Epidemiologie und mikrobiologische Diagnostik der Sepsis

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Institut für Medizinische Mikrobiologie, Universitätsklinikum Münster

Bad Honnef-Symposium

Empfehlungen zur kalkulierten Initialtherapie bakterieller Erkrankungen bei Erwachsenen

Bonn, 21.-22. März 2016

Block C

„Et bliev nix wie et wor“

Sepsis; Definition Version „X“

„Et bliev nix wie et wor“

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Sepsis is not a specific illness but rather a syndrome encompassing a still-uncertain pathobiology.

- Word count: 9506
- Occurrence of the term:
  „**pathogen**“ or similar: n = 3 (=0,03%)
  „**infection**“: n = 65 (=0,68%)

- **BK-Diagnostik zu langsam für primäre Sepsis-Therapie**
- **nur in max. 30-40% der Sepsisfälle Erregernachweis**

Box 2. Key Concepts of Sepsis

- Sepsis is the primary cause of death from infection, especially if not recognized and treated promptly. Its recognition mandates urgent attention.
- Sepsis is a syndrome shaped by pathogen factors and host factors (eg, sex, race and other genetic determinants, age, comorbidities, environment) with characteristics that evolve over time. What differentiates sepsis from infection is an aberrant or dysregulated host response and the presence of organ dysfunction.
- Sepsis-induced organ dysfunction may be occult; therefore, its presence should be considered in any patient presenting with infection. Conversely, unrecognized infection may be the cause of new-onset organ dysfunction. Any unexplained organ dysfunction should thus raise the possibility of underlying infection.
- The clinical and biological phenotype of sepsis can be modified by preexisting acute illness, long-standing comorbidities, medication, and interventions.
- Specific infections may result in local organ dysfunction without generating a dysregulated systemic host response.

Epidemiologie

Estimated population prevalence of sepsis and severe sepsis in Germany ("pre-DRG era")

Prospective, observational, cross-sectional 1-day point-prevalence study in 2003 (454 ICUs from a representative nationwide sample of 310 hospitals)

(including septic shock)

Characteristic 3,877 patients included	Sepsis %	95% CI	Severe sepsis %	95% CI
Overall	12.4	10.9–13.8	11.0	9.7–12.2
Stratum				
1 (non-university, ≤ 200 beds)	9.8	7.2–12.5	6.0	3.9–8.1
2 (non-university, 201–400 beds)	11.5	9.1–13.8	9.5	7.3–11.6
3 (non-university, 401–600 beds)	15.5	11.7–19.2	9.0	6.0–12.0
4 (non-university, > 600 beds)	14.5	10.2–18.8	15.3	11.4–19.2
5 (university)	10.5	3.9–17.2	19.3	13.1–25.4
Gender				
Male	11.5	9.5–13.5	11.9	10.1–13.6
Female	13.5	11.5–15.6	9.7	8.3–11.1
Age (years)				
< 50	12.0	9.0–15.0	11.2	8.4–14.0
50–65	12.4	9.7–15.0	12.2	9.6–14.8
> 65	12.6	10.7–14.4	10.4	8.9–11.9

Number of newly diagnosed cases of

- **Sepsis**: approx. 79,000/a = 116/100,000 inhabitants
- **Severe sepsis**: 75,000 /a = 110/100,000 inhabitants

approx. 154,000 cases of sepsis/a in Germany

Engel et al., Intensive Care Med (2007) 33:606–618 **SEPNET**

Hospital mortality of patients with severe sepsis in Germany

Characteristic	Hospital mortality[a] Percentage	95% CI
Overall	55.2	50.2–60.2
Stratum		
1 (non-university, ≤ 200 beds)[c]	48.8	34.6–63.3
2 (non-university, 201–400 beds)	52.0	42.3–61.7
3 (non-university, 401–600 beds)	46.8	33.0–60.8
4 (non-university, > 600 beds)	60.6	50.8–69.7
5 (university)	60.0	50.0–69.3
Gender		
Male[c]	56.5	49.9–62.8
Female	53.8	46.0–61.5
Age (years; tertiles)[d]		
18–59	46.0	37.5–54.7
60–72	60.8	52.2–68.7
≥ 73	58.6	49.9–66.8
Septic shock		
No[c]	47.3	40.3–54.5
Yes	62.4	55.2–69.2

Engel et al.,
Intensive Care Med
(2007) 33:606–618

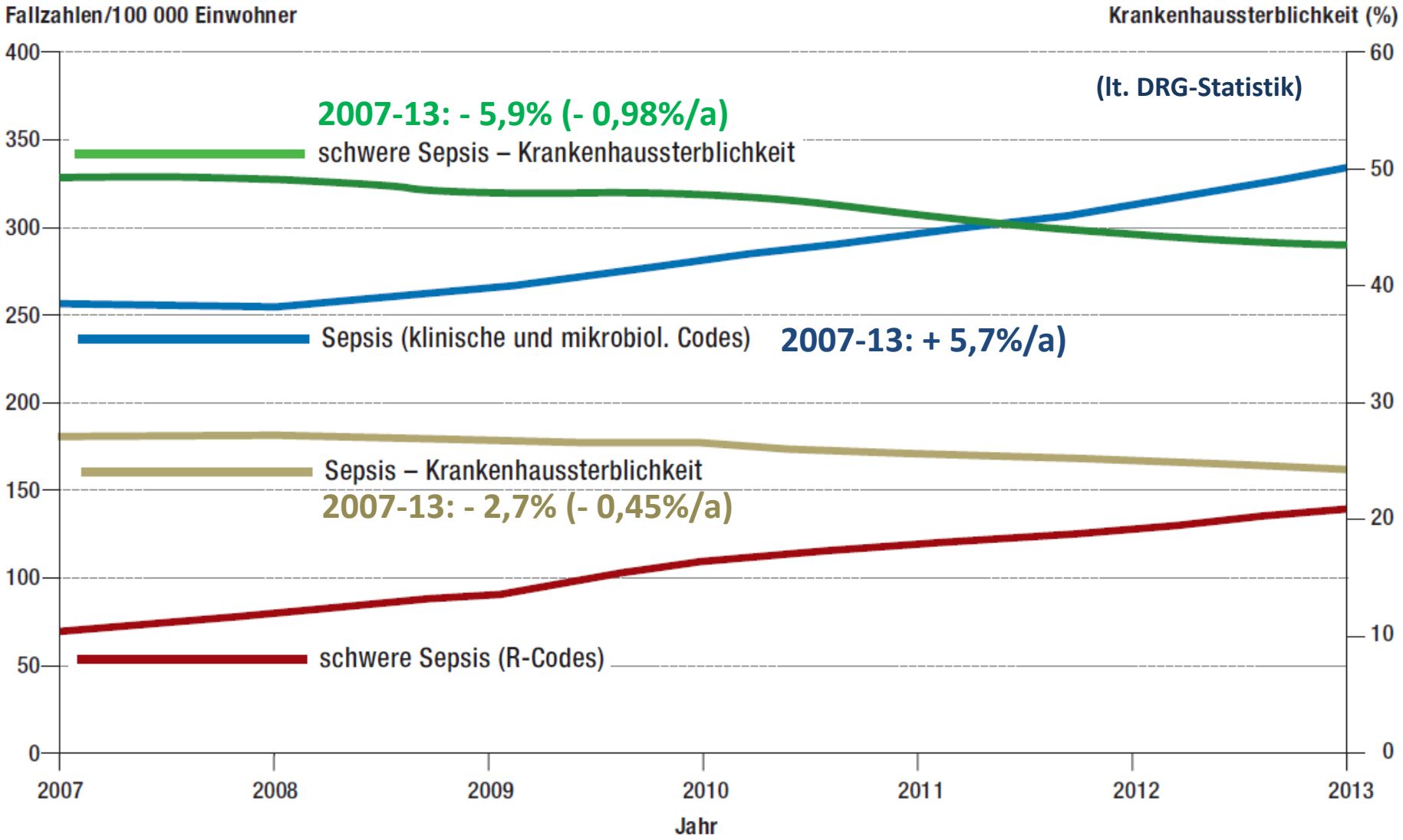
SEPNET

Fallzahlen, Sterbefälle, Häufigkeits- und Sterblichkeitsraten der Sepsis in Deutschland, 2013 (lt. DRG-Statistik)

