SUPPLEMENTAL MATERIAL

POSTER P1356

THE UPDATED TOPICS OF THE EFLM EUROPEAN URINALYSIS GUIDELINE 2023

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Chapter 1. Recommendations for Medical needs

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
1	Epidemiology and clinical symptoms of the target diseases, as well as diagnostic and prognostic significance of the chosen tests are recommended to guide the clinical use of urinalysis tests.	1, B	1
2	Urinalysis tests should be requested based on assessment of risk for severe disease. The specific tests should be planned between laboratories and clinics, to balance benefits against resource.	1, C	1.1
3	General screening strategies for low-risk and routine patients (work-flow optimisation) is to be separated from targeted diagnostics for high-risk patients.	1, C	1.1 – 1.3
4	Asymptomatic bacteriuria must not generally be sought, in order to avoid unnecessary antimicrobials and multiresistant strains of uropathogens. Exceptions include pregnant women, immunocompromised patients, and patients undergoing some urological or gynaecological operations.	1, A	1.2.2
5	Quantitative specific protein measurements are recommended as primary investigations for high-risk patients for detection and follow-up of kidney disease.	1, A	1.3.1
6	Either advanced automated counting or visual microscopy of urine particles is recommended to detect specifically a renal disease in low and high-risk patients with proteinuria .	1, B	1.3.2
7	Requisition and reporting of urinalysis tests using electronic interfaces is encouraged, with local diagnostic algorithms. Electronic transfer improves exchange of systematic information between clinicians and laboratories, including specimen details.	1, B	1.4.2

[a] *Strengths of Recommendations (SoR) are: 1= strong, 2 = weak recommendation.*
Levels of Evidence (LoE) are: A = high, B= moderate, C= low quality of evidence, D = consensus by the experts.
*R*ating was adopted to laboratory medicine from the GRADE system [Gyatt GH et al, BMJ 2008].

Gyatt GH, Oxman AD, Vist GE, Kunz R, Falck-Ytter Y, Alonso-Coello P, Schünemann HJ, for the GRADE Working Group. GRADE: an emerging consensus on rating quality of evidence and strength of recommendations. Brit Med J 2008;336:924-6.

Chapter 2. Recommendations for Patient Preparation

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
8	Interaction with patients shall be improved to invite patients to become active in decision-making on their disease. This would encourage them to learn how to collect a mid-stream urine (MSU) specimen in the best achievable way, in order to minimise contamination .	1, C	2.1.1
9	Laboratories shall maintain an educational material bank and enforce routine co-operation with their clinical units in order to improve preanalytical processes, including preparation of patients for delivering their urine specimens.	1, C	2.1.1 and 3.5
10	The recommended quality indicator for MSU specimens is a desirable rate < 10%, and a maximum rate < 15% of polymicrobial growth at 10^4 CFU/mL (or 10^7 CFB/L) in urine culture, calculated at laboratory level.	1, C	2.1.1 and 3.2
11	Chemical measurements and particle counts from single-voided urine specimens are improved by reporting concentration of urine. Chemical measurands are recommended to be reported as measurand-to-reference ratios, e.g., albumin-to-creatinine ratio. Particle counts should be reported with results of urine relative density, conductivity, or osmolality.	 1, A 1, B	2.2.1
12	Reporting bladder incubation time is recommended to improve interpretation of significance of low bacterial counts, or fragile particles in urine (urgency, or dilute urine if < 4 hours).	2, C	2.2.3

