Bloodstream infections (BSI)

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BSI

Primary = a condition where the infection is the bloodstream itself

- Infective endocarditis
- endarteritis, thrombophlebitis
- catheter related BSI

21.11.2023
Prof. Nemec: Introduction to HAI, Catheter Infection; Surgical Site Infections; Hospital-Aquired & Ventilator-Associated Pneumonia

Secondary

- pneumonia
- pyelonephritis
- wound infections
- ...

The term sepsis

life-threatening organ dysfunction caused by a dysregulated host response to infection

Definition Sepsis-3, 2016

Sepsis, if not recognized and treated early, is the primary cause of death from infection

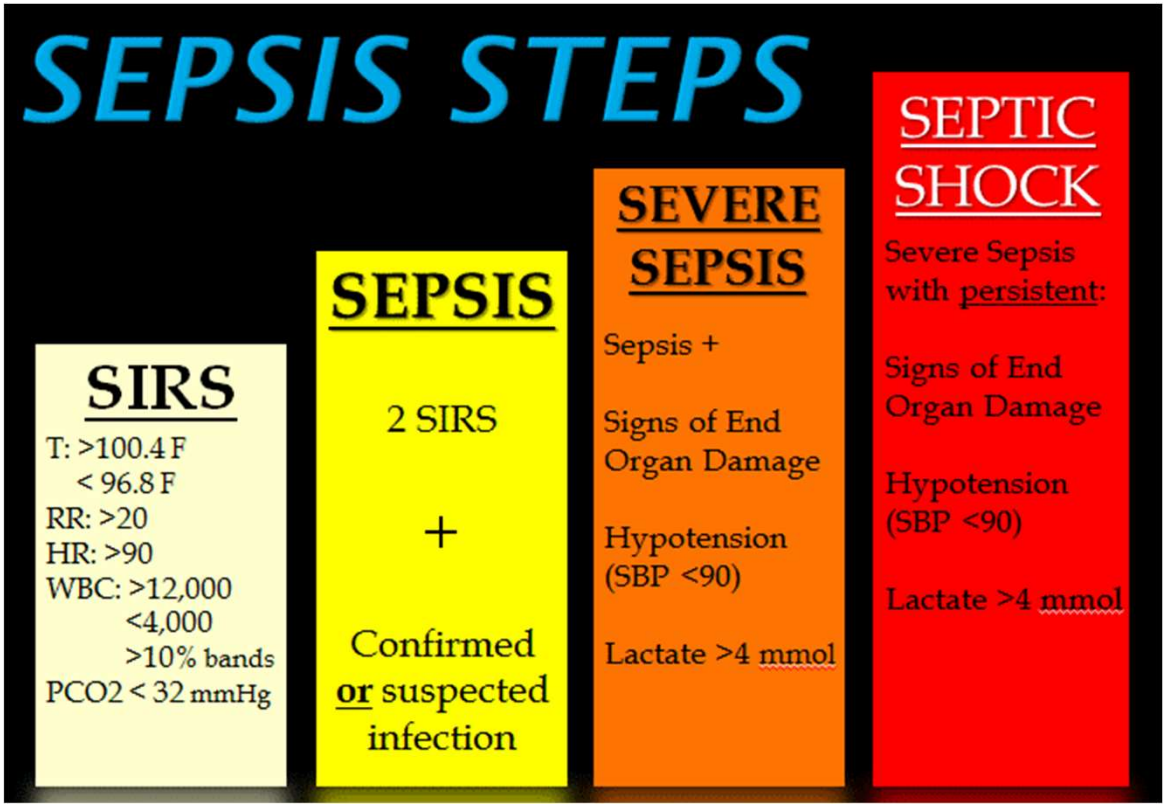
The term sepsis

Definition Sepsis-1, 1992
SIRS due to infection

Box 1. SIRS (Systemic Inflammatory Response Syndrome)

Two or more of:

- Temperature >38°C or <36°C
- Heart rate >90/min
- Respiratory rate >20/min or $Paco_2$ <32 mm Hg (4.3 kPa)
- White blood cell count >12 000/mm^3 or <4000/mm^3 or >10% immature bands



The term sepsis

Definition Sepsis-2, 2003

supplemented by a list of diagnostic criteria

including alteration of consciousness, oedema, positive fluid balance, hyperglycaemia, etc.