	Sepsis inkl. schwere Sepsis u. septischer Schock	**schwere Sepsis** inkl. septischer Schock (R65.1!, R57.2) (% Sepsis, gesamt)	**septischer Schock** (R57.2) (% Sepsis, gesamt)
Fälle	**279.530**	**115.421 (41,3%)**	**33.815 (12,1%)**
Todesfälle	**67.849**	**50.349 (74,2%)**	**19.891 (29,3%)**
adjustierte Rate/ 100 000 Einwohner	**335**	**138**	**40**
Krankenhaus-sterblichkeit (%)	**24,3**	**43,6**	**58,8**

Fleischmann et al., Deutsches Ärzteblatt 2016 | Jg. 113 | Heft 10

Häufigkeitsrate pro 100 000 Einwohner standardisiert auf die Bevölkerungsstruktur 2010 und Krankenhausletalität von Sepsis und schwerer Sepsis (inklusive septischem Schock) in Deutschland, 2007–2013

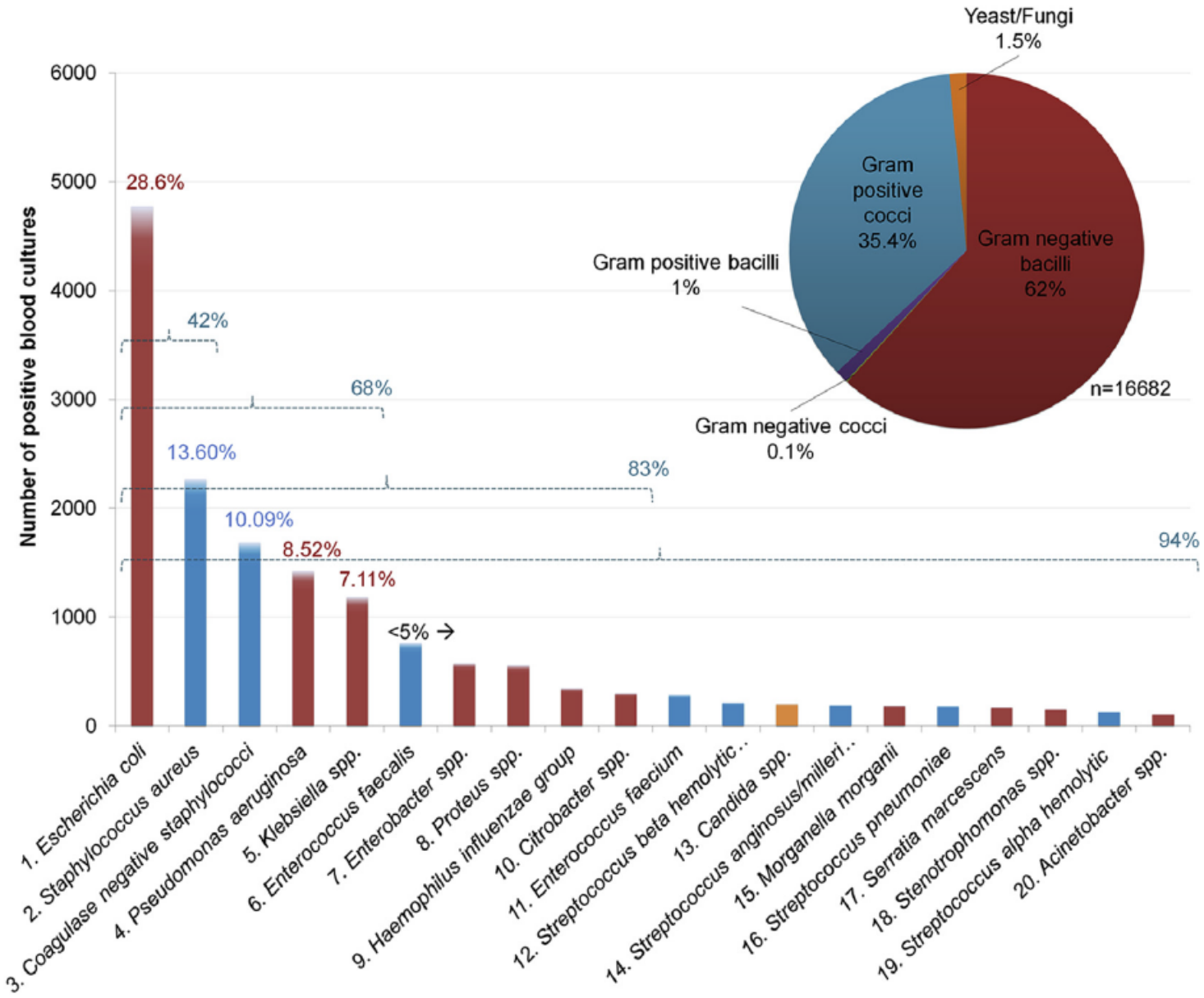


1,21% ⇦ Sepsisfälle/Krankenhausfälle ⇨ 1,54%

nach Fleischmann et al., Deutsches Ärzteblatt 2016 | Jg. 113 | Heft 10

Causative pathogens of BSIs

Opota et al., CMI 2015



Top 20 microbes identified from positive blood cultures during 1 year.

Data from our 1000-bed tertiary-care university hospital (Lausanne, Switzerland) during the year 2013 (16 682 identifications).

Das Problem

The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3)

JAMA. 2016;315(8):801-810. doi:10.1001/jama.2016.0287

Identified Challenges and Opportunities

Assessing the Validity of Definitions When There Is No Gold Standard

Sepsis is not a specific illness but rather a syndrome encompassing a still-uncertain pathobiology. At present, it can be identified by a constellation of clinical signs and symptoms in a patient with suspected infection. Because no gold standard diagnostic test exists, the task force sought definitions and supporting clinical criteria that were clear and fulfilled multiple domains of usefulness and validity.

110 Jahre Blutkulturdiagnostik

Emanuel Libman
(1872-1946)

→ Studie mit >700 Blutkulturen (1906)

→ erste Richtlinie zur Blutkulturdiagnostik

of Ratisbon; Marshal Macdonald, who won Wagram, and was made a Marshal on the field of battle, a man who was a gallant and loyal gentleman all his days: Marshal Suchet, who had been a junior officer in Napoleon's company, when the latter was a captain; Marshal Davout, the hero of Auerstadt; General Junot, whose wife Napoleon wished to marry, when she was a young girl—Junot, reckless to gallantry, who resembled Mad Anthony Wayne of our Revolutionary struggle; and General Foy, who was sent to Turkey to fight the Russians and the English, and was wounded fifteen times in his various arduous campaigns. It seems a pity that Larrey's old friend and patient, Lannes, is not near him. This celebrated Marshal's body lies in the Cemetery of Montmartre.

