EFLM European Urinalysis Guideline, update 2023

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ELMÜ kliinilise mikrobioloogia sektsiooni koosolek

Rakvere

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Guideline staatus, Timo Kouri

- **We are still working** with the revisions proposed to the primary version. The expected publication will be in Clin Chim Acta in 2024 as a special issue. You can follow the pace from our website: https://www.eflm.eu/site/page/a/1466

Chapter 7. Bacteriology, page 202

- Meditsiinilised näidustused uriini külviks:

(1) Suspicion of acute pyelonephritis or febrile urinary tract infection

(2) Suspicion of hospital-acquired urinary tract infections (possibility of reduced antibiotic sensitivity)

(3) Suspicion of urinary tract infection in patients with a predisposing disease, such as

diabetes, anomaly of the urinary tract, recurrent stone disease, or immunocompromised state

(4) Patients failing first line antimicrobial chemotherapy

(5) Febrile patients with indwelling catheters

(6) Clinical suspicion of urinary tract infection in men (symptomatic)

(7) Clinical suspicion of urinary tract infection in pregnant women (symptomatic)

(8) Suspicion of urinary tract infection in children and adolescents (symptomatic)

(9) Reccurrent UTI

Uriini külvi eesmärk

to identify aetiological agents of urinary tract infection, i.e., relevant pathogens, but also mixed flora (> 2 species) as a sign of contamination

to estimate the concentration of bacteria

to offer susceptibility testing for antimicrobial treatment

to look for a relapse or re-infection in patients not responding to antimicrobial treatment

Patogeenide klassifikatsiooni alused I

Primary pathogens: põhjustavad infektsioone normaalses urotraktis

Secondary pathogens: harva põhjustavad infektsioone normaalses urotraktis, sageli esinevad haiglainfektsioonide tekitajana

Doubtful pathogens: võivad koloniseerida urotrakti ja aeg-ajalt põhjustavad haiglainfektsioone

Contaminants: reeglina sattuvad uriini proovivõtu ajal, kui kontaminatsioon on välistatud, soovitav uus proov etioloogilise rolli kinnitamiseks

Patogeenide klassifikatsioon I

- **I. Primary pathogens**
- *E. coli*
- *S. saprophyticus*

- **II. Secondary pathogens**
- *Enterobacter* spp.
- *Citrobacter* spp.
- *M. morganii*
- *Serratia* spp.
- *Klebsiella* spp.
- *Proteus* spp.
- *P. aeruginosa*
- *Enterococcus* spp.
- *S. aureus*
- *Actinotignum schaalii*
- *Aerococcus* spp. *(Aerococcus urinae, Aerococcus sanguinicola)*
- *C. urealyticum*
- *Alloscardovia omnicolens?*

Patogeenide klassifikatsioon II

- **III. Doubtful pathogens**
  - *Streptococcus agalactiae*
  - Yeast
  - *Acinetobacter* spp.
- **IV. Contaminants**
- *Staphylococcus*, coagulase negative (except *S. saprophyticus*)
- *Corynebacterium* spp (except *C. urealyticum*) Muud korünebakterid???
- *Gardnerella vaginalis*
- *Lactobacillus* spp. (except *L. delbrueckii*)

ASM Manual 2023 sept

Võimalikud UTI tekitajad – Klass II?

- *C. diphtheriae* - nephrostomy catheter+related infections
- *C. amycolatum* -UTI
- *C. argentoratense* - catheter-related infections
- *C. aurimucosum*- UTI (mostly male patients), female urogenital tract (also associated with complications during pregnancy, including spotaneous abortions)
- *C. coyleae*- complicated UTI (also with urgency urinary incontinence and overactive bladder)
- *C. glucuronolyticum*- genitourinary tract infections (mainly males)
- *C. imitans*- UTI
- *C. jeikeium*- catheter-related infections, UTI
- *C. macginleyi*- UTI associated with use of permanent bladder catheter
- *C. minutissimum*- lower urinary tract
- *C. mycetoides*- UTI
- *C. pseudodiphtheriticum*- UTI
- *C. renale*- UTI
- *C.riegelii*- UTI
- *C. simulans*- UTI
- C. striatum-UTI
- *C. tuberculostearicum*- UTI
- *C. urealyticum*- UTI, cystitis, pyelonephritis

Patogeenide klassifikatsioon – küsimus Pauli poolt Timo Kourile

According to the **2023 ASM manual**, many *Corynebacteria* can be potential causes of UTIs (*C. amycolatum, C. argentoratense, C. aurimucosum, C. coyleae, C. glucuronolyticum, C. imitans, C. jeikeium, C. macginleyi, C. minutissimum, C. mycetoides, C. pseudodiphtheriticum, C. renale, C. riegelii, C. simulans, C. striatum, C. tuberculostearicum, C. urealyticum*) - should these be considered as secondary pathogens?

After application of MALDI-TOF we can find lot of new species and some of these have been reported to cause UTI.