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
13	The first morning urine is recommended to be collected after an 8-hour period of recumbency, and after an incubation of 4-8 hours in the bladder. The second morning urine is suggested be considered in ambulatory patients, and a random urine in emergency patients as needed.	1, B	3.1.1 - 3.1.3
14	Measurand-to-reference ratios, e.g., relating measurands to creatinine concentrations in urine, from single-voided specimens are recommended to replace timed urine collections for chemical measurements because of the lower incidence of non-conformities. Verification of the intended measurand to a new patient group is needed before clinical application.	1, A	3.1.5
15	The recommended quality specification for mid-stream urine (MSU) specimens is a desirable rate < 10%, and a maximum rate < 15% of polymicrobial growth at 10^4 CFU/mL (or 10^7 CFB/L) in urine culture, calculated at laboratory level.	1, C	2.1.1 and 3.2
16	Mid-stream collections are strongly recommended for single voided urine specimens, because of the lower level of contaminants as compared to first-stream specimens. The use of antiseptics is not recommended.	1, B	3.2.1
17	Single catheter urine or suprapubic aspiration specimen is recommended to establish the diagnosis of UTI in children or older patients without urinary control.	1, B	3.2.3
18	Urine specimens must not be taken from the collection bag of a permanent indwelling catheter. A specimen shall be collected after removing the old catheter and taking the sample through the new catheter.	1, B	3.2.4
19	Urine specimens from specific collection pads or bags may be used to exclude UTI in small infants, but they become easily contaminated. Consider spontaneously voided specimens. Non-standard diapers are not recommended. Positive growth shall be confirmed by single catheter or SPA urine collection.	1, B	3.2.6
20	The actual time of urine collection is recommended to be documented and reported to the analytical site together with the specimen, to allow assessment of acceptability of the specimen after the preanalytical delay and storage conditions before analysis.	1, B	3.3
21	Preservation of urine specimens is obligatory if the sample is not analysed within 2-6 hours after voiding. Consider refrigeration if applicable. Guidance to criteria of successful preservation is given in this guideline.	1, B	3.3 and 3.5
22	Technical features of urine collection containers given in this guideline are recommended to be followed by the manufacturers to improve the quality of clinical urine specimens. The given specifications are open for revisions after technical or clinical evidence.	1, B	3.4

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
23	Clinical laboratories are recommended to express clearly, which level of analytical performance (Levels 1-3) is the target, when they are establishing their measurement procedures. For nominal scale examinations, the relevant diagnostic performance should be described accordingly.	1, B	4

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Chapter 5. Recommendations for Chemistry

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
24	Multiple (multiproperty) test strips are still recommended as screening tools for low-risk patient populations because of their cost-efficiency. They are NOT recommended for urine diagnostics of high-risk patients if insensitive.	1, A	5.2.1
25	No laboratory tests are recommended for low-risk non-pregnant female patients with typical symptoms of uncomplicated cystitis.	1, A	5.2.1.1 and 7.1.1
26	Laboratory tests to screen for UTI are recommended to include tests for detection of at least leukocytes and bacteria.	1, A	5.2.1.1
27	Rapid tests are recommended to be requested from elderly patients after a clinical intention to treat only because of a high prevalence of asymptomatic bacteriuria.	1, A	5.2.1.1
28	Concentration is suggested to be measured from urine specimens of pediatric patients, to alert of non-representative dilute specimens.	2, B	5.2.1.1
29	Sensitive albuminuria screening for incipient chronic nephropathy is not recommended at an epidemiological level because of costs of follow-up investigations. A targeted screening of high-risk patient populations is recommended.	1, B	5.2.1.3
30	Urine concentration is recommended to be reported together with all chemical and particle examinations from single-voided urine specimens.	1, B	5.2.1.4
31	Plasma hydroxybutyrate measurements are recommended for the follow-up of comatose ketoacidosis patients instead of urine strip tests.	1, B	5.2.1.5
32	From specimens of intensive care and in-patient groups with needs of improved accuracy, urine concentration is suggested to be measured by using refractometry or osmolality.	2, B	5.2.2.1
33	Urine strip tests are recommended to be read with instruments both in laboratories and points-of-care, using qualified procedures to avoid human errors in interpretation of results.	1, A	5.2.2.2
34	Performance of test strip measurements is recommended to be verified against quantitative measurement procedures and monitored internally by using continuous reflectance values from reflectometers, and control solutions close to the limit of positivity of each measurement.	1, B	5.2.3
35	Sensitive detection of renal disease in high-risk groups requires measurements of both urine albumin, and a tubular marker in urine, such as α1-microglobulin, in the diagnostics of kidney disease. Measurement of urine total protein remains important in screening for free light chains in urine (Bence Jones proteinuria). Estimation of GFR (eGFR) is of primary importance in the follow-up of the detected kidney disease.	1, B	5.3.1.2
36	Physiological and biochemical limits of each measurand for urine volume rate (concentration) need to be considered when interpreting them clinically.	1, B	5.4.2
37	The EFLM Urinalysis Guideline endorses the diagnostic strategy for renal stone formers given by the European Association of Urology on Urolithiasis.	1, B	5.5.1
38	Preservation of measurands related to renal stones is no more recommended for 24-hour urine collections by patients at home. Additions of preservatives may be needed after receiving the specimen at the laboratory, depending on local preanalytical processes.	1, A	5.5.2