Those of us that go to Paris and look at the tomb of Baron Larrey can feel with justice that there is buried a soldier, a patriot; a great, learned, and brilliant surgeon; a brave, truthful, and loyal man; a gentleman; and a benefactor of the human race.

ON SOME EXPERIENCES WITH BLOOD-CULTURES IN THE STUDY OF BACTERIAL INFECTIONS.[1]

By E. Libman, M. D.,
Adjunct Visiting Physician and Assistant Pathologist
Mt. Sinai Hospital, New York.

When, a few months ago, you honored me by asking me to present something here, I was much concerned. I felt unequal to the task of addressing you, and I was at a loss as to the choice of my subject. After a few days' thought I decided that the subject which has been announced to you would be an advantageous one in a number of ways.

In the first place, I could combine the paper with a demon-

The organisms found were: streptococci, the pneumococcus, *Micrococcus aureus*, *Micrococcus citreus*, *Micrococcus albus*, *Bacillus pyocyaneus*, paracolon bacillus, *Bacillus coli*, *Bacillus proteus vulgaris* and the gonococcus.

blood of a child suffering from streptococcic intestinal infection (1), in the clinic of my friend and teacher, Professor Escherich, I have been much interested in systemic bacterial infections, and, during the past eight years I have attempted from time to time to study especially the general infections by the pyogenic cocci. The number of cases which we have studied by means of cultures is between 700 and 750. Not all are of value. Many were made at request in cases which proved to be examples of fever due to tuberculosis, or cases not bacterial in origin. Some were unsuccessful for one reason or another. I shall not attempt to cover the entire material—that would be impossible. Only certain points will be taken up and digressions will be made here and there so as to mention observations that are unusual or particularly interesting. The literature (2) will not be discussed as I prefer to speak at this time of our own experiences. The subject of infections by the typhoid bacillus will be omitted and only such pneumococcus infections as occurred independently of pneumonia will be included.

While the paper will not be a connected one,—the breadth of the subject prevents that—I shall take up the following main points:

8. Discussion of positive blood-cultures.
9. Diagnostic points.
10. The prognosis in cases in which bacteria have been found in the blood.

1. Terminology.

The terminology (3) that I shall use is one based on the work itself and will, I hope, be justified by the observations I shall record. When bacteria attack any part of the body we call the resultant lesion a local infection. There may or may not be evident toxemia; usually there is. If such a local infection is so situated that it is not diagnosed we can call the lesion a cryptic infection. If there is toxemia we have a cryptogenetic toxemia.

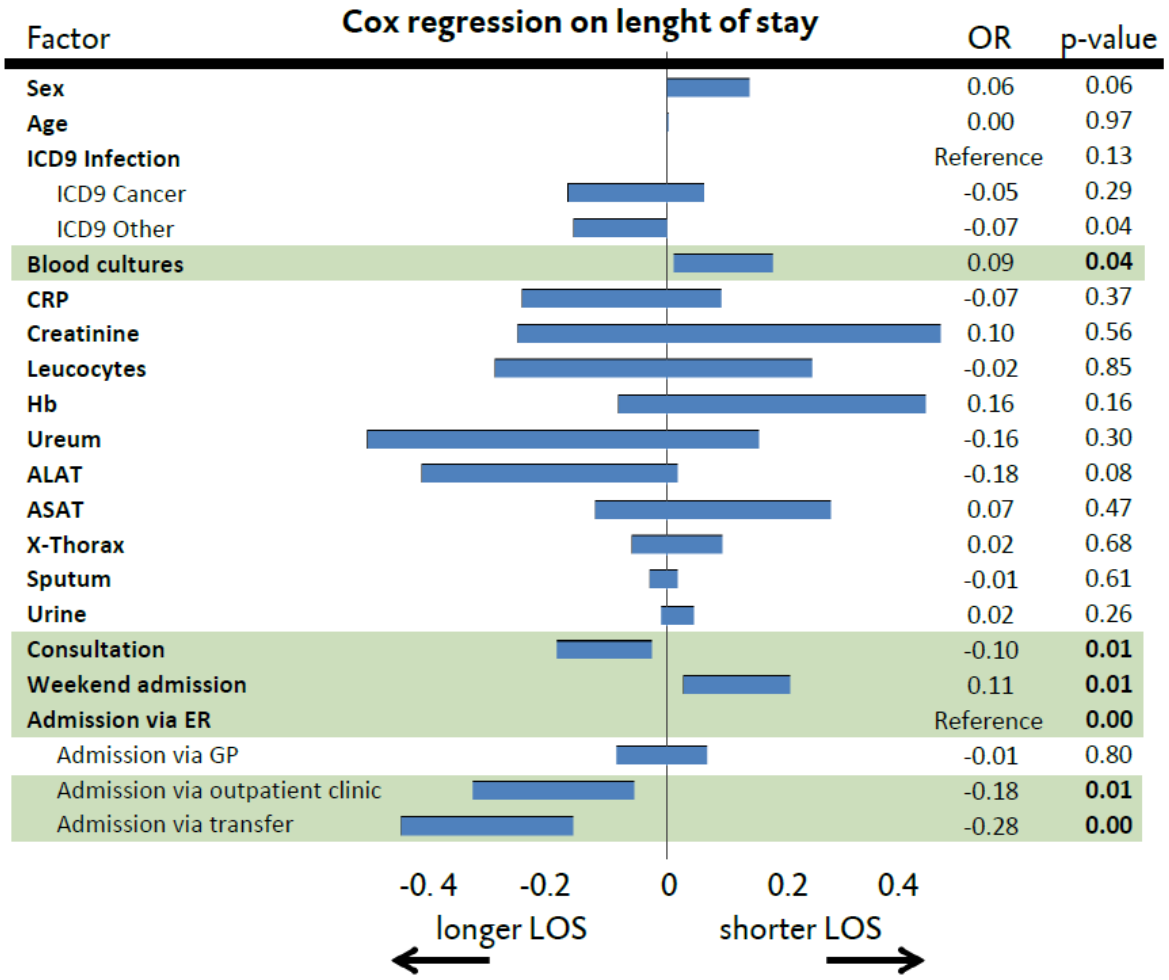
If bacteria are present in the blood we have a bacteriemia, or systemic infection. Such a bacteriemia may or may not be accompanied by the establishment of secondary foci (metas-

[1] Read before the Medical Society of the Johns Hopkins Hospital, February 5, 1906.