Infection[a]

Documented or suspected *and* some of the following[b]:

General parameters

Fever (core temperature >38.3°C)
Hypothermia (core temperature <36°C
Heart rate >90 bpm or >2 SD above the normal value for age
Tachypnea: >30 bpm
Altered mental status
Significant edema or positive fluid balance (>20 ml/kg over 24 h)
Hyperglycemia (plasma glucose >110 mg/dl or 7.7 mM/l) in the absence of diabetes

Inflammatory parameters

Leukocytosis (white blood cell count >12,000/µl)
Leukopenia (white blood cell count <4,000/µl)
Normal white blood cell count with >10% immature forms
Plasma C reactive protein >2 SD above the normal value
Plasma procalcitonin >2 SD above the normal value

Hemodynamic parameters

Arterial hypotension[b] (systolic blood pressure <90 mmHg, mean arterial pressure <70, or a systolic blood pressure decrease >40 mmHg in adults or <2 SD below normal for age)
Mixed venous oxygen saturation >70%[b]
Cardiac index >3.5 l min^{-1} m^{-2}[c,d]
Organ dysfunction parameters
Arterial hypoxemia ($PaO_2/FIO2$ <300)
Acute oliguria (urine output <0.5 ml kg^{-1} h^{-1} or 45 mM/l for at least 2 h)
Creatinine increase ≥0.5 mg/dl
Coagulation abnormalities (international normalized ratio >1.5 or activated partial thromboplastin time >60 s)
Ileus (absent bowel sounds)
Thrombocytopenia (platelet count <100,000/µl)
Hyperbilirubinemia (plasma total bilirubin >4 mg/dl or 70 mmol/l)

Tissue perfusion parameters

Hyperlactatemia (>3 mmol/l)
Decreased capillary refill or mottling

The term sepsis

life-threatening **organ dysfunction** caused by a **dysregulated host response** to infection

today's sepsis (sepsis-3) corresponds to severe sepsis (sepsis-1),
i.e. distinguishes sepsis from uncomplicated BSI

Clinical criteria: SOFA (sequential organ failure assessment)

Table 1. Sequential [Sepsis-Related] Organ Failure Assessment Score[a]

	Score				
System	0	1	2	3	4
Respiration					
Pao_2/Fio_2, mm Hg (kPa)	≥400 (53.3)	<400 (53.3)	<300 (40)	<200 (26.7) with respiratory support	<100 (13.3) with respiratory support
Coagulation					
Platelets, $\times 10^3/\mu L$	≥150	<150	<100	<50	<20
Liver					
Bilirubin, mg/dL (μmol/L)	<1.2 (20)	1.2-1.9 (20-32)	2.0-5.9 (33-101)	6.0-11.9 (102-204)	>12.0 (204)
Cardiovascular	MAP ≥70 mm Hg	MAP <70 mm Hg	Dopamine <5 or dobutamine (any dose)[b]	Dopamine 5.1-15 or epinephrine ≤0.1 or norepinephrine ≤0.1[b]	Dopamine >15 or epinephrine >0.1 or norepinephrine >0.1[b]
Central nervous system					
Glasgow Coma Scale score[c]	15	13-14	10-12	6-9	<6
Renal					
Creatinine, mg/dL (μmol/L)	<1.2 (110)	1.2-1.9 (110-170)	2.0-3.4 (171-299)	3.5-4.9 (300-440)	>5.0 (440)
Urine output, mL/d				<500	<200

no standardised diagnostic test for sepsis is available

Microbiological diagnostics

Blood culture

Molecular diagnostics

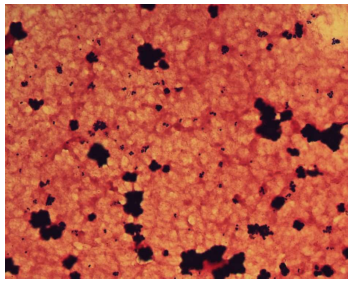
Blood culture

1- 3 days

positive

negative

5 days



Gram staining

1 day

culture on solid media

2 hours

preliminary identification

identification and AST

1 day

What characteristics should the ideal dg. test have:

	Blood culture:
• cheap	yes
• reliable	sensitivity 50% only
• rapid (ultra-rapid)	takes dozens of hours
• unaffected by antibiotic treatment	certainly affected by this (x resins)
• distinguishing the finding of a pathogen from contamination	not straightforward
• with information on appropriate ATB treatment	upon AST ... or ...