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Chapter 6. Recommendations for Particle Analysis

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
39	Urine particle analysis has a role in the diagnostics of urinary tract infections, haematuria, and kidney diseases.	1, A	6.1.1
40	Urine crystals are not recommended to be looked for, nor be reported, for all specimens. In specific situations, urinary crystals may indicate an inherited or metabolic disease, or a drug precipitated in the kidneys, causing stone formation or renal failure. Most commonly, crystals or amorphous precipitate interfere with identification of other particles in urine.	1, A	6.1.1
41	Laboratories are recommended to clearly discuss and describe their basic and advanced differentiation of urinary particles with their clinicians, in order to harmonise clinical interpretation of their results.	1, B	6.1.2
42	Phase-contrast optics is recommended in the detection and discrimination of urine particles both in routine and reference microscopy.	1, A	6.2.2
43	Laboratories should verify one of the (Level 2) procedures of visual microscopy for their routine analysis to ensure accuracy of their results.	1, B	6.2.3
44	The standard unit for urine particle counts is particles/litre (L), the SI unit. Unit of routine clinical reports is recommended to be harmonised as nationally decided.	1, C	6.2.3
45	Automated particle analysers need to be verified before being implemented into routine, based on the published performance specifications (against Level 3 procedure), as repeated in these guidelines. Performances in detecting urinary tract infections or kidney diseases need special attention.	1, A	6.4.1
46	It is recommended to adopt relevant statistical procedures when presenting verification data for urine particles.	1, B	6.4.2
47	Based on the verification, appropriate review rules need to be defined and implemented to support reliability of all results.	1, B	6.4.3

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Chapter 7. Recommendations for Bacteriology