Effects of doing blood cultures

JH Dik[1], JR Lo Ten Foe[1], B Sinha[1], P Nannan Panday[2], R Hendrix[1,3], MJ Postma[4] & AW Friedrich[1]
[1]Department of Medical Microbiology, University Medical Center Groningen, [2]Clinical Pharmacy, University Medical Center Groningen, [3]Certe, Groningen, [4]Department of Epidemiology, University of Groningen

25th ECCMID EP052
Copenhagen, Denmark
25 – 28 April 2015
ESCMID



Performing blood cultures during admission for patients with a suspected infection was **correlated with**:

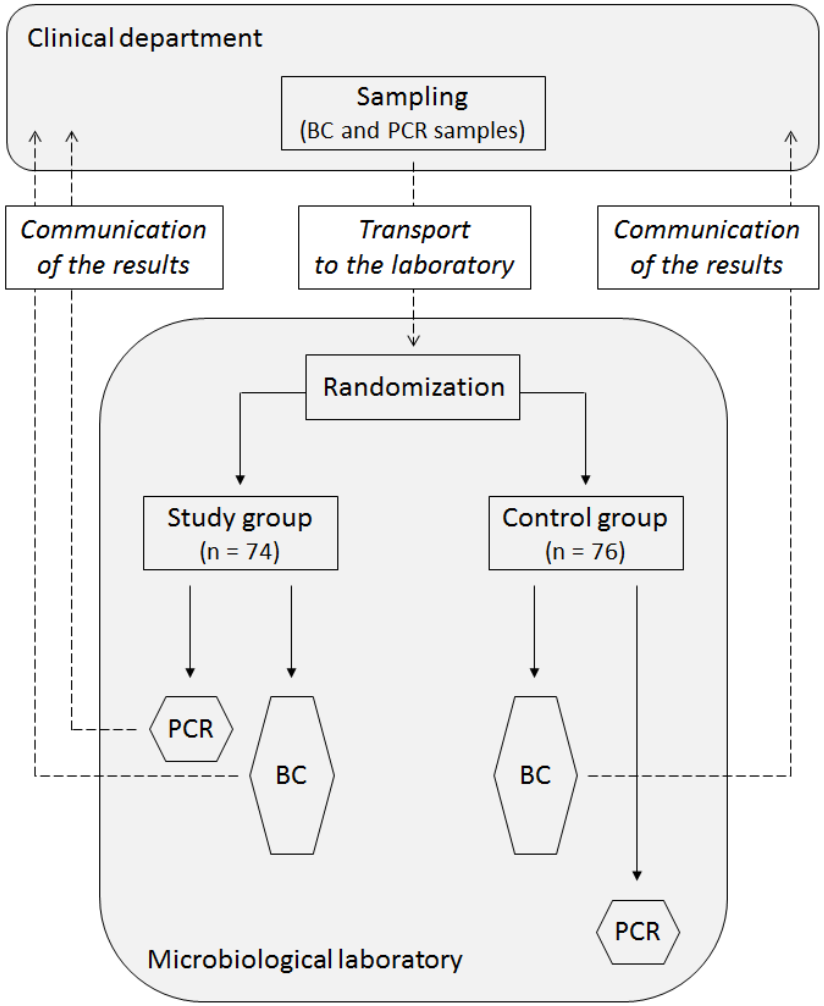
- **Significant shorter stay in the hospital** (16.85 days vs. 13.35 days; P<0.001)
- **Less total costs per patient** (€4,788); i.e. saving of €981,441/a for the University Hospital

Patients had to be started with broad spectrum antibiotics during admission with a minimum of 3 days.
Patients with (n=580) and without (n=205) blood cultures drawn at the day of admission.

Med Microbiol Immunol (2015) 204:585–592

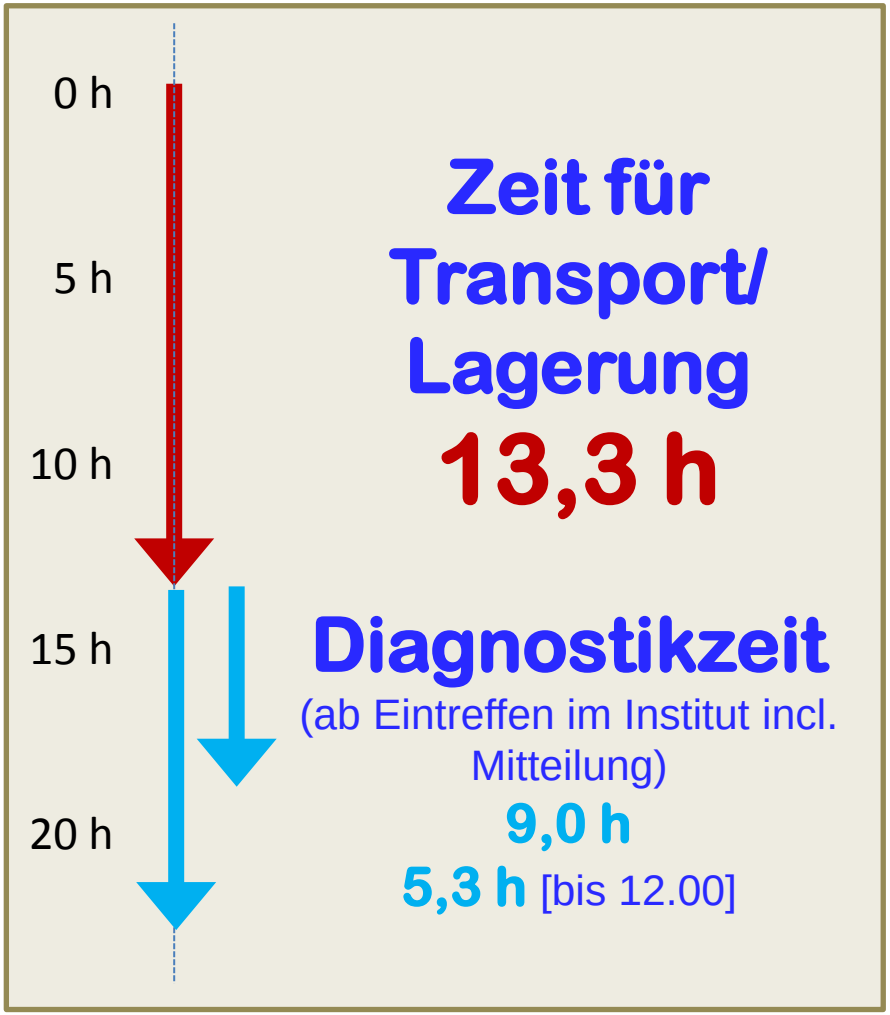
Impact of multiplex PCR on antimicrobial treatment in febrile neutropenia: a randomized controlled study

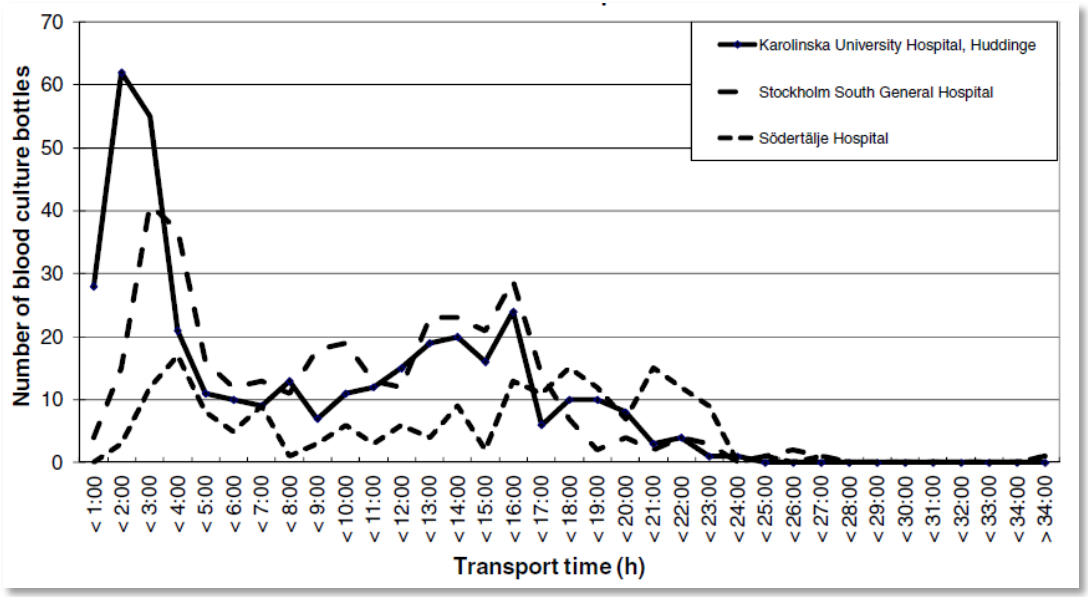
Evgeny A. Idelevich · Gerda Silling · Yvonne Niederbracht · Hanna Penner · Maria Cristina Sauerland · Sascha Tafelski · Irit Nachtigall · Wolfgang E. Berdel · Georg Peters · Karsten Becker · Molecular Diagnostics of Sepsis study group