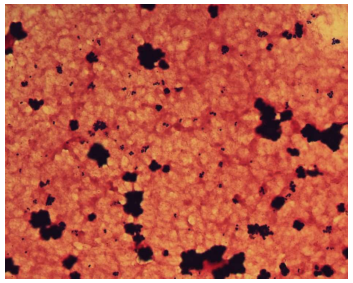
Blood culture

1- 3 days

positive

negative

5 days



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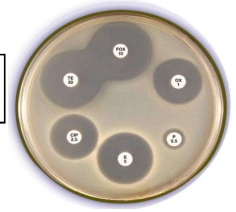


1 hour

identification and some AMR genes

43 targets

Tabulka 2. Analyty detekované testem BioFire BCID2 Panel

Grampozitivní bakterie		
Enterococcus faecalis	*Staphylococcus* spp.	*Streptococcus* spp.
Enterococcus faecium	*Staphylococcus aureus*	*Streptococcus agalactiae* (skupina B)
Listeria monocytogenes	*Staphylococcus epidermidis*	*Streptococcus pneumoniae*
	Staphylococcus lugdunensis	*Streptococcus pyogenes* (skupina A)

Gramnegativní bakterie	
Komplex *Acinetobacter calcoaceticus-baumannii*	*Enterobacterales*
Bacteroides fragilis	Komplex *Enterobacter cloacae*
Haemophilus influenzae	*Escherichia coli*
Neisseria meningitidis (opouzdřená)	*Klebsiella aerogenes*
Pseudomonas aeruginosa	*Klebsiella oxytoca*
Stenotrophomonas maltophilia	Skupina *Klebsiella pneumoniae*
	Proteus spp.
	Salmonella spp.
	Serratia marcescens

Kvasinky		
Candida albicans	*Candida krusei*	*Cryptococcus neoformans/gattii*
Candida auris	*Candida parapsilosis*	
Candida glabrata	*Candida tropicalis*	

Geny antimikrobiální rezistence				
CTX-M	KPC	*mecA/C*	NDM	*vanA/B*
IMP	*mcr-1*[a]	*mecA/C* a MREJ (MRSA)	OXA-48-like	VIM

Molecular diagnostics

10 hours (intensive)

broad-range PCR (16S rRNA gene)
+ Sanger sequencing

Use of 16S on various materials

	Heart valves	Joint aspirates	Blood ICU
Samples total	75	230	476
Samples positive	55	135	186
Samples positive by both culture and 16S PCR	11	73	87
Samples positive by 16S PCR only	44	59	73
Samples positive by culture only	0	3	26
Added values of 16S PCR (% from all samples)	56 %	19 %	7 %
False negativity of 16S PCR (% from all samples)	0 %	2 %	7 %

Molecular diagnostics

10 hours (intensive)

broad-range PCR (16S rRNA gene)
+ Sanger sequencing

3.5 hours

multiplex PCR and T2MR

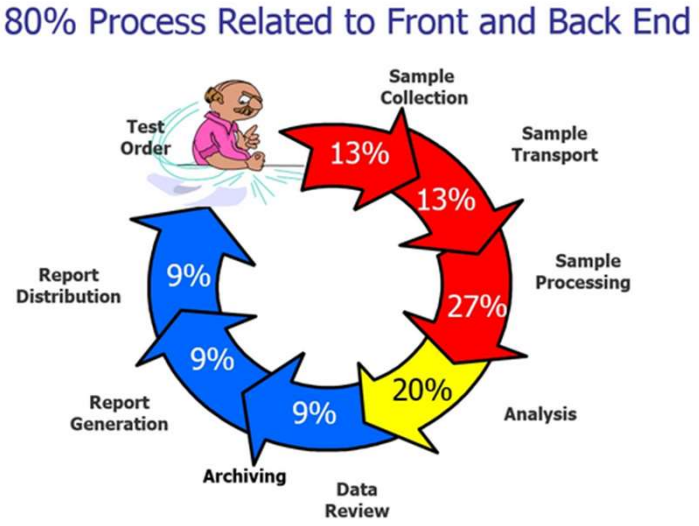
T2MR and „ESCAPE“

- a group of six virulent and resistant bacteria (in the T2MR list, *E. coli* replaces *Enterobacter*)
- health care-associated infections
- may escape conventional ATB therapy due to their MDR phenotype