Patogeenide klassifikatsioon – Timo Kouri vastus

Dear Paul

- Since I am not a microbiologist, the detailed classification of uropathogens is not my topic. The provisional list has been collected by Prof Martine Pestel-Caron, Rouen, France, and discussed with the other microbiologists, e.g., Prof Sören Schubert, Munich, Germany.
- The detailed classification of individual pathogens may be less important than the consequences in the laboratory workflow, in particular within classes III - IV. The tentative Table 7-3 (see below) is a list of examples - and not a complete classification - with some modifications to earlier classifications, and additions of new suggested pathogens.
- While looking at the current tentative table 7-3 for your meeting (please, wait for the final version), you are allowed to work based on your local epidemiology as well, in addition to the EARS-Net and EUCAST co-operation.

Yours,

Timo Kouri

Sööde I

No single culture medium allows growth of all uropathogens.

Chromogenic medium is strongly recommended as the primary routine agar.

As compared to other media such as Cystine-Lactose Electrolyte Deficient (CLED) agar, it allows rapid identification of the most frequent microorganisms causing urinary tract infections (particularly *E. coli*).

It also supports detection of polymicrobial growth thanks to the hydrolysis of different chromogenic substances by species specific enzymes

Thus, using chromogenic agar allows to reduce workload of the laboratory technicians, material required for bacterial identification (no need for large supplementary tests to identify *E. coli*), and to improve turn-around time for patient results with lower costs

Sööde II

- Clinical microbiologists should additionally consider necessity of specific procedures, such as culturing urine specimens on blood agar under 5% CO2 atmosphere for 48 hours:

  These clinical cases may include patients with defined urological diseases, or cases of positive leukocyturia with negative culture results and needs to detect emerging fastidious Gram-positive pathogens.

Sööde III

- Furthermore, for urine specimens collected using urological procedures (e.g., cystoscopy, nephrostomy) or for prostatic secretions, a chocolate agar could be recommended as an optimum approach
- Urine samples showing the presence of yeast on microscopy can be inoculated on chromogenic yeast culture medium such as ChromAgar. This allows a direct presumptive identification of *Candida albicans*, *C. tropicalis* and *C. krusei*.

Külv ja koguse hindamine

- Inoculum: The volume of urine that is inoculated onto a culture medium affects the limits of detection of bacteriuria. It is to be noted that **1-µL disposable loop inoculum is less optimal in detecting low count bacteriuria**. Statistical reliability starts at 10^4 CFU/mL (10^7CFB/L) with a 1-µL inoculum that results in 10 colonies on plate.
- Because of the uncertainty, the 2-3 colonies growing on a plate are still within a grey zone of detection, and only > 5 colonies/plate differ statistically from a negative result. This must be considered when expressing culture results or adopting limits of significant growth

10 µl külviaasa kasutamine

- Kateeteruriin
- Aspiratsiooni teel saadud uriin (suprapubic aspirates)
- Invasiivselt kogutud uriin (operatsiooni ajal, nefrostoomist?)
- Inkubeerida 16-24 tundi 33-37°C juures
  - Vajadusel inkubeerida kuni 48 tundi (invasiivselt kogutud uriin, leukotsüütuuria ilma kasvuta kliinise infektsiooniga patsiendil, nõudlikke patogeenide kahtlusel)
  - Veriagari lisamine 5% CO_2 kuni 48 tundi

Mikroobi koguse määramine?

Pesade arv söötmel	Külv 1µl (PMÜ/ml)	Külv 10µl (PMÜ/ml)	Külv 100µl (PMÜ/ml)
< 10 pesa	10^3-10^4	10^3	10-10^2
10-100 pesa	10^4-10^5	10^3-10^4	10^2-10^3
>100 pesa	>10^5	>10^4	>10^3