Sepsis-„Schnell“diagnostik unter Routinebedingungen

(Mo-Fr 7.30 – 18.00)





Rönnberg et al., Diag. Microbiol. Infect. Dis. 76 (2013) 286–290

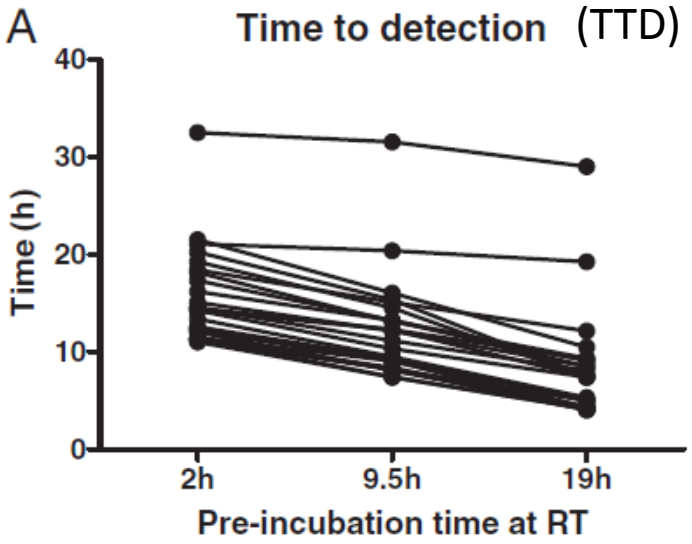
Distribution of transport time for individual blood culture samples

Median (IQR) laboratory transport time for 3 tertiary-care hospitals by time of sampling

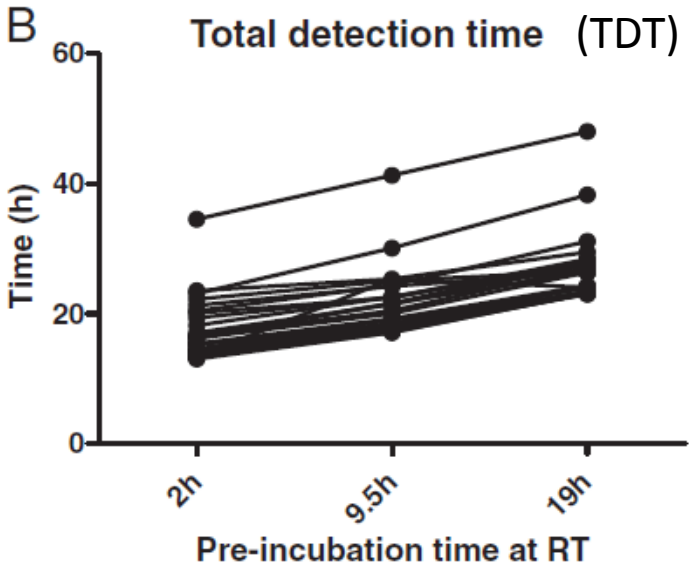
	Karolinska University Hospital, Huddinge		Stockholm South General Hospital		Södertälje Hospital	
	No. of samples	Median (IQR)	No. of samples	Median (IQR)	No. of samples	Median (IQR)
Weekdays	274	4 (2–13)	250	8 (3–13)	133	14 (4–18)
Weekends	102	10 (2–15)	98	11 (6–15)	52	17.5 (11–21)
8–16	161	2 (1–3)	117	3 (2–5)	90	18 (4–21)
16–24	154	13 (10–15)	159	13 (11–15)	70	16 (13–17)
24–8	61	6 (4–7)	72	6 (4–8)	25	7 (4–9)

IQR = interquartile range.

Rönnberg et al., Diag. Microbiol. Infect. Dis. 76 (2013) 286–290



Time difference between the time point at which the samples are **placed in the blood culture system** and the time point at which the blood culture bottle **signals for positivity**



Time difference between the **time point of sampling** and the time point at which the blood culture bottle **signals for positivity**. (Transport time + TTD)

- Unfortunately, the shorter TTD obtained with longer transport times **did not compensate** the time period outside the blood culture system
- **TDT** invariably **increased with longer transport time.**

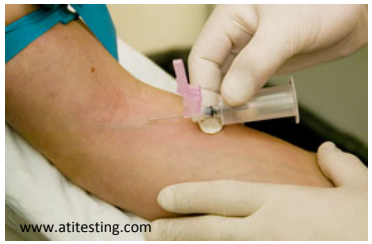
TTD (A) and TDT(B) of single bacterium in simulated blood culture bottle after three different pre-incubation periods.

RT: room temperature

Commercially available systems for the direct identification of microbes from positive BCs

System (Manufacturer)	Methods	Time to result	Microorganism coverage	Resistance and virulence markers	Sensitivity Specificity Correlation with conventional methods (%)
PNA FISH and QuickFISH (AdvanDx, Woburn, MA, USA)	FISH	<1–3 hours	4 Gram positive 4 Gram negative 5 Fungi	0	97–100 90–100 96–99
AccuProbe (Gen-Probe, San Diego, CA, USA)	FISH	<1 hour	*Staphylococcus aureus* *Enterococcus* spp. *Streptococcus pneumoniae* *Streptococcus* group A *Streptococcus* group B	0	80.8–100 98.7–100 nr
Verigene (Nanosphere, Northbrook, IL, USA)	Microarray	2.5 hours	12 Gram positive 9 Gram negative	*mecA*, *van*A/B, KPC, NDM, CTX-M,VIM, IMP,OXA12	81–100 98–100 nr
Prove-it Sepsis (Mobidiag, Esbo, Finland)	Microarray	3.5 hours	60 bacteria 13 fungi	*mecA*	95% 99% nr
FilmArray (Idaho Technology, Salt Lake City, UT, USA)	Multiplex PCR	1 hour	8 Gram positive 11 Gram negative 5 Fungi	*mecA*, *van*A/B, KPC	97–95 91–98 nr
Xpert MRSA/SA BC (Cepheid, Sunnyvale, CA, USA)	Real-time PCR	1 hour	*S. aureus*	*mecA*	100 99–100 nr
StaphSR assay (BD GeneOhm, San Diego, CA, USA)	Multiplex PCR	1–2 hours	*S. aureus*	*mecA*	96–100 95–98 nr
StaphPlex (Genaco Biomedical Products, Huntsville, AL, USA)	Multiplex PCR + Microarray	5 hours	*S. aureus*	*mecA* (+ PVL)	100 95–100 92
MALDI-TOF MS Brucker Daltonics (Bremen, Germany) bioMérieux (Marcy l'Etoile, France)	Mass-spectrometry	<1 hour	<1000[a]	not in routine	– – 76–99