Escherichia coli	E (Ec)
Staphylococcus aureus	S
Klebsiella pneumoniae	K
Acinetobacter baumannii	A
Pseudomonas aeruginosa	P
Enterococcus faecium	E

What characteristics should the ideal dg. test have:

	Molecular diagnostics:
• cheap	no
• reliable	better than blood culture
• rapid (ultra-rapid)	perharps yes
• unaffected by antibiotic treatment	yes
• distinguishing the finding of a pathogen from contamination	yes and no
• with information on appropriate ATB treatment	no



Back to blood culture

Blood culture

Gold standard of microbiological diagnostics of sepsis (BSI)

To collect	Traditional approach	Novel approach
Which material	blood (with skin swap)	blood ---
When	when the temperature rises	on suspicion of BSI
How	„paired blood cultures" **2x to 3x twin bottles**	Single sampling **1x four to six bottles**

one blood culture ≠ one bottle
one blood culture = a set of bottles taken at a given time, or all bottles taken as part of a septic episode diagnostics

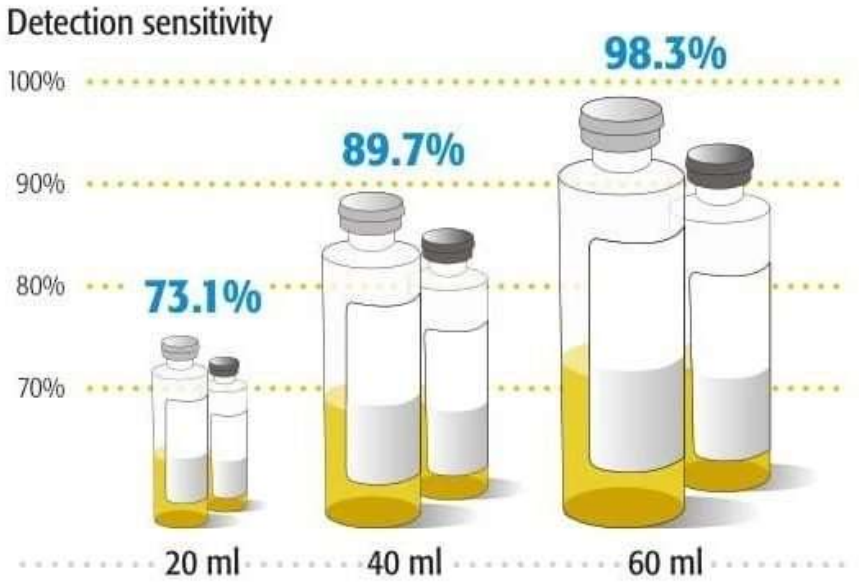
Collection of a sufficient amount of blood