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No	Recommendations	SoR (1-2), and LoE (A-D) [a]	Chapter discussed
48	Commensal urogenital microbiota are not recommended to be sought nor treated in asymptomatic individuals (Asymptomatic bacteriuria).	1, A	7.1.1 and 1.2
49	Low-risk patient groups with symptoms related to urinary tract infection are recommended to be screened for the presence of infection by using a validated questionnaire, to reduce routine workflow in bacteriology laboratory. Rapid tests for leukocytes and bacteria are recommended for emergencies in the diagnostics of unclear and other cases.	1, A	7.1.1 and 1.2
50	Urine specimens from most routine patients suspected for UTI are recommended to be sent to quantitative urine culture and possible antimicrobial susceptibility testing. Sensitive screening procedures are encouraged to reduce the number of specimens from the routine workflow. Diagnostic processes of specimens from high-risk patient groups are recommended to be organised as nationally or locally defined.	1, A	7.1.2 and 1.2
51	No control cultures are recommended from patients with lower UTI if becoming asymptomatic after an antimicrobial treatment.	1, A	7.1.3
52	Classification of uropathogens has been slightly updated. In addition to uropathogenicity, predisposing host conditions, quality of specimen collection, results from particle analysis (leukocytes and bacteria), and quantity and types of species grown in culture are recommended to be considered when assessing the diagnostic value of detected bacteriuria.	1, A	7.2.1
53	New species *Aerococcus* spp., *Actinotignum schaalii* and *Corynebacterium urealyticum* are proposed in the list of class II uropathogens.	2, B	7.2.2
54	Bacterial identification using Matrix-assisted laser desorption ionization time-of-flight mass spectrometry (MALDI-TOF MS) is strongly recommended for medium-sized and large laboratories (> 100 specimens/day), to improve patient prognosis with accuracy and reliability of identification to the species level, and shortened delay of reporting.	1, A	7.3.3
55	Limitations of the MALDI-TOF MS in detecting bacteriuria at low colony counts (less than 10^4 CFU/mL, or 10^7 CFB/L) must be understood in organising laboratory processes for urine specimens with a possibility of significant low bacteria counts. MALDI-TOF MS cannot be recommended for urine specimens in routine laboratories without a preculturing step.	1, A	7.3.3
56	Chromogenic agar is strongly recommended as primary agar medium to identify Escherichia coli (most frequent uropathogen) easily, quickly, and inexpensively (no need for a panel of tests to define the species). A second agar (such as blood agar) is recommended in clinically defined cases and for fastidious organisms.	1, B	7.4.1
57	Reproducible detection of low colony counts at 10^3 CFU/mL (10^6 CFB/L) requires an inoculum of at least 10 µL, adopting one of the recommended methods of inoculation.	1, A	7.4.2
58	Aerobic incubation at 35 ± 2 °C for 16-24 hours is sufficient for primary uropathogens. Agar plates from specimens of pyuria patients remaining negative after this incubation should be incubated for additional 24 hours under aerobic conditions. For special urine specimens, blood agar plates are recommended to be incubated under 5% CO_2 atmosphere for 48 hours in addition to aerobic conditions, to detect possible fastidious organisms.	1, A	7.4.2
59	A qualified reference examination (Level 3 procedure) is recommended to be used for bacterial cultures (1) to verify a required performance of routine bacterial culture (at Level 2), or (2) to assess any instruments in bacteriology intended to detect, quantify, or identify bacterial species for clinical diagnostics against the suggested performance specifications as needed.	1, A	7.4.4
60	No recommendation is given to the unit for reporting urine bacterial cultures. A national harmonisation is recommended to avoid confusion among professionals and patient risks.	Not given	7.5.1
61	A flowchart for routine urine specimens is recommended as a practical advice to bacteriology laboratories to organise their workflows, starting from mid-stream urine specimens. It is open for modifications based on specific specimens or patient populations, as well as local epidemiology of uropathogenic species in the laboratory.	1, B	7.5.2
62	Bacteria and yeast detected from urine specimens need to be identified to the species level to satisfy proper clinical diagnostics, and to be able to assess their antimicrobial susceptibility. Limitations of different identification methods are recommended to be considered to avoid deficient identifications or misclassifications.	1, A	7.6
63	This guideline recommends documents of the European Committee on Antimicrobial Susceptibility Testing (EUCAST) for procedures of antimicrobial susceptibility testing (AST), including reminders of limitations of each method. No rapid or direct AST can be recommended for routine workflow at the moment. The microbiology laboratories shall adhere to national antimicrobial stewardship in their AST reports.	1, A	7.7
64	The suggested practical procedures or tools for verification of routine bacterial examinations aim to help in the assessment of various changes in routine workflows. The level of satisfactory assessment in each case must be judged against relevant references, such as the ISO 15189 standard.	1, B	7.8