Opota et al., CMI 2015



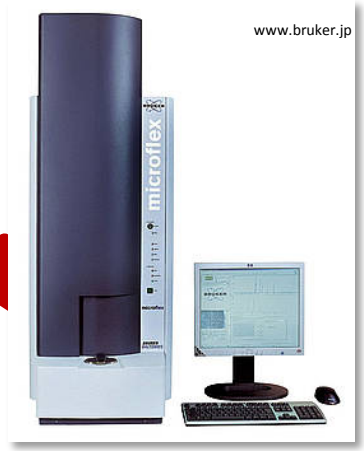
Semiautomated blood culture instrument (≥1 – 7 days)

Conventional cultivation on solid agar medium **(≥1 – 2 days)**

Biochemical procedures and susceptibility testing **(≥1 – 2 days)**

MALDI Sepsityper®

- **MALDI Biotyper®**
  For Direct Pathogen Identification from Positive Blood Culture Bottles



53.1 min
(mean time)

- 6.3 min for lysis-centrifugation
- 32.2 min for extraction and pellet drying
- 11.2 min for spotting
- 3.4 min for MALDI-TOF MS measurement

Applied method saved on average 23.5 h for yeast identification

Idelevich et al., PLOS ONE 2014

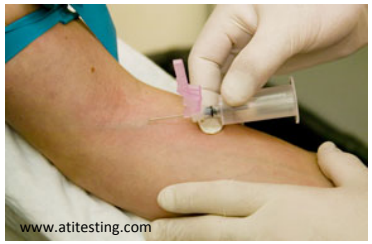
Evaluation of Three Rapid Diagnostic Methods for Direct Identification of Microorganisms in Positive Blood Cultures

Raquel M. Martinez,* Elizabeth R. Bauerle, Ferric C. Fang, Susan M. Butler-Wu

Journal of Clinical Microbiology p. 2521–2529
July 2014 Volume 52 Number 7

Definitive ID	No. of cultures	No. (%) of cultures correctly identified by: MALDI-TOF MS (%) Genus (>1.6)	MALDI-TOF MS (%) Species (>1.8)	*Quick*FISH (%)	BC-GP (%)
Staphylococci	58	57 (98.3)	51 (87.9)	57 (98.3)	58 (100)
Enterococci	16	16 (100)	16 (100)	16 (100)	16 (100)
Enterobacteriaceae	35	34 (97.1)	32 (91.4)	33 (94.3)	—
Non-*Enterobacteriaceae*	11	6 (54.5)	5 (45.5)	11 (100)	—
Yeast	5	3 (60)	3 (60)	5 (100)	—

- MALDI-TOF MS with Sepsityper (Bruker) processing
- *Quick*FISH (AdvanDx)
- Verigene Gram-Positive Blood Culture (BC-GP; Nanosphere)



Semiautomated blood culture instrument (≥1 – 7 days)

Conventional cultivation on solid agar medium **(≥1 – 2 days)**

~~Biochemical procedures and~~ susceptibility testing **(≥1 – 2 days)**

- **zusätzliche Kosten**
- **personalaufwendig**
- **schwierig in die Laborroutine integrierbar**

MALDI Sepsityper®

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  For Direct Pathogen Identification from Positive Blood Culture Bottles

53.1 min
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Applied method saved on average 23.5 h for yeast identification

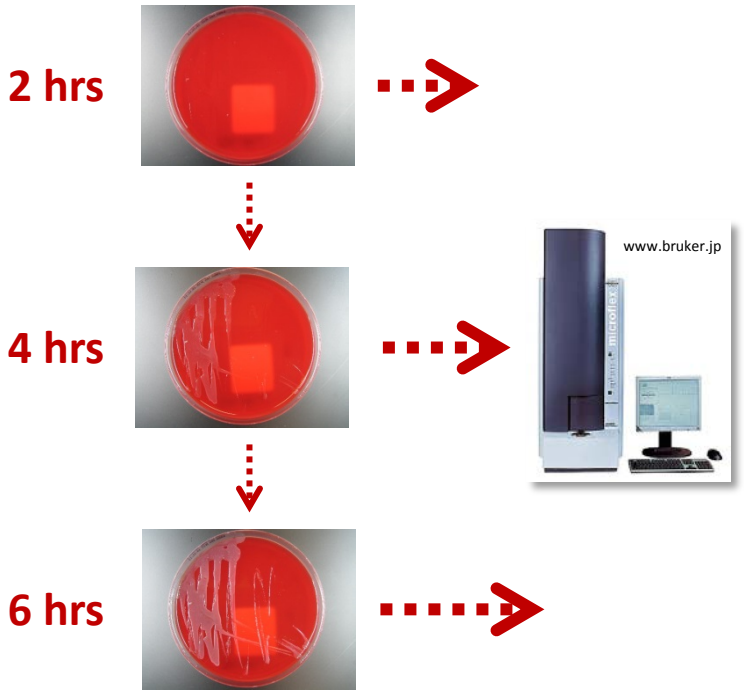
Idelevich et al., PLOS ONE 2014

Rapid identification of microorganisms from positive blood cultures by MALDI-TOF mass spectrometry subsequent to very short-term incubation on solid medium

E. A. Idelevich, I. Schüle, B. Grünastel, J. Wüllenweber, G. Peters and K. Becker

Institute of Medical Microbiology, University Hospital Münster, Münster, Germany

Clin Microbiol Infect 2014; **20**: 1001–1006



Cultivation times to successful identification:

	Species level (score ≥2) (%)	Genus level (score ≥1.7) (%)
Gram-positive aerobic cocci, *n* = 86		
≤2 h	1 (1.2)	5 (5.8)
≤4 h	16 (18.6)	42 (48.9)
≤6 h	55 (64.0)	77 (89.5)
≤8 h	83 (96.5)	84 (97.7)
≤12 h	85 (98.8)	85 (98.8)
24 h	86 (100)	86 (100)
Mean identification time, h	5.9	4.7
Gram-negative aerobic rods, *n* = 42		
≤2 h	32 (76.2)	37 (88.1)
≤4 h	40 (95.2)	41 (97.6)
≤6 h	41 (97.6)	41 (97.6)
≤8 h	41 (97.6)	41 (97.6)
≤12 h	41 (97.6)	41 (97.6)
24 h	41 (97.6)	41 (97.6)
Mean identification time, h	2.0	1.7

- **Very early and reliable identification from positive BCs**
- **Without additional time and cost expenditure**

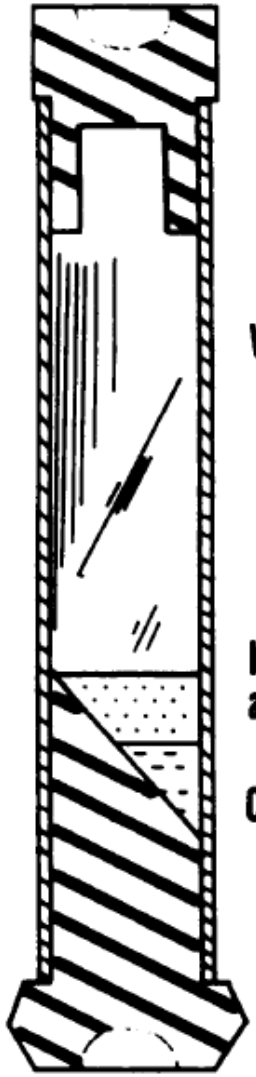
0095-1137/78/0007-0052$02.00/0
JOURNAL OF CLINICAL MICROBIOLOGY, Jan. 1978, p. 52–54