- essential to increase the sensitivity

only 1 to 10 bacterial cells in 1 mL of blood

Desired blood volume: 40 to 60 mL

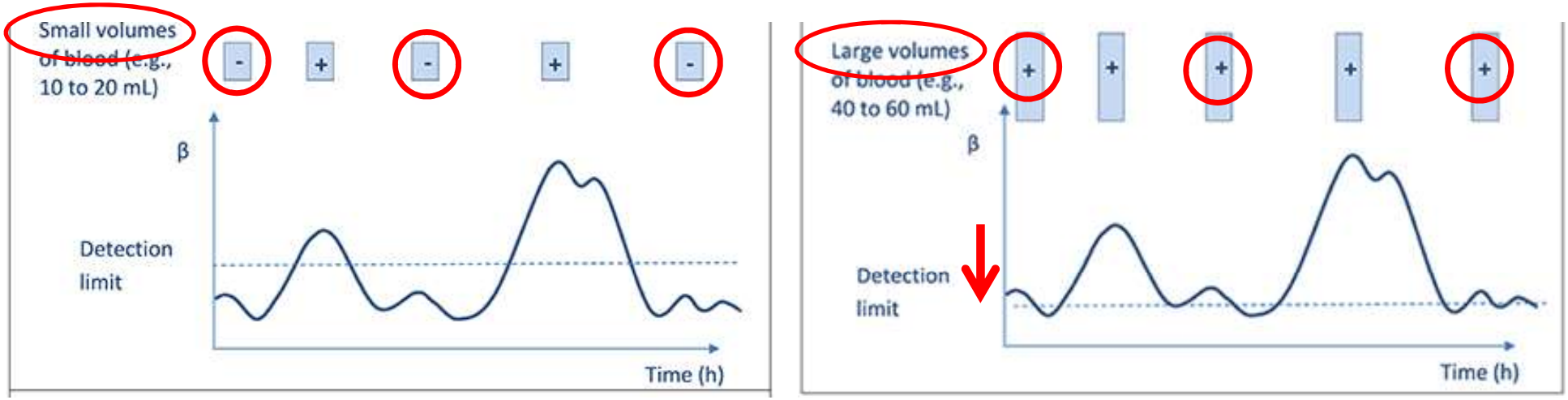
Taking just one single vial is useless



Lee et al. Detection of bloodstream infections in adults: how many blood cultures are needed? 2007.

Collection of a sufficient amount of blood

- essential to increase the sensitivity

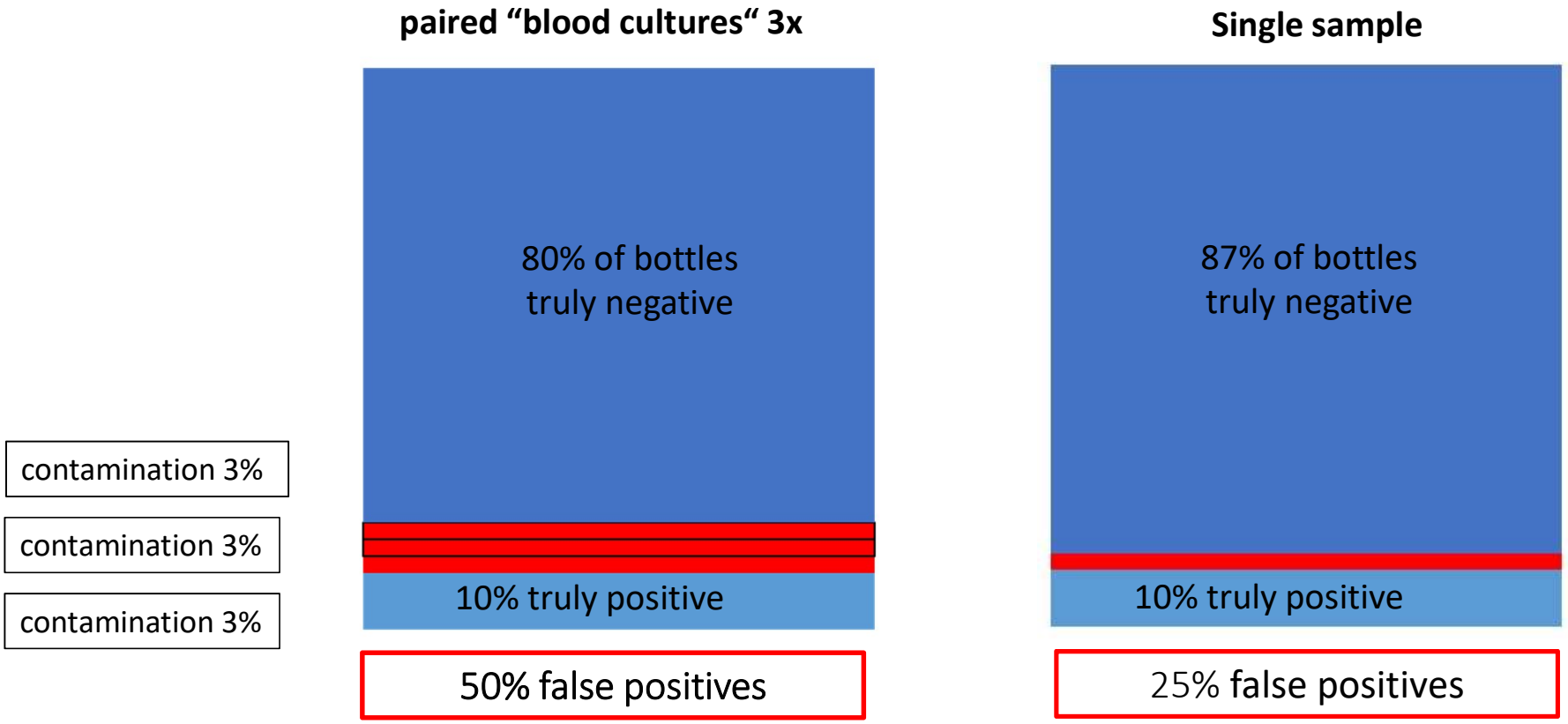


Intermittent bacteraemia for less than 24 hours is exceptional

Single sample

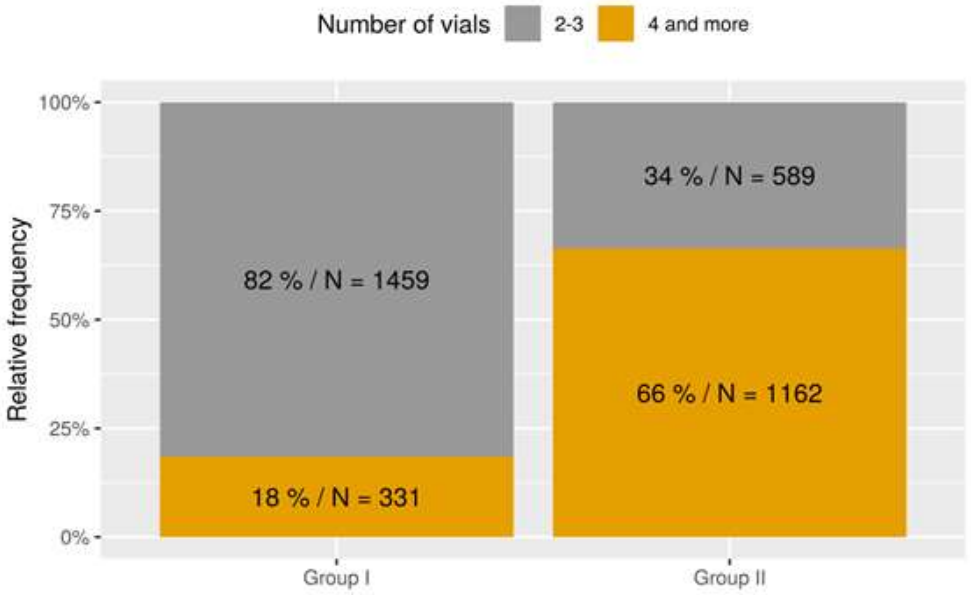
- essential to increase the specificity

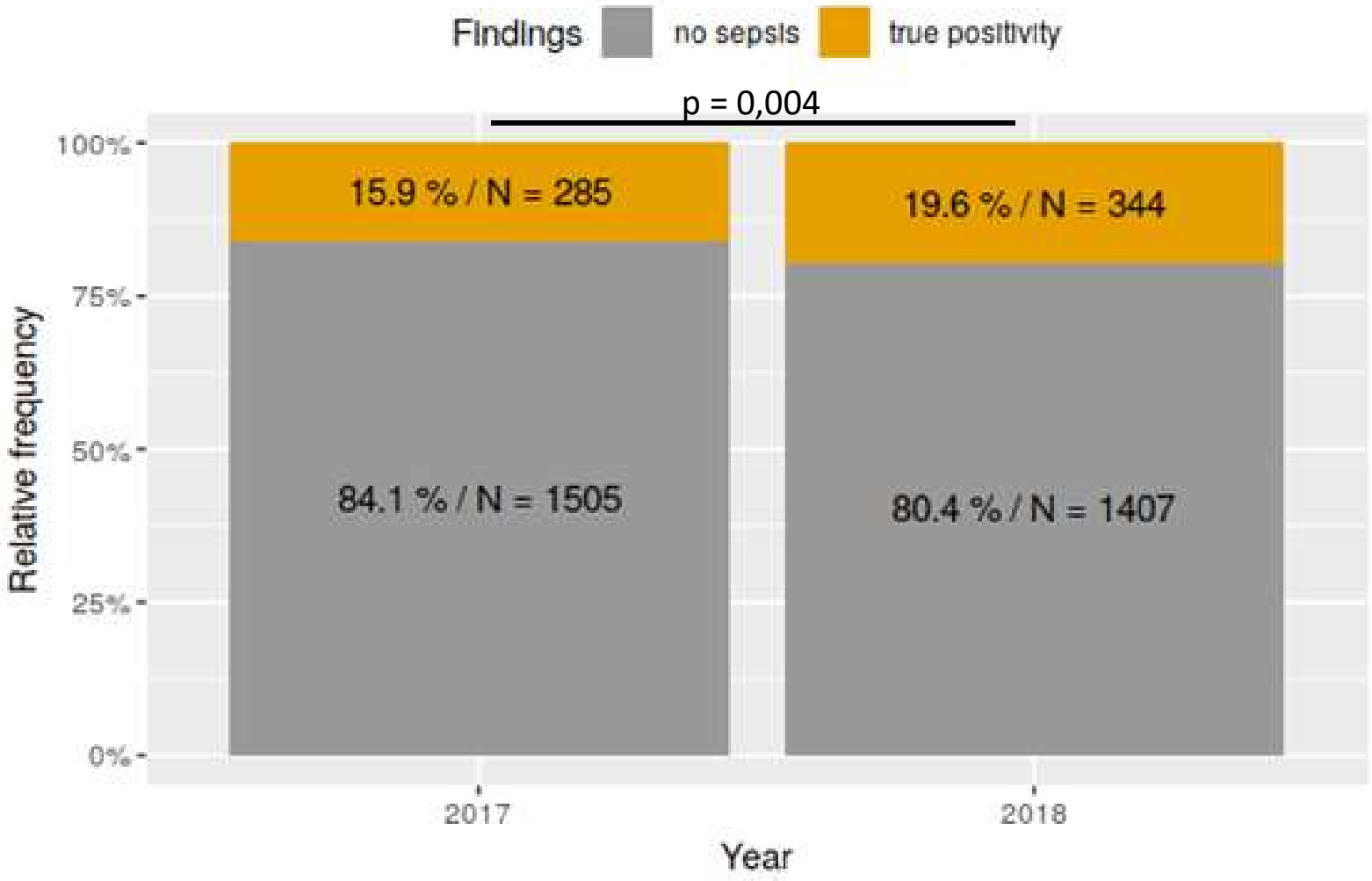
Common contaminants: coagulase negative staphylococci, *Corynebacterium* spp., *Micrococcus* spp., *Bacillus* spp., *Cutibacterium acnes*.



Single sample in Motol

	Jan to June 2017	Oct 2017 to Apr 2018
# blood culture (%)	1790	1751
# 2 to 3 bottles	81.5 %	33.7 %
# 4 and more bottles	18.5 %	66.3 %




Findings
no sepsis
true positivity
p = 0,004
100%
75%
50%
25%
0%
Relative frequency
15.9 % / N = 285
84.1 % / N = 1505
19.6 % / N = 344
80.4 % / N = 1407
2017
2018
Year

Practical aspects of blood culture collection

- Sufficient amount of blood, **40 to 60 ml** = 4 to 6 bottles (10 mL each)
  Fill the bottles completely (orientation according to the scale on the side of the bottle)
- Aerobic and anaerobic bottles in ratio **1 : 1**; to fill **aerobic bottles as the first in order**
- Mycotic bottle can be added to the basic set

- collection from the periphery
- start automatic blood incubation as early as possible

Management of sepsis (from microbiologcal perspective)

- broad-spectrum AB therapy timely (within one hour of occurrence):

  beta-lactam (carbapenem or piperacilin/tazobactam or cefepim)

  + aminoglycoside (amikacin or gentamicin)

  potentially + clindamycin (or linezolid) if toxin is produced

- blood cutlure

  + sometimes molecular diagnostics

Infective endocarditis

- predisposing factors: valve replacement, pacemaker, iv. addicts, rheumatic fever

- blood culture (repeatedly)
- echocardiography

Causing agens:

S. aureus, streptococci (viridans), enterococci, HACEK, non culturable (*bartonella, coxiella*), candida

HACEK: *Haemophilus aphrophilus* (today *Aggregatibacter*), *Aggregatibacter actinomycetemcomitans*, *Cardiobacterium hominis*, *Eikenella corrodens*, *Kingella kingae*

Kingella Kingae