Pre- and Post-analytical Aspects in Medical Microbiology Diagnostics: Diagnostic Stewardship and Role of EQA

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Disclosure

De spreker heeft

- Geen financiële banden met de IVD industrie
- Geen sponsoring door belanghebbende industrie
- Geen honoraria van belanghebbende industrie
- Geen aandeelhouder van belanghebbende industrie
- Geen andere relaties met belanghebbende industrie die gezien kunnen worden als belangenverstrengeling

Outline

- A short introduction to clinical microbiology lab and procedures ≈ laboratory medicine
- Pre- and post-analytical phase in medical microbiology
- What we do as EQA (SKML)
- What can we do more?

CLINICAL MICROBIOLOGY

Intro to Clinical Microbiology: subspecialties

- Bacteriology (including tuberculosis)
  - Mainly culture (also microscopy (Gram stain), serology and molecular)
- Virology
  - Mainly serology and molecular
- Mycology
  - Mainly culture with microscopy, also molecular and serology
- Parasitology
  - Mainly microscopy, some serology

Intro to Clinical Microbiology: why testing?

- To in- or exclude infection
- To guide antimicrobial therapy
- (Epidemiological purposes)
- (Prevention purposes)

Participoll (1)

How important is clinical data for EQA for clinical microbiology on which test to be performed :

- A: Totally not important
- B: May be important
- C: I don’t know – I don’t care
- D: Very important

Clinical Microbiology ≈ Laboratory Medicine (1)

- Mostly departing from clinical suspicion of infection

- Samples
  - Mostly ‘simple’ but can be ‘precious’
  - All ‘types’, all organs

- Personnel
  - Medical technologists
  - Clinical microbiologists: (in the Netherlands) medical doctor

Clinical Microbiology ≈ Laboratory Medicine (2)

- Type of tests
  - Mainly culture (bacteriology)
  - But also molecular diagnostic and serology
  - Large part of work: antimicrobial susceptibility tests

- Type of instruments
  - In general less automated

Clinical Microbiology ≈ Laboratory Medicine (3)

- Mainly need clinical questions
- Additional tests based on clinical information (close contact with clinicians)
- May be subjective regarding testing and reporting
  - Quantification vs. semi-qualitative
    - 10 CFU/ ml sonication fluid?
  - Presence of microorganism: not necessarily infection

Clinical Microbiology ≈ Laboratory Medicine (4)

Werkblad (Alt+R)

	14-04-2022	15-04-2022	16-04-2022	19-04-2022	20-04-2022	2
	BA	NV	COFL1			
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			MIDV Pseudomona..			

Arts: Hoek, RAS (AGB:03022994)

Materiaal	**Sputum**	**Afname:** 13-04-2022, 08:00
		Ontvangst: 14-04-2022
Onderzoek	**Aerobe kweek inclusief B. cepacia**	**Status: Voorlopige uitslag**
Labnr	20220735675102	Aanvraag: 14-04-2022
		Autorisatie: 21-04-2022

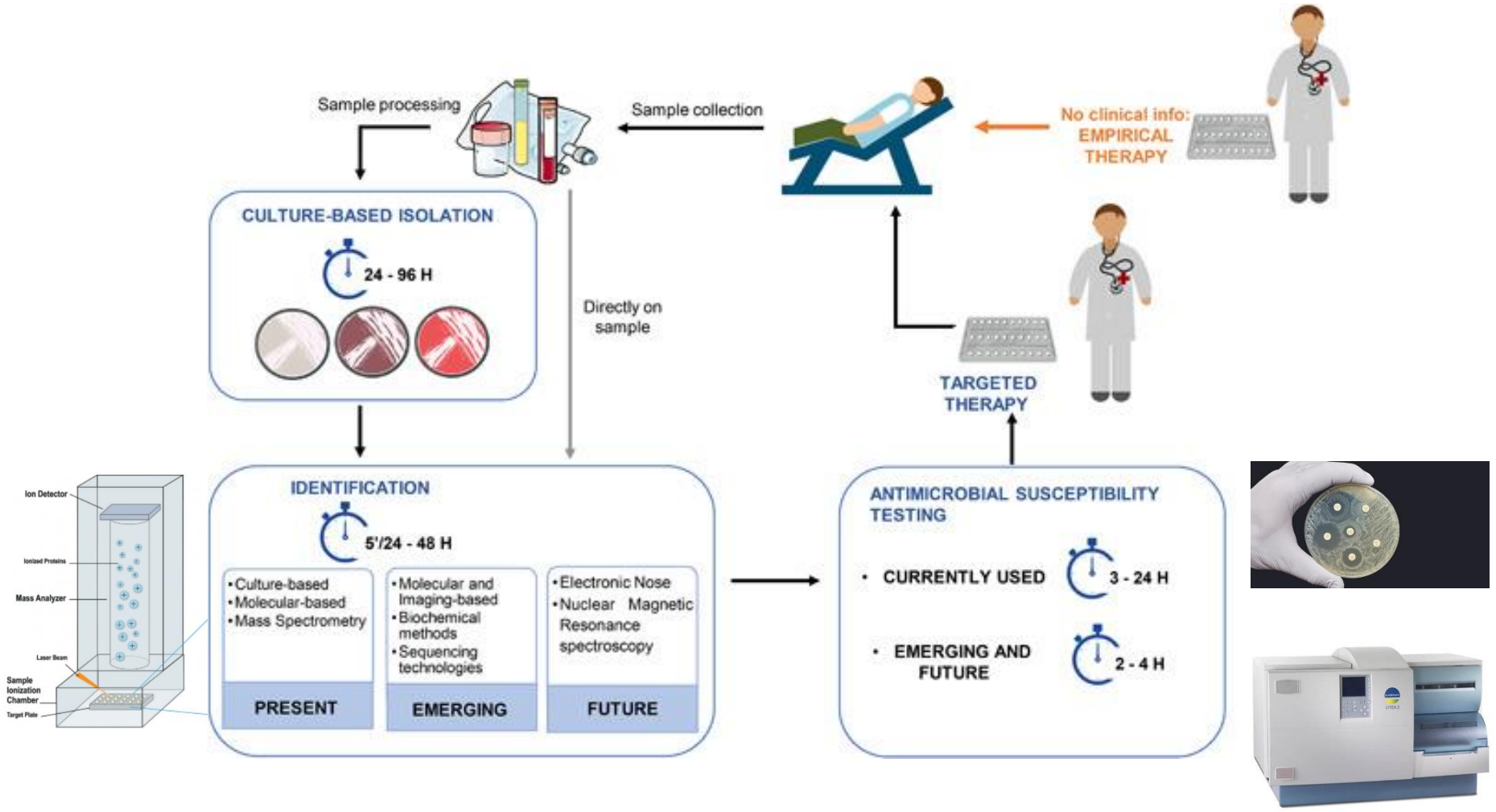
Interne opmerkingen		
27-04 13:07	*041191*	*mdcol invalid> opnieuw. (12)*
28-04 16:01	*043658*	*R-ino MDCOL lijkt niet rein. inderdaad herhalen volgende week (31)*

Resultaten

Commensale flora groei 1
Geen Burkholderia cepacia complex gekweekt
Micro-organisme 1 Haemophilus influenzae
groei 2
Micro-organisme 2 Pseudomonas libanensis (P. fluorescens groep)
groei 1
Dit betreft een voorlopig en/of onvolledig antibiogram, het definitieve antibiogram volgt.

Gevoeligheid:	**Micro-organisme 1 Haemophilus influenzae**	**Micro-organisme 2 Pseudomonas libanensis (P. fluorescens groep)**
amoxicilline	S	

Bacteriology workflow



Maugeri, et al. Biotech Journal. 2019, with modification

PRE-ANALYTICAL PHASE

Participoll (2)

Which of the following pre-analytical aspects are important to be considered in taking blood culture?

- A: Time of the day (Circadian rythym)
- B: Presence of fever
- C: Withdraw blood from arterial line
- D: Withdraw blood from central venous catheter

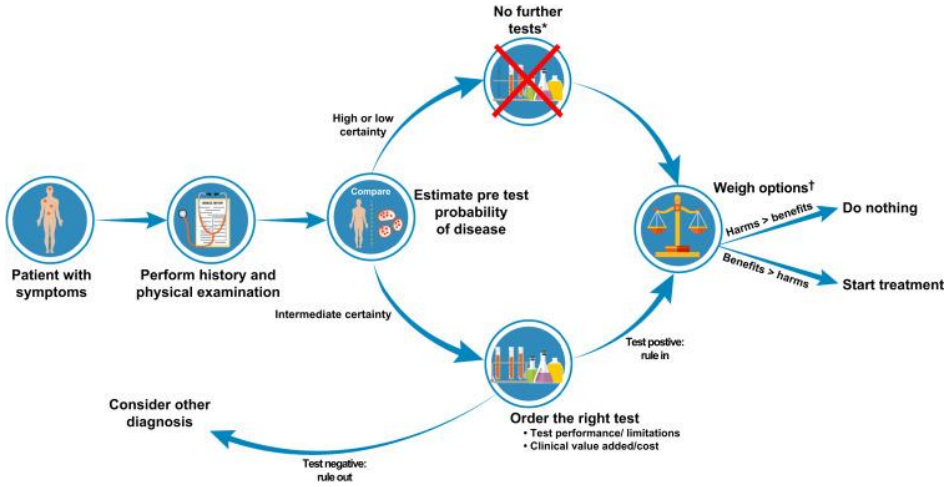
Pre-analytical phase: ordering

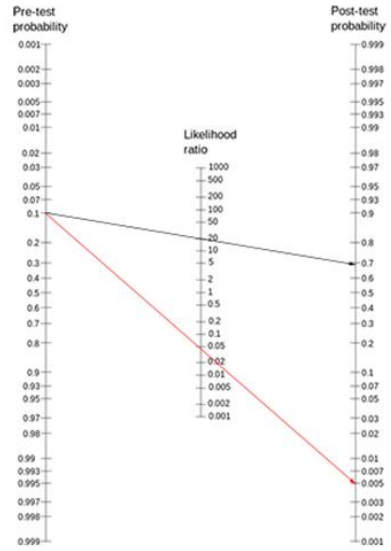
- Diagnostic stewardship
  - Best for patient, doctor
  - Best for environment

The Unintended Contribution of Clinical Microbiology Laboratories to Climate Change and Mitigation Strategies: A Combination of Descriptive Study, Short Survey, Literature Review and Opinion

Erlangga Yusuf • Ad Luijendijk • Geesje Roo-Brand • Alexander W. Friedrich

- Bayesian





Pre-analytical phase: patient preparation

- Vs. clinical chemistry
  - No circadian rhythm
  - (No) influence of diet
- Refrain from antibiotics use when possible
- Importance of specimens collection
  - Contaminants
  - False negative
  - Rubbish in rubbish out → incorrect therapy

Pre-analytical phase: specimen collection

- Right method (e.g. mid-stream or first urine portion, not from arterial blood)
- Proper source (e.g. CSF in bacterial brain abscess)
- Proper time (e.g. endocarditis)
- Proper volume (e.g. blood culture)

Pre-analytical phase: transport

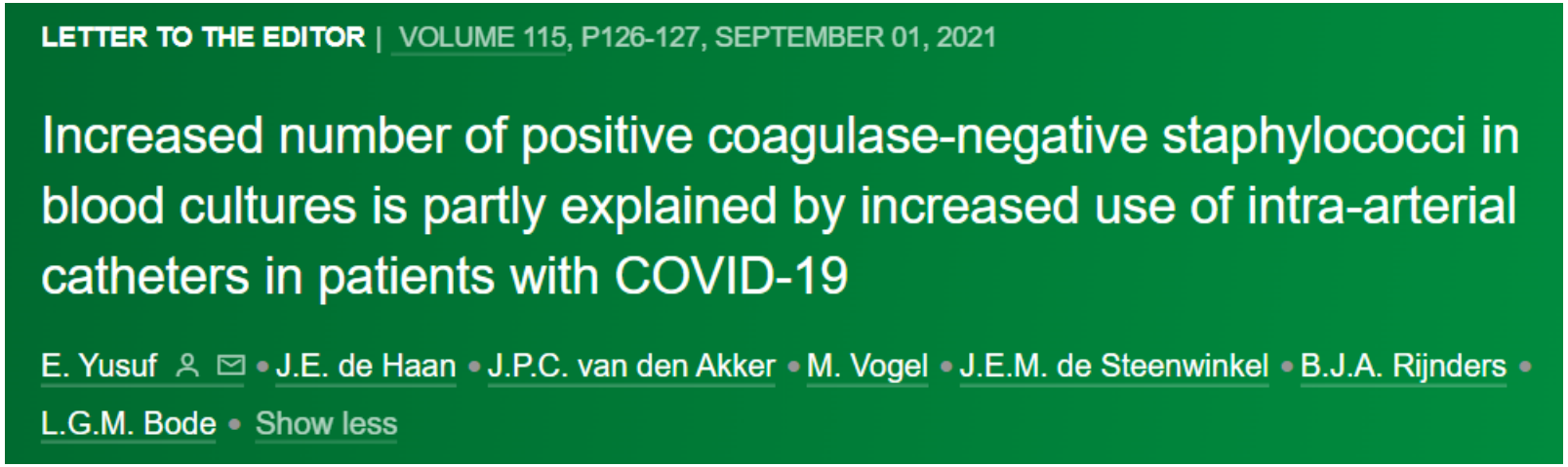
- Transport:
  - Proper container
  - Proper transport (e.g. swabs in UTM or VTM)

- Correct agar plates
  - Suited to clinical question
  - i.e. choc agar for *Haemophilus influenza* or *Neisseria gonorrhea*

Pre-analytical: what can go wrong (1)

- Ordering: wrong test

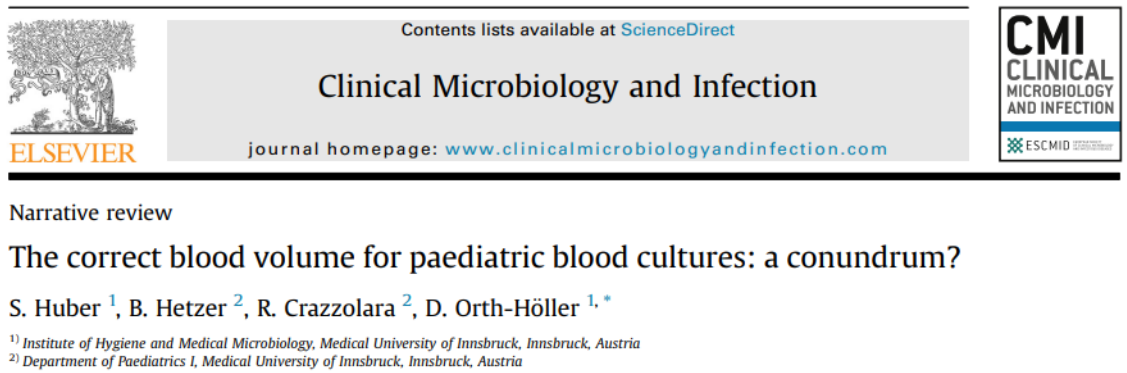
- Patient preparation:
  - Antibiotic use
  - Improper antiseptic
  - Inappropriate source



Pre-analytical: what can go wrong (2)

- Transport
  - Contamination (e.g. passing pathology department)
  - No conservative for urine
  - Dry swabs

- Specimen collection
  - Experience (nurses, interns, residents)
  - ‘Complicated’ samples (e.g. biopsies)



Contents lists available at ScienceDirect

Clinical Microbiology and Infection

journal homepage: www.clinicalmicrobiologyandinfection.com

Narrative review

The correct blood volume for paediatric blood cultures: a conundrum?

S. Huber [1], B. Hetzer [2], R. Crazzolara [2], D. Orth-Höller [1,*]

[1] Institute of Hygiene and Medical Microbiology, Medical University of Innsbruck, Innsbruck, Austria
[2] Department of Paediatrics I, Medical University of Innsbruck, Innsbruck, Austria

POST-ANALYTICAL

Post-analytical (1)

- Evaluation of test results
  - Contamination?
  - Make sense?
  - Never heard before microorganism
  - Interpretation of antibiogram correctly?

- Release of test results
  - Timeliness

Post-analytical (1): antibiogram and resistance

Materiaal	Wondvocht	Afr
5838324487	oppervlakkig	
Onderzoek	**Aerobe banale kweek**	**Status**
Labnr	20220743792101	

Resultaten

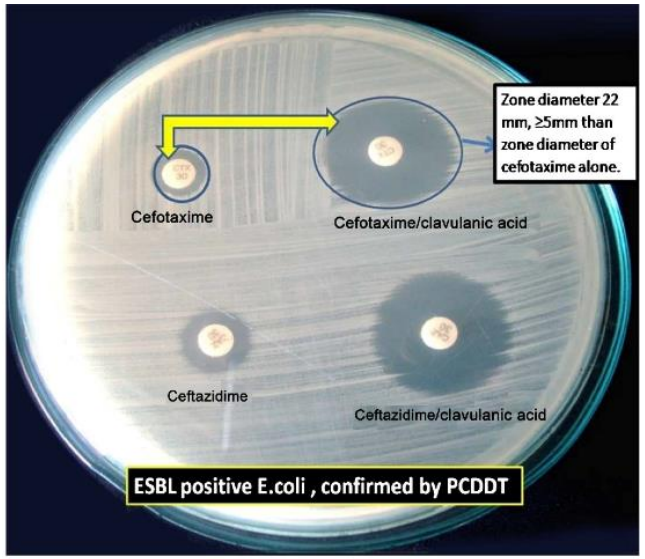
Afnamelocatie materiaal ontbreekt; hierdoor zijn microbiologische en klinische interpretatie van dit onderzoek niet optimaal.

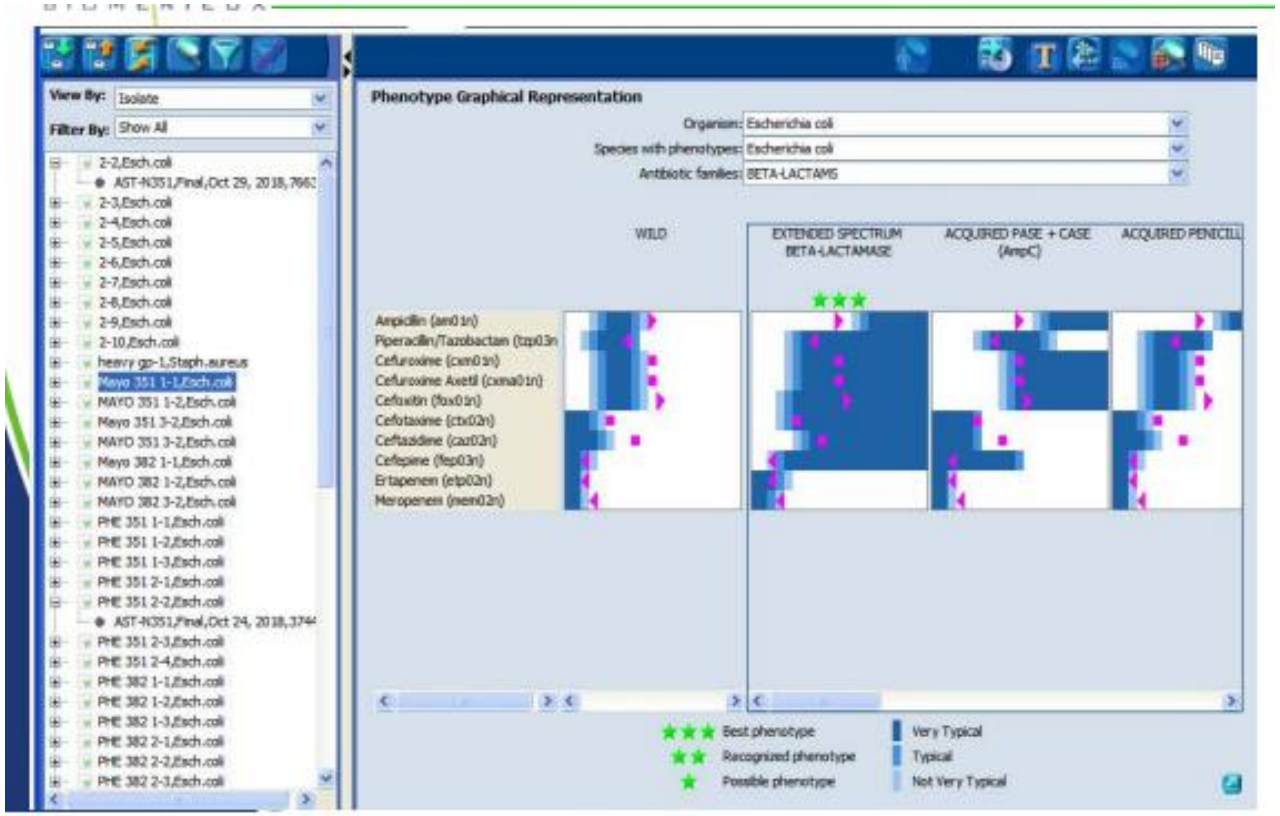
Micro-organisme 1 **Escherichia coli**
groei 2

Micro-organisme 2 **Staphylococcus aureus**
groei 1

Gevoeligheid:	Micro-organisme 1 Escherichia coli				Micro-organisme 2 Staphylococcus aureus			
				MIC				MIC
flucloxacilline					S			
amoxicilline		R	>	16				
augmentin		R	>	16				
piptazobactam		S	≤	4				
imipenem	#	S	≤	0,25				
meropenem	#	S	≤	0,25				
cefuroxim		S		4	S			
cefotaxim		S	≤	0,25				
cefoxitin	#	S	≤	4				
ceftazidime	#	S	≤	0,12				
gentamicine		S	≤	1	S	≤	0,5	
tobramycine	#	S	≤	1				

Post-analytical (2): expert system





SKML

What SKML sent as EQA

- Short clinical case

- Asking for
  - Presence of pathogen bacteria
  - Identification of the bacteria
  - Antimicrobial susceptibility test results

- Spiked material

What SKML sent as EQA

- Not merely presence or absence of microorganism, but integrated with clinical data

- Including thus:
  - Differential diagnosis
  - Adequate lab procedure
  - Correct identification (species, genus)
    - Sometimes species level does matter
  - Correct AST
    - Sometimes intrinsic resistance

Examples

Monster	**A**
Materiaal	Wonduitstrijk (diep)
Gegevens	Man van 67-jaar die 6 weken geleden sternotomie heeft ondergaan ivm. Coronary Artery Bypass Grafting (CABG).
Vraagstelling	Pathogene bacteriën? Indien in Qbase voor de gekweekte pathogene bacteriën een gevoeligheid wordt gevraagd, deze testen volgens EUCAST. (Extra vraag: is de isolaat mucoid?) BA, CHOC, MCC, BBA

Monster	**B**
Materiaal	Faeces
Gegevens	45-j vrouw met klachten van chronische diarree. Verschillende PCR op banale verwekkers van diarree in de afgelopen 6 maanden waren negatief.
Vraagstelling	Pathogene bacteriën? Indien in Qbase voor de gekweekte pathogene bacteriën een gevoeligheid wordt gevraagd, deze testen volgens EUCAST. YERK ~~VOLGT PCR, CLOT~~

Examples (1)

Monster B	Meting	Rapportage	Metho
Amikacine			
Amoxicilline			
Ampicilline			
Augmentin			
Azithromycine			
Cefepime			
Cefotaxim			
Cefoxitin			
Cefoxitin screen			
Ceftazidim			
Cefuroxim			
Ceftriaxone			
Ciprofloxacine			
Clarithromycine			
Clindamycine			
Colistine			
Co-trimoxazol			
Doxycycline			
Erythromycine			
Flucloxacilline			
Fusidinezuur			
Gentamicine			
Imipenem			
Levofloxacine			
Meropenem			
Metronidazol			
Nitrofurantoine			
Nofloxacine			
Oxacilline			
Penicilline			
Piperacilline			
Piperacilline/tazobactam			
Rifampicine			
Teicoplanine			
Tetracycline			
Tobramycine			
Vancomycin			

Resistentie mechanisme	Resultaat (ja/nee/nvt/niet interpeteerbaar)
CRE	
ESBL	
Plasmidaal AmpC	
MLSB induceerbaar	
MRSA	
HLGR	
VRE	

SKML EQA, what we test

- Mainly analytical
  - Normally not a problem → most labs using the same instruments
- Pre- analytical
  - Somehow limited: ordering wrong test
  - Not: patient preparation, specimen collection, transport
- Post-analytical
  - Various labprotocols regarding identification
  - Not for expert rules regarding antibiogram

Should we improve our EQA?

- Probably yes

- But still, not all pre-analytical aspects can be tested
  - We can’t sent specimens

- Post-analytical aspects
  - Open for discussion
  - No ‘ golden standard ‘ of lab protocols regarding antimicrobial susceptibility test

Quality in daily practice (1)

- Close contact with clinicians
  - Diagnostic stewardship and pre-analysis
  - Antimicrobial therapy
- Antimicrobial treatment guidelines
- Teaching and training
- Possibility of repetitive culture → patients who are not responding
- In the lab
  - Technical authorization (double)
  - Medical authorization

Quality in daily practice (2)

- Teaching and training
- Possibility of repetitive culture → patients who are not responding
- In the lab
  - Technical authorization (double)
  - Medical authorization

Conclusion and discussion

- Clinical microbiology: part of clinical thinking
- SKML assesses some of these aspects, but not all
- Any idea to improve is welcome

Idea? Questions? Remarks?

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Thanks to

- Clinical Microbiologist Section Bacteriology
  - Claudy Olivera dos Santos
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  - Jakko van Ingen
  - Lieke Reubsaet
  - Maarten Schijffelen
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