinical setting (coagulase-negative staphylococci [CoNS] are significant in patients with prosthetic valves but not in those with native valves)
- Multiple blood cultures positive for the same organism
- Shorter incubation time for recovery
- The degree of severity of clinical illness

Worldwide Change in Microbiology
ICE Prospective Data



IE In Egypt: Microorganisms Isolated From Blood Culture:

Blood culture was positive in 30.3% of 156 patients, so blood culture-negative endocarditis (BCNE) represented 69.7% of patients



(El Kholy et al. Impact of serology and molecular methods on improving the microbiologic diagnosis of infective endocarditis in Egypt, 2015)

Challenges in Diagnosis of IE

- Rising rates of *S. aureus* endocarditis
- Healthcare- associated endocarditis
- Increased rates of antimicrobial resistance
- High rates of culture-ve in some regions: 56.4% in Algeria Vs. 2.5- 31% in Europe
- Immunocompromized patients
- Cardiovascular Implantable Devices

S aureus BSI Vs. IE

- A major clinical challenge is that at least 25% of *S aureus* BSI represent IE or metastatic infections.
- The question is whether a continuous bacteremia in the presence of an IV line is representative of IE.
- Blood cultures should only be drawn through IV lines for the purpose of diagnosing catheter-related BSIs and have limited value for answering this clinical challenge.
- An important clue to continuous bacteremia/IE is the presence of *S aureus* bacteriuria associated with hematuria. Hematuria in the setting of IE is due to embolic renal infarction or immunologically mediated glomerulonephritis.

Causes of Culture -ve IE

- Inappropriate Blood Culture
- Fastidious microorganisms

Fastidious!

- ***Brucella spp.***
- **Nutritionally deficient Streptococci**
- **HACEK organisms**
  - *Haemophilus spp.*
  - *Actinobacillus*
  - *Cardiobacterium hominis*
  - *Eikenella corrodens*
  - *Kingella kingae*
- ***Coxiella burnetti* (Q fever)**
- ***Bartonella species* (cat scratch disease)**
- ***Legionella, Mycoplasma***
- ***Chlamydia***
- ***Aspergillus* species**
- ***Lactobacillus* species**

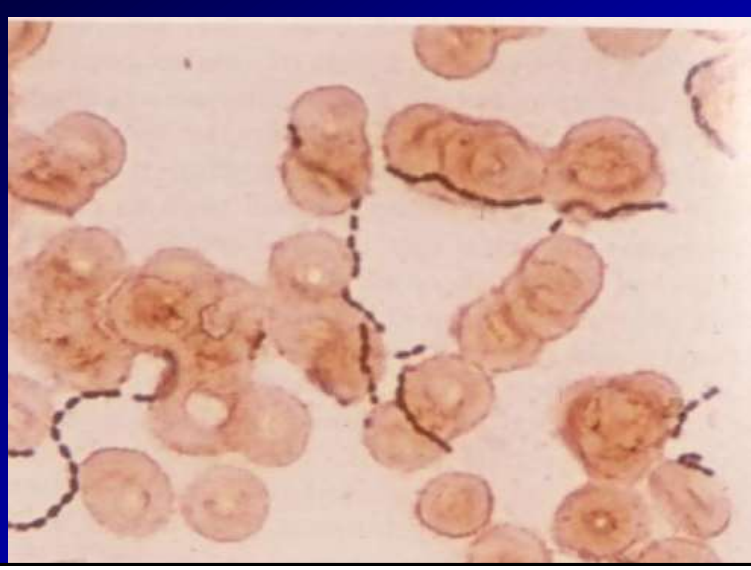
Improved Lab Diagnosis

- Improve yield of culture techniques
- Serological Methods
- Molecular Detection