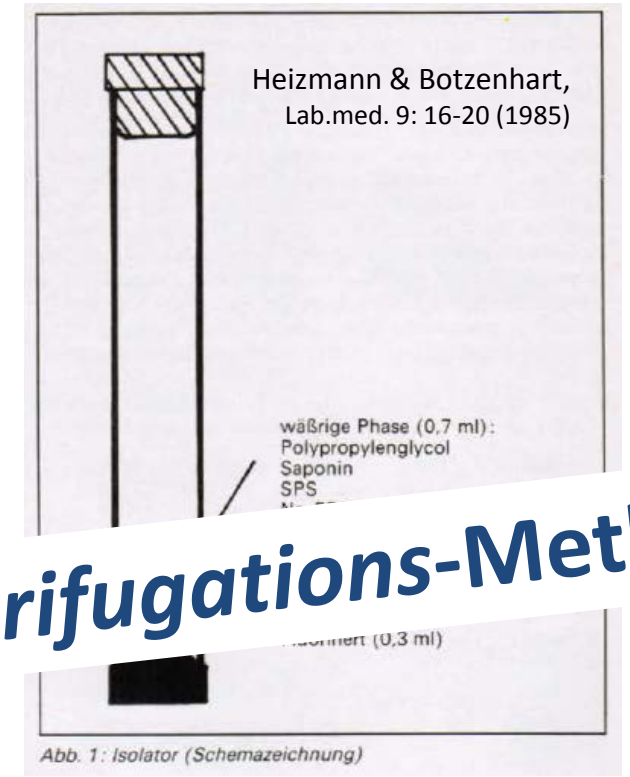
Vol. 7, No. 1
Printed in U.S.A.

New Centrifugation Blood Culture Device

G. L. DORN* AND K. SMITH

Department of Microbiology, Leland Fikes Research Institute, and Granville C. Morton Cancer and Research Hospital, Divisions of Wadley Institutes of Molecular Medicine, Dallas, Texas 75235





Heizmann & Botzenhart,
Lab.med. 9: 16-20 (1985)

Abb. 1: Isolator (Schemazeichnung)

Lysis-Zentrifugations-Methode

and time. The best overall average recovery (93%) was obtained at 3,000 × *g* for 30 min. With

⇨ **qualitatives und quantitatives *Blutkulturverfahren***

Direct blood culturing on solid medium outperforms an automated continuously monitored broth-based blood culture system in terms of time to identification and susceptibility testing

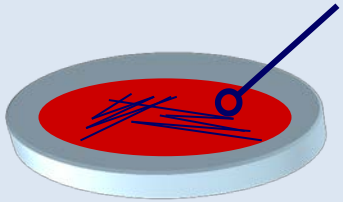
E. A. Idelevich, B. Grünastel, G. Peters and K. Becker

New Microbe and New Infect 2016; 10: 19–24

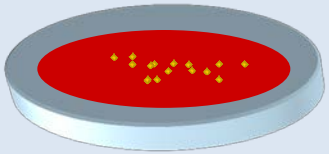
10 ml of spiked blood

Isolator tube

Centrifugation (3000 g for 30 min)



Incubation at 36°C in air with 5% CO_2

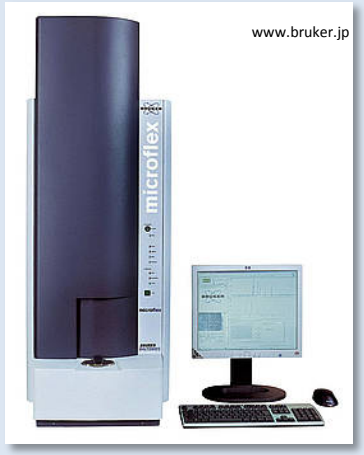


(neu)

Hourly observation of growth for **microcolonies**

Automated BC system
(BACTEC™ 9240; BD Diagnostics)

MALDI-TOF MS
(Microflex LT system; Bruker Daltonics)



Direct blood culturing on solid medium outperforms an automated continuously monitored broth-based blood culture system in terms of time to identification and susceptibility testing

E. A. Idelevich, B. Grünastel, G. Peters and K. Becker

New Microbe and New Infect 2016; 10: 19–24

Organism	Concentration (CFU/mL)	Time to MALDI-TOF MS identification after direct blood culture method (h)			Time to BACTEC positivity signal (h)
		High confidence (score ≥2.0)	Low confidence (score ≥1.7)	Modified threshold (score ≥1.5 and three identical propositions)	
Escherichia coli	100	7	7		
	10	7			
	1				
Pseudomonas					
Sta					
Stap					13.9
				14	16.1
			15	15	17.8
Enter		9 (8[a])	8	8	10.7
	10	9	9	9	11.9
	1	10	10	10	13.0
Streptococcus pneumoniae	100	9	8	8	10.2
	10	9	9	9	11.5
	1	12	12	12	12.4
Haemophilus influenzae	100	11	11	11	16.3
	10	11	11	11	18.6
	1	11	11	11	20.0

[a]Time to identification was reduced by on-plate extraction.
[b]Time to identification was reduced by on-plate extraction followed by additional shots.
[c]No Vitek 2 antimicrobial susceptibility testing is routinely performed for *H. influenzae*.

⇨ **Spezies-Identifikation durchschnittlich 3,3 h eher als Wachstumsdetektion durch automatisiertes System**

Direct blood culturing on solid medium outperforms an automated continuously monitored broth-based blood culture system in terms of time to identification and susceptibility testing

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Organism	Concentration (CFU/mL)	Time to Vitek 2 AST after direct blood culture method (h): Time until Vitek 2 inoculation	Duration of Vitek 2 AST	Total time to Vitek 2 result	Time to BACTEC positivity signal, h
Escherichia coli	100	7			
	10				
					12.7
				19.8	14.0
			11.8	25.8	13.9
		14	14	28.0	16.1
	1	17	13	30.0	17.8
Enterococcus faecalis	100	8	11.5	19.5	10.7
	10	9	11.8	20.8	11.9
	1	10	12	22.0	13.0
Streptococcus pneumoniae	100	9	13.8	22.8	10.2
	10	10	13.8	23.8	11.5
	1	12	10.3	22.3	12.4
Haemophilus influenzae	100	—[c]	—	—	16.3
	10	—	—	—	18.6
	1	—	—	—	20.0

[c]No Vitek 2 antimicrobial susceptibility testing is routinely performed for *H. influenzae*.

⇨ **Empfindlichkeitstestung durchschnittlich 2.5 h eher gestartet als Wachstumsdetektion durch automatisiertes System**

Direkte Blutkultivierung von Hefen auf Festmedium

Organism and concentration	Time to species identification applying direct lysis-centrifugation-cultivation method		Time to positivity applying automated BC system	
	Sabouraud agar	Chocolate agar	BACTEC Mycosis-IC/F	BACTEC Plus Aerobic/F
Candida albicans				
100 cfu/ml	14	15	16.4	17.8
10 cfu/ml	15	18	19.1	21.3
1 cfu/ml	17	20	23.1	24.6
Candida glabrata				
100 cfu/ml	15	26	16.2	38.2
10 cfu/ml	15	27	19.5	47.7
1 cfu/ml	16	30	23.6	56.6
Candida krusei				
100 cfu/ml	15	15	16.9	17.5
10 cfu/ml	15	18	19.3	20.2
1 cfu/ml	17	19	23.0	22.1
Candida tropicalis				
100 cfu/ml	15	13	15.6	16.5
10 cfu/ml	15	16	17.2	19.2
1 cfu/ml	16	17	20.5	20.9

Idelevich *et al*, ECCMID 2015

Rapid Identification and Susceptibility Testing of *Candida* spp. from Positive Blood Cultures by Combination of Direct MALDI-TOF Mass Spectrometry and Direct Inoculation of Vitek 2

Evgeny A. Idelevich*, Camilla M. Grunewald, Jörg Wüllenweber, Karsten Becker

PLOS ONE | DOI:10.1371/journal.pone.0114834 December 9, 2014

Positive monomicrobial BCs from 15 patients including:

- 13 aerobic
- 5 anaerobic
- 5 fungal
- 1 paediatric bottle

Candida species identification rates by using direct MALDI-TOF MS method

Species	Total number of samples	Number of identified samples	Identification rate, %
C. glabrata	12	7	58.3
C. albicans	9	6	66.7
C. dubliniensis	2	1	–[a]
C. krusei	1	1	–[a]
Total	**24**	**15**	**62.5**

Commercially available molecular assays for the diagnosis of sepsis using whole blood as sample type

Diagnostic technique		No. of pathogens detected	Sensitivity	Specificity
Xpert MRSA/SA *(Roche)*	Real-time PCR	2	75–100	98.4–99.4
SeptiFast *(Roche)*	Multiplex real time PCR assay for bacterial and fungal pathogens	25, plus mecA as reflex test	60–95	74–99
VYOO *(SIRS-Lab)*	Multiplex PCR with gel electrophoresis	34plus mec A, vanA/ B/C, SHV, CTX-M	30–51	n.d.
SepsiTest *(Molzym)*	Broad-range PCR with sequencing	>300 pathogens	61–88.5	83.5–85.8

*Concordance with blood culture-dependent assays; n.d., not determined

Liesenfeld et al., Eur. J. Microbiol. Immunol.

Patient outcome and hospital costs for patients with bloodstream infection treated using routine medical management with or without the SeptiFast test

	Routine management (Mean ± *SD*)	Routine management plus SeptiFast (Mean ± *SD*)	*p* value
28-day mortality	13 (27%)	14 (26%)	n.s.
6-month mortality	20 (37%)	20 (41.6%)	n.s.
Stay in ICU	31.0 ± 19.4	22.9 ± 29.9	<0.05
Stay in hospital	21.3 ± 23.4	18.3 ± 21.4	<0.05
Stay in ICU survivors	24.1 ± 21.9	18.3 ± 11.4	<0.05
Number of antibiotics used per patient	5.1 ± 3.1	4.2 ± 2.2	<0.05
Antibiotic treatment cost per patient	3576 €	2812 €	<0.05
Cost of ICU stay	32798 €	24246 €	<0.05
Cost of ward stay	5824 €	4988 €	<0.05
Total cost	42198 €	32228 €	<0.05

n.s., not significant

acc. data from Alvarez et al., Anaesth. Intensive Care 40, 958–963 (2012)

Liesenfeld et al., Eur. J. Microbiol. Immunol.

Randomized controlled clinical trial evaluating multiplex polymerase chain reaction for pathogen identification and therapy adaptation in critical care patients with pulmonary or abdominal sepsis

Sascha Tafelski[1]*, Irit Nachtigall[1]*, Thomas Adam[2], Stefan Bereswill[2], Jana Faust[1], Andrey Tamarkin[1], Tanja Trefzer[1], Maria Deja[1], Evgeny A Idelevich[3], Klaus-Dieter Wernecke[4,5], Karsten Becker[3], Claudia Spies[1] for the Molecular Diagnostics of Sepsis Study Group

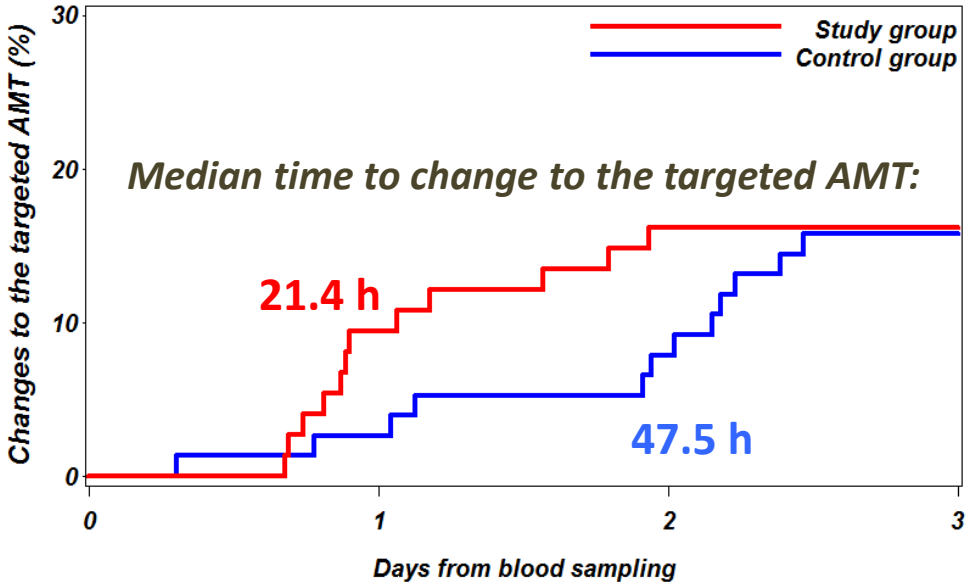
Journal of International Medical Research
2015, Vol. 43(3) 364–377

Med Microbiol Immunol (2015) 204:585–592
DOI 10.1007/s00430-014-0385-7

ORIGINAL INVESTIGATION

Impact of multiplex PCR on antimicrobial treatment in febrile neutropenia: a randomized controlled study

Evgeny A. Idelevich · Gerda Silling · Yvonne Niederbracht · Hanna Penner · Maria Cristina Sauerland · Sascha Tafelski · Irit Nachtigall · Wolfgang E. Berdel · Georg Peters · Karsten Becker · Molecular Diagnostics of Sepsis study group



- Significant reduction in the time required for initial pathogen identification by PCR (15.9 h), compared with standard BC (38.1 h); (P<0.001) [Tafelski et al.].
- PCR method accelerates change to the targeted antimicrobial therapy (AMT) in febrile neutropenic patients (*P* = 0.018) [Idelevich et al.]

„Wat wellste maache?“

- Definition der Sepsis „in progress“
- ungebrochene, Patientencharakteristika-bedingte Bedeutung der Sepsis bzgl. Morbidität, Letalität und Gesundheitsökonomie
- therapeutische Limitierungen durch (multi-) resistente Erreger
- BK-Diagnostik ist essentiell trotz bestehender Limitationen!
- nur teilweiser Fortschritt bei der Erfüllung der klinischen Anforderungen an die mikrobiologische Diagnostik (sensitiv, spezifisch und **schnell!!!**)
  - inakzeptable Transport- und Lagerungszeiten (Station, Labor)
  - nur partielle Vorteile durch DNA-basiertem Direktnachweis – bisher kein Durchbruch in der Sepsis-Routinediagnostik
  - zu lange Kultivierungszeiten
  - erfolgreiche Beschleunigung der Zeiten für Identifizierung und Empfindlichkeitstestung durch
    - MALDI TOF MS
    - Einsatz von Mikrokolonien nur kurzzeitig bebrüteter Festnährmedien

„Wat ~~wollste~~ maache?“
sollste

⇨ **Beschleunigung**

der mikrobiologischen Sepsisdiagnostik