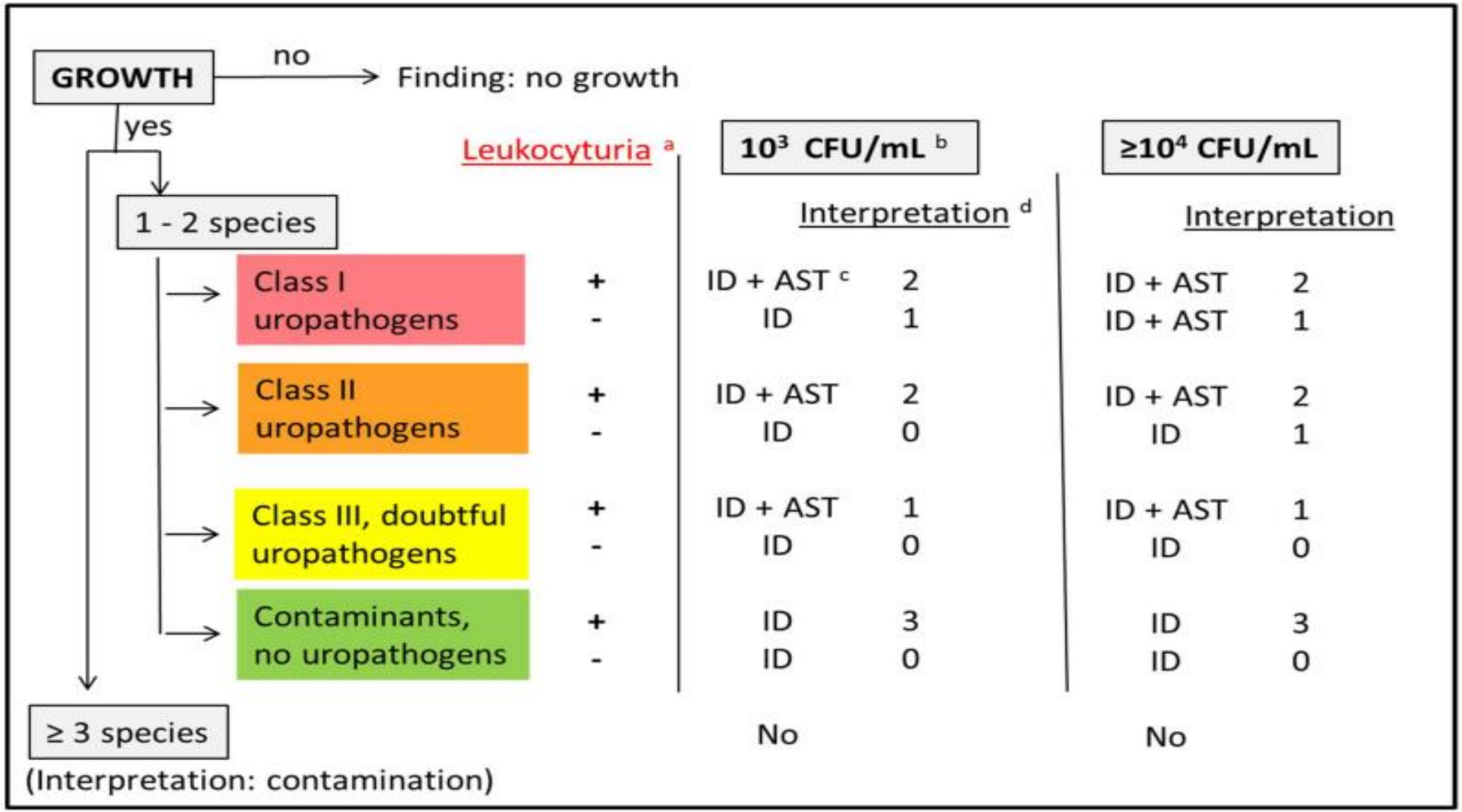
Mikroobi koguse määramine?

- Kas peame kusagil avaldama tabeli, mis on kõigile arusaadav ja vastuvõetav erinevate külviaasade kasutamisel?
- Kas peame ka 100 µl koguse kohta tabelisse panema?
- Kas peame täpsustama ka TEHIKus avaldatud loendi?
  - Praegused valikud
    - < 10^3 PMÜ/mL
    - 10^3–10^4 PMÜ/mL
    - 10^4–10^5 PMÜ/mL
    - > 10^5 PMÜ/mL
    - 10–10^2 PMÜ/mL
    - 10^2–10^3 PMÜ/mL

Leukotsütuuria

- Presence of leukocyturia should be assessed at a cut-off of about 30 WBC x10^6/L, with a grey zone 10-30 WBC x10^6/L [Kouri T et al, CCA 2021] keeping in mind that leukocyturia can be absent in patients with neutropenia
- Leukotsüütide arvu skaala ribatestil (ITK näide):
  - Neg
  - 15 (jäljed)
  - 70; 125; 500 (Leu/µL)
- Milline väärtus korreleerub 30 WBC x10^6/L?

Tulemuste tõlgendamise algoritm I



Tulemuste tõlgendamise algoritm II

- **0** = Detected microorganisms probably **do not cause a UTI** (even with corresponding symptoms).
- **1** = Detected microorganisms **possibly cause** UTI in selected clinical presentations

(immunocompromised patients, early infection…) with appropriate clinical picture.

- **2** = Detected microorganisms with significant colony counts. **UTI is probable** with appropriate clinical picture.
- **3** = No microorganisms detected with the used culture procedure. Antibiotic treatment? In presence of appropriate clinical picture, consider tests specific for other microbes, e.g., *Chlamydia, Mycoplasma, Ureaplasma, M. tuberculosis, N. gonorrhoeae*.

Tulemuste tõlgendamise algoritm III

- Eestikeelsed tõlgendused eraldi loendisse ja kasutama need rutiinselt?
- Töörühm juhendi adapteerimiseks Eesti tingimustesse (patogeenid, kogused, leukotsütuuria, kommentaarid etc?

- Clinical effectiveness of point of care tests for diagnosing urinary tract infection: a systematic review
  - Eve Tomlinson, Hayley E. Jones, Rachel James, Chris Cooper, Christina Stokes, Samina Begum, Jessica Watson, Alastair D. Hay, Mary Ward, Howard Thom, Penny Whiting