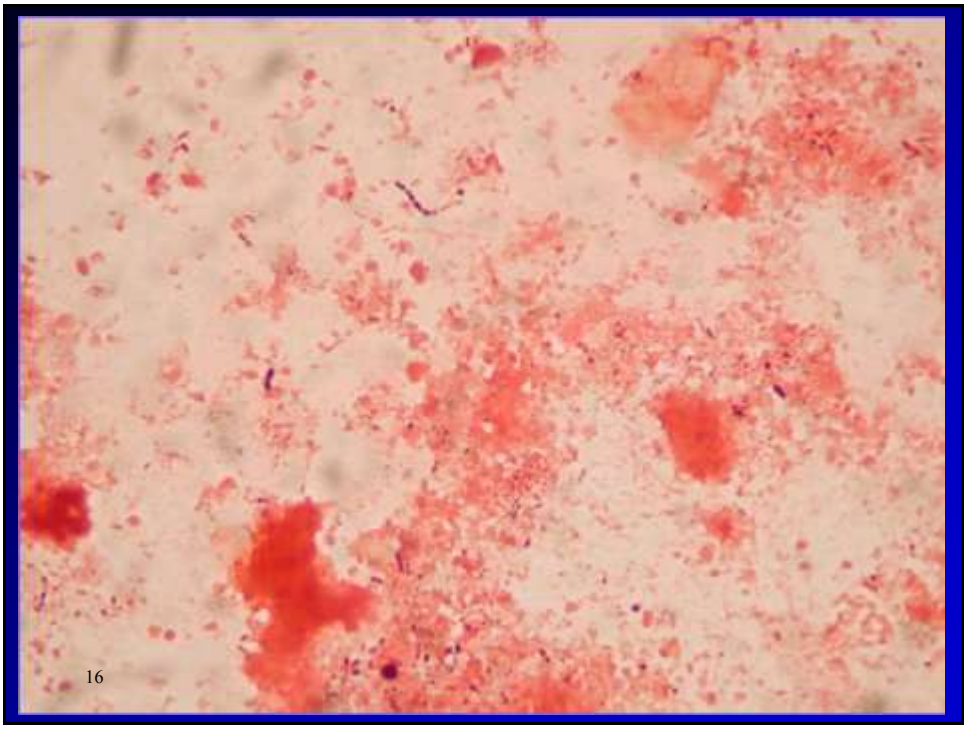
Increasing Yield of Blood Culture

- Communication with Lab: more sets (3) & more incubation time (3 weeks)
- Volume: BC result is volume- dependant:
  - In adults 10 ml/ bottle are required.
  - Adequate sets: 2-3/ 24 hrs or 4 sets at 1 hr interval
- Timing: Before Antimicrobials
- Skin site preparation:
  - Choice of the Site
  - Avoid contamination from skin or draw through intravenous (IV) lines.

Streptococcus In Direct Gram stain of positive blood culture



Aspergillus in Excised Valve



Fungal infective endocarditis

- Most types of fungal IE have a low rate of positive blood culture results. At best, only 50% of *Candida* species are associated with positive blood culture results.
- *Aspergillus* and other molds are almost never retrieved from the bloodstream.
- Fungal endocarditis must always be considered in the clinical setting of culture-negative IE that fails to respond to appropriate antibiotic therapy.
- Antigen and antibody detection

Pacemaker infective endocarditis

- Establishing the diagnosis of pacemaker IE is difficult because of its subtle presentation, especially late-onset disease.
- The addition of pocket infection and the presence of pulmonary emboli to the Duke criteria have increased the rate of diagnosis from 16% to 87.5% of cases.
- Fever and/or a positive blood culture result without evidence of a primary source in patients with a pacemaker or implantable cardioverter-defibrillator should be considered to represent device-associated IE until proven otherwise.

Cultures of Cardiovascular implantable electronic devices (CIED)

- The AHA 2010 guideline update on CIED infections recommends that, when the CIED is explanted, culture of the lead-tip and Gram stain and culture of the generator-pocket tissue be obtained.
- However, percutaneous aspiration of the generator pocket should not be performed for diagnostic evaluation of CIED infection.

Serological Diagnosis

Useful if

- Blood Culture is –ve
- Fastidious organisms

Disadvantages:

- Cross reactions: e.g. Bartonella and Chlamydia
- High titers in endemic areas & with other chronic infections

Interpretation of the serology results:

- Positive titer for *Brucella* when antibody titers ≥ 1/320
- *Bartonella* endocarditis when IgG titers ≥1:800

Coxiella burnetii

- A single serum specimen is diagnostic if:
- Anti-phase I IgG antibody titer of >1:800 and IgA titer of >1:100 by MIF test indicate Q fever endocarditis (Duke Major)
- Usually high antibody response to both phase I and phase II Ag

Aspergillus Galactomannan Antigen

- using the Platelia EIA (Bio-Rad, Marnes-La-Coquette, France).
- Patients with an index >0.5 were considered positive for *Aspergillus* antigen

Molecular Techniques

Advantages:

- Detection by DNA amplification using PCR:
  - Multiplex
  - Broad- range PCR
- Needs no viable microorganisms
- Identify fastidious & non- culturable.
- Sera, valve or other tissue can be used

Limitations of Molecular Techniques

- Cost and availability of equipment
- Depend on the quality and nature of the specimen
- Affected by inhibitory substances in specimens
- Contamination
- No. and quality of DNA sequences in data base
- Results are not quickly available
- Choose a procedure standardized for clinical diagnosis

Lab Algorithm in Cairo University

Blood Culture: At least 3 sets (6 bottles), if negative:

- Serum:
  - Serological testing for *Brucella, C.burnetii, Bartonella, M.pneumoniae, Legionella, Chlamydia*
  - Galactomannan antigen
- Multiplex PCR: sepsis screen
- Broad range PCR followed by sequencing: under validation

Excised valves:

- Microbiology: Direct exam (Gram Stain, KOH Preparation for Fungi) & Culture
- Histopathology: Microorganisms & tissue reaction

Conclusions

IE remains a diagnostic challenge

- Blood culture remains the corner stone
- Increased yield of bacteria from Bl culture:
  - **Without antibiotics administered before sampling**
  - **By increasing the volume of blood**
- Fastidious bacteria need rich media, prolonged incubation time, and special culture conditions
- Serology: important diagnostic role in culture-ve endocarditis caused by *Brucella, Bartonella* and *Coxiella &* Galactomannan Ag detection
- Molecular techniques: promising in spite of limitations

Thank You