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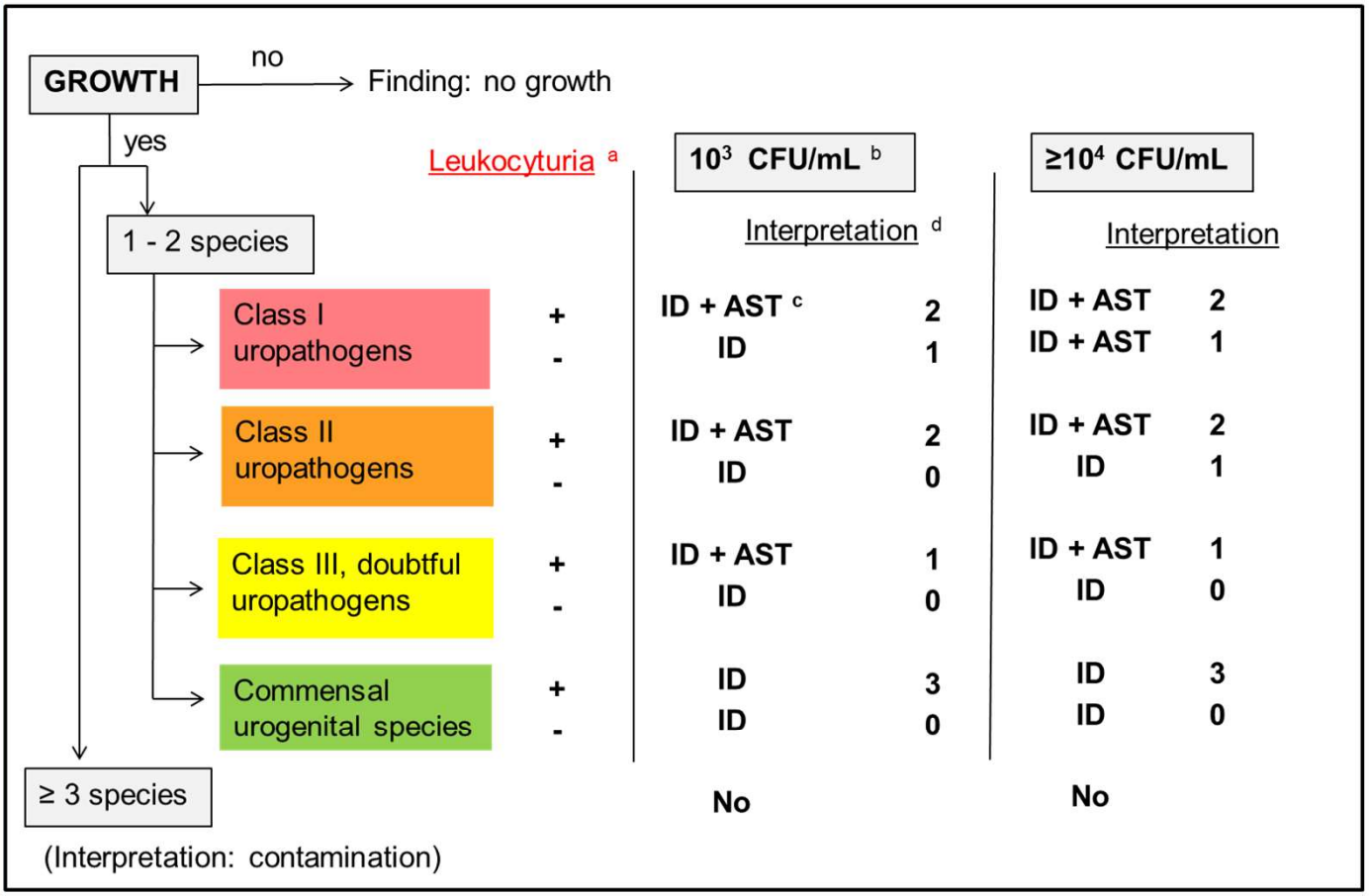
Figure 1

Workflow of primary cultures from routine urine specimens



[a] Presence of leukocyturia ≥ 30 WBC x10^6 /L, with a grey zone 10 – 30 WBC x10^6/L [Kouri T et al, CCA 2021].
[b] Recommendation to perform AST, antimicrobial susceptibility test and/or ID = identification to species level.
[c] Clinical interpretations 0-3 given as comments along with the report to the clinicians:

Interpretation:

0 = „ Urinary tract infection with cultivated microorganisms improbable, even with corresponding symptoms".
1 = „ If corresponding symptoms are present, urinary tract infection with cultivated microorganisms is possible".
2 = „ If corresponding symptoms are present, urinary tract infection with cultivated microorganisms is probable".
3 = „If corresponding symptoms are present, urinary tract infection with yet undetected microorganisms is likely, e.g. Chlamydia, Mycoplasma, Ureaplasma, *M. tuberculosis*, *N. gonorrhoeae*, etc.".

ID = Identification to species level AST = antimicrobial susceptibility test, CFU = colony-forming units