

# **Sepsis from a microbiological perspective**

Veronika Holá

Institute for Microbiology

Faculty of Medicine, Masaryk University  
and St. Anne's Faculty Hospital in Brno

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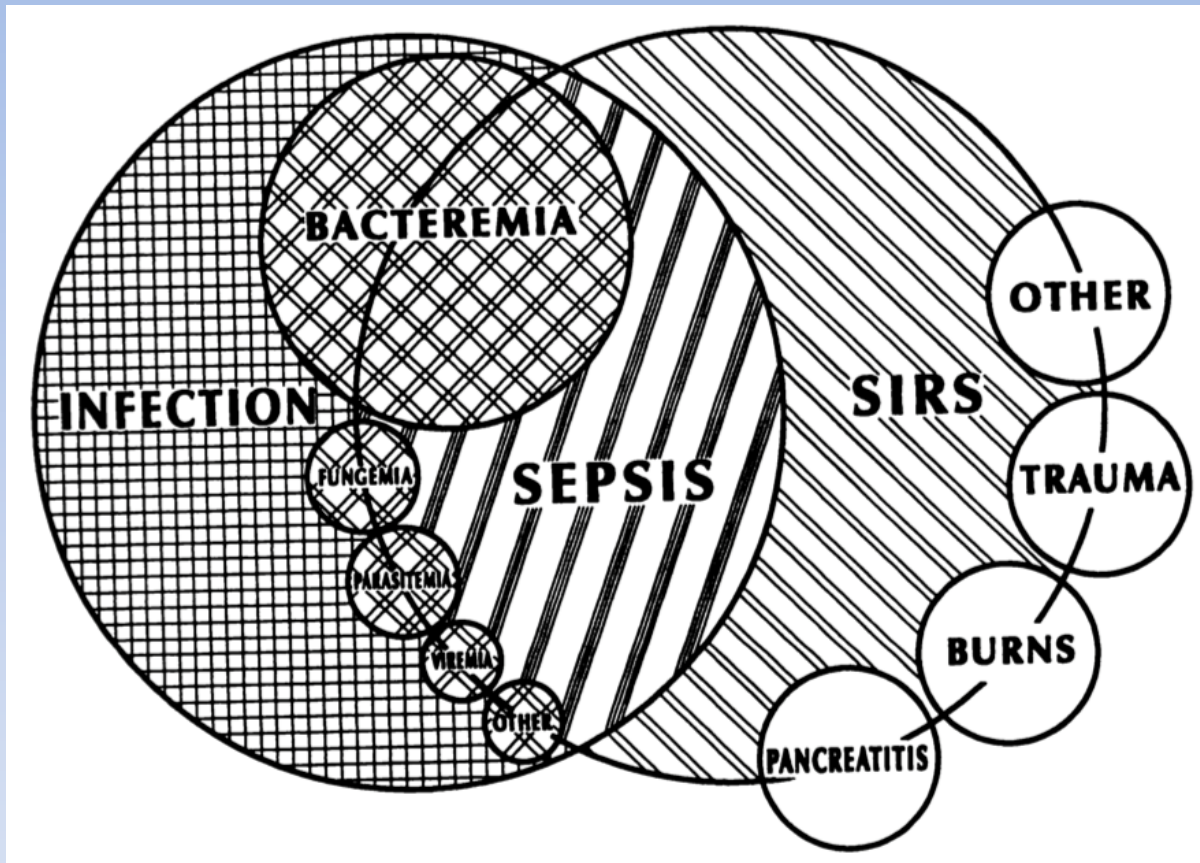
# Sepsis

- **Definition of sepsis**
- Septic haemodynamic
- Presence of infection
- SIRS

# Response of the macroorganism

- Systemic Inflammatory Response Syndrome (SIRS)
- Sepsis = SIRS + infection
- Severe sepsis = sepsis + signs of organ dysfunction
- Septic shock = severe sepsis + haemodynamic changes

# Infection, SIRS, sepsis



Bone, R., Balk, R., Cerra, F., Dellinger, R., Fein, A., Knaus, W., Schein, R., et al. (1992). Definitions for sepsis and organ failure and guidelines for the use of innovative therapies in sepsis. The ACCP/SCCM Consensus Conference Committee. American College of Chest Physicians/Society of Critical Care Medicine. *Chest*, 101(6), 1644-1655.

# Sepsis

- Cytokine storm
- **Systemic Inflammatory Response Syndrome (SIRS)**
- Reaction of immune system to microbial products
- SIRS include
  - 1) Body temperature  $<36\text{ }^{\circ}\text{C}$  or  $>38\text{ }^{\circ}\text{C}$
  - 2) Heart rate greater than 90 beats per minute
  - 3) Tachypnea (high respiratory rate),  $>20$  breaths per minute  
or arterial partial pressure of carbon dioxide  $<4.3\text{ kPa}$  (32 mmHg)
  - 4) White blood cell count  $<4000\text{ cells/mm}^3$  ( $4 \times 10^9\text{ cells/L}$ ) or  $>12,000\text{ cells/mm}^3$  ( $12 \times 10^9\text{ cells/L}$ )  
or the presence of  $>10\%$  immature neutrophils (band forms) - "left-shift"
- The septic patients meet criteria for SIRS

# Bedside dg. of sepsis

- Clinical symptoms
  - Temperature
  - Respiratory rate
  - Pulse rate
  - Nausea
  - Confusion
  - Blood pressure
  - Urine secretion
- + Laboratory markers
  - Number of leukocytes
  - Haemocoagulation
  - Respiratory-metabolical acidosis
  - Organ dysfunction
  - Inflammatory markers

# SIRS criteria x SOFA score x qSOFA score

- SOFA score - Sequential organ failure assessment score
- Based on six different scores
  - Respiratory, cardiovascular, hepatic, coagulation, renal and neurological systems
- qSOFA - simplified
  - Low blood pressure (SBP  $\leq$  100 mmHg)
  - High respiratory rate ( $\geq$  22 breaths/min)
  - Altered mentation (GCS  $<$  15)

# Sepsis vs. microbaemia

**Bacteriaemia**



**Starting sepsis**



**Interaction with immunity system**



**Cytokines → endothelium of capillars + inflammation**



**Systemic Inflammatory Response Syndrome (SIRS)**

**+**

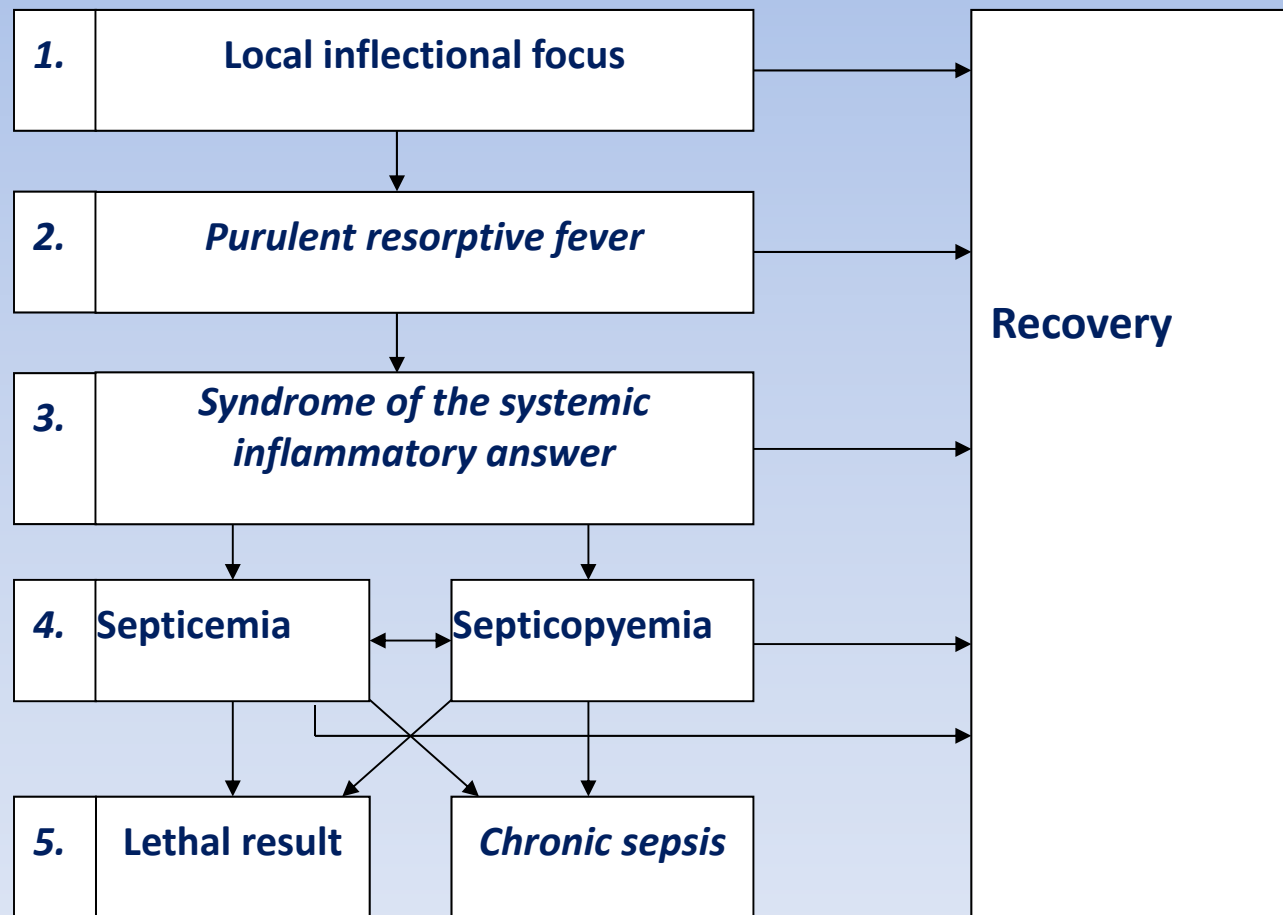
**Compensatory Anti-inflammatory Response Syndrome  
(CARS)**



# Sepsis vs. microbaemia

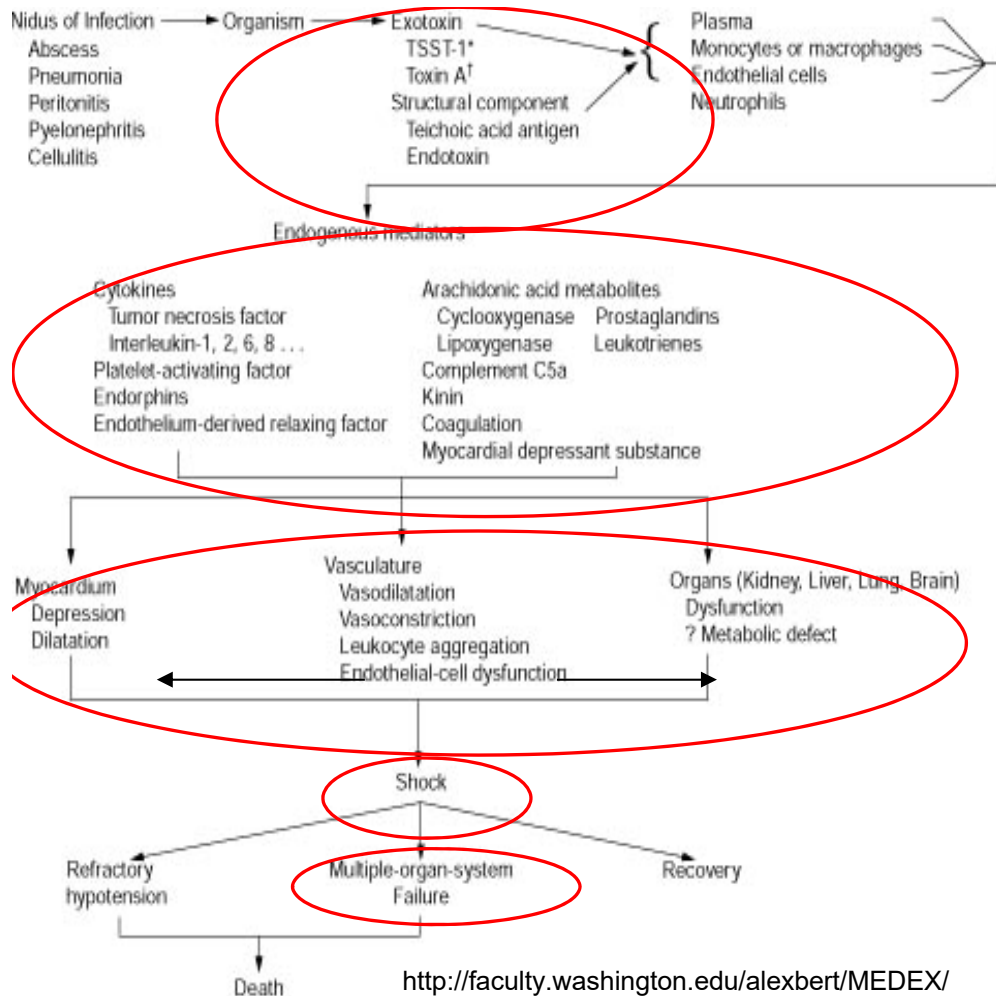
- Sepsis **x** bacteraemia and bacteraemia **x** sepsis
- Blood normally sterile
- **Not necessarily** present in developed sepsis
- High risk of multi-organ failure
- **Sepsis** - mortality
- **Septic shock**

# The phases of the development of the generalized infection



# Pathogenesis of sepsis

- Microbial process
- Necessary conditions
- Most bacteria – only in attenuated patient



- Clinical symptoms
- Pathological physiology
  - Local x generalized inflammation
- Laboratory markers



# Organ dysfunction in sepsis

- Lungs
- Kidneys
- Heart
- Livers
- Intestine
- Brain
- Adrenals
- Pancreas (B-cells)
- Coagulation system (DIC)
- Leukocytes (PMNs)

# Therapy of sepsis

- Intensive
- Complex
- ATB treatment not satisfactory
- Need of shock treatment
- Event. surgical intervention

# Spectrum of etiological agents of sepsis

- Autumn 2017 lecture
  - Sepsis in localised infections
  - Wound sepsis
  - Fulminant sepsis
  - Urosepsis
  - Intraabdominal sepsis
  - Nosocomial sepsis
  - Sepsis puerperalis
  - Newborn sepsis
  - Blood stream infections
- **Catheter-related BSI & sepsis**

# Catheter related sepsis

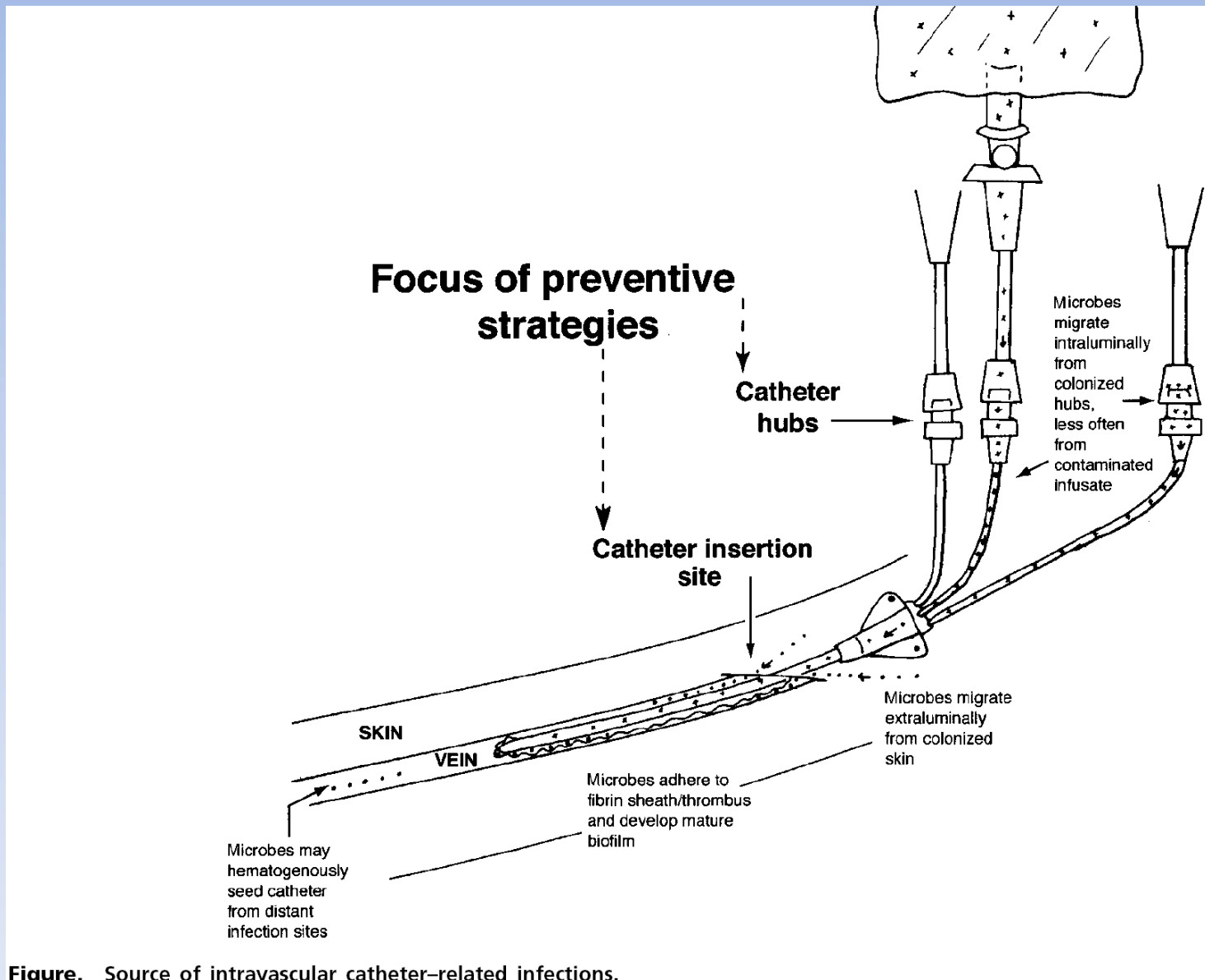


Figure. Source of intravascular catheter-related infections.



# Catheter related sepsis

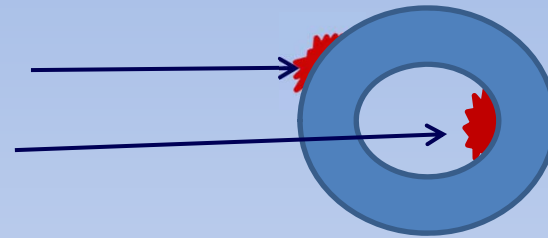
- Catheter-related blood stream infection
- Colonisation of catheter
- Suspect catheter-associated infection
- Local infection of catheter

# Venous catheters

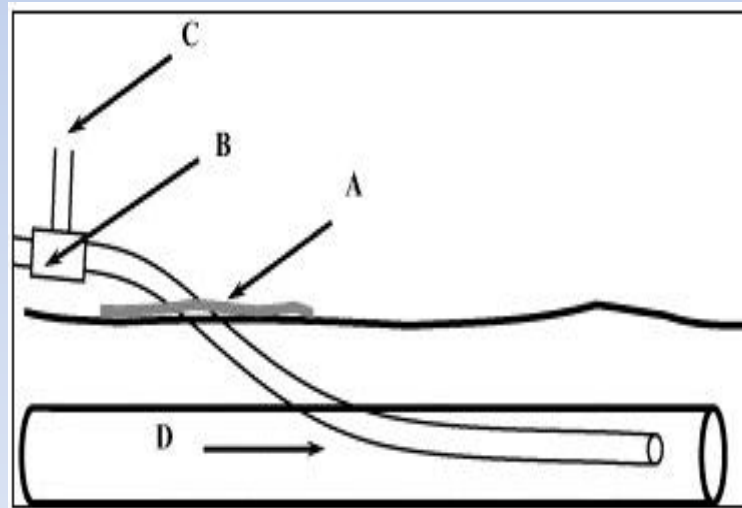
- Peripheral venous catheters
- Peripheral arterial catheters
- Swan-Ganz catheters
- Central venous catheters (CVC)
- Tunnelised CVC
- Implanted venous ports

# Infection of the catheter

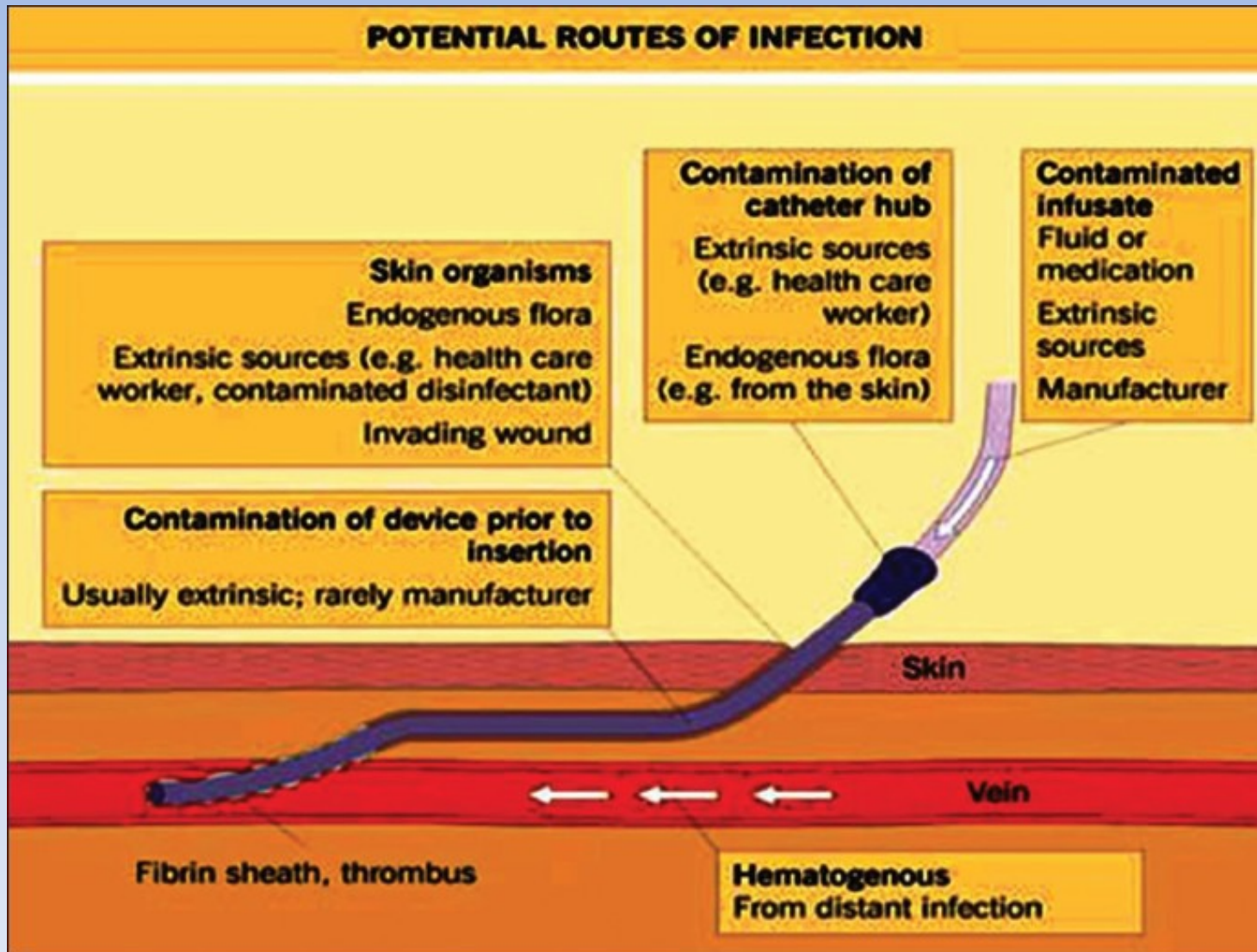
- **Infection**
  - Extraluminal
  - Intraluminal



- **Source of the infection**



# Infection of the catheter



# BSI related sepsis

- Catheter sepsis
- Trombophlebitis
- Central sepsis
  - Endarteritis and (trombo-)phlebitis
  - Endocarditis
    - Accute endocarditis
    - Subaccute and chronic endocarditis → sepsis lenta
    - „Culture-negative“ endocarditis

# Etiology of CRBSI I.

CoNS  
 Enterobacteria  
 PSSP  
 STAU  
 ECSP & SRSP  
 yeasts  
 Other

TABLE 1. Frequency of microorganism isolation from 774 sonicated catheter cultures

Organism	Frequency <sup>a</sup>	%
Coagulase-negative staphylococci	376	36.4
<i>Pseudomonas aeruginosa</i>	143	13.9
Enterococci	103	10.0
Yeasts	95	9.2
<i>Staphylococcus aureus</i>	60	5.8
<i>Enterobacter</i> species	45	4.4
<i>Escherichia coli</i>	40	3.9
<i>Corynebacterium</i> species	34	3.3
Alpha-hemolytic streptococci	27	2.6
<i>Serratia</i> species	19	1.8
<i>Klebsiella</i> species	18	1.7
<i>Bacillus</i> species	18	1.7
<i>Acinetobacter</i> species	12	1.2
<i>Proteus</i> species	10	1.0
Other	32	3.1

<sup>a</sup> A total of 1,032 organisms were isolated.

(Sherertz et al. , 1990)

Table 1. Incidence rates and distribution of pathogens most commonly isolated from monomicrobial nosocomial bloodstream infections (BSIs) and associated crude mortality rates for all patients, patients in intensive care units (ICU), and patients in non-ICU wards.

Pathogen	BSIs per 10,000 admissions	Percentage of BSIs (rank)			Crude mortality, %		
		Total (n = 20,978)	ICU (n = 10,515)	Non-ICU ward (n = 10,442)	Total	ICU	Non-ICU ward
CoNS	15.8	31.3 (1)	35.9 (1) <sup>a</sup>	26.6 (1)	20.7	25.7	13.8
<i>Staphylococcus aureus</i> <sup>b</sup>	10.3	20.2 (2)	16.8 (2) <sup>a</sup>	23.7 (2)	25.4	34.4	18.9
<i>Enterococcus</i> species <sup>c</sup>	4.8	9.4 (3)	9.8 (4)	9.0 (3)	33.9	43.0	24.0
<i>Candida</i> species <sup>c</sup>	4.6	9.0 (4)	10.1 (3)	7.9 (4)	39.2	47.1	29.0
<i>Escherichia coli</i>	2.8	5.6 (5)	3.7 (8) <sup>a</sup>	7.6 (5)	22.4	33.9	16.9
<i>Klebsiella</i> species	2.4	4.8 (6)	4.0 (7) <sup>a</sup>	5.5 (6)	27.6	37.4	20.3
<i>Pseudomonas aeruginosa</i>	2.1	4.3 (7)	4.7 (5)	3.8 (7)	38.7	47.9	27.6
<i>Enterobacter</i> species	1.9	3.9 (8)	4.7 (6) <sup>a</sup>	3.1 (8)	26.7	32.5	18.0
<i>Serratia</i> species <sup>b</sup>	0.9	1.7 (9)	2.1 (9) <sup>a</sup>	1.3 (10)	27.4	33.9	17.1
<i>Acinetobacter baumannii</i>	0.6	1.3 (10)	1.6 (10) <sup>a</sup>	0.9 (11)	34.0	43.4	16.3

(Wisplinghoff et al., 2004 )

# Etiology of CRBSI II.

- Biofilm & Resistance**

G+ 60-70%  
 CoNS  
*S. aureus*  
 Enterococci and streptococci

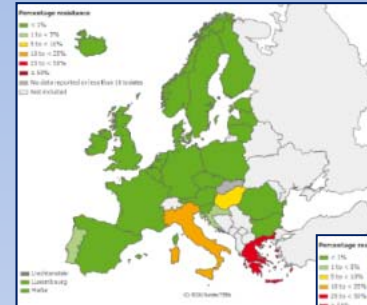
G-  
 Enterobacteria  
*Pseudomonas, Burkholderia, Stenotrophomonas, aj.*

Yeasts  
 Other

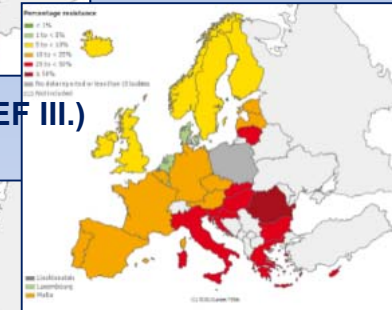
- Specificity of the examination**



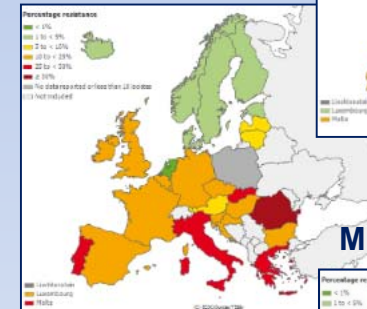
**Karbapenemases**  
*K. pneumoniae*



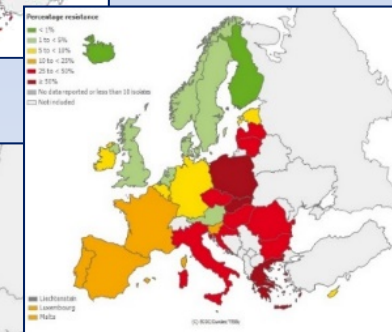
**Karbapenemases**  
*P. aeruginosa*



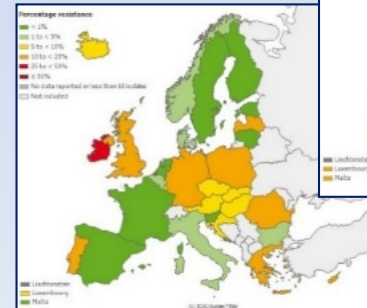
**MDR (FQ, AMG, CEF III.)**  
*K. pneumoniae*



**MRSA**



**VRE**  
*E. faecium*



**PREVENTION OF CATHETER-RELATED  
INFECTIONS  
IS PREFERABLE TO TREATMENT**



# Prevention of CRBSI – catheter insertion

- **Aseptic character of catheter insertion**
  - +
    - **Experienced personnel**
      - +
        - **High-quality subsequent care**
- Place of the catheter insertion
- No. of catheter lumen
- Surface treatment of the entry
- Better connection systems and in-line filtration
- Implanted ports and tunnelisation

# Prevention of CRBSI – catheter care

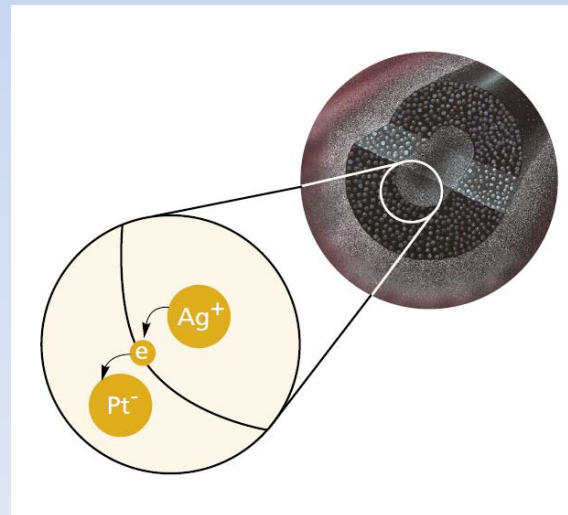
- Aseptic manipulation
- Experienced personnel
- Care management
- Minimalisation of manipulation
- Regular control
- Treatment of site of insertion by disinfectants × No ATB ointments
- Prophylactic administration of anticoagulants × No systemic prophylaxis with ATB
- Regular exchange of short-term catheters × No preventive exchange of long-term catheters (CVC)
- Regular exchange of infusion sets and accessories

# Prevention of CRBSI – catheter

- Material
- Surface treatment
- Impregnation of catheter by antimicrobial compounds

# Prevention of CRBSI – catheter

- Impregnation with antiseptics
- Impregnation with ATB
- Impregnation with Ag
- Other chemicals used for catheter surface impregnation (*in vitro*)



# Microbiological dg. of sepsis

- Rapidity
- Sensitivity
- Specificity
- Correct sampling technique

# Catheter sepsis

- Diagnosis of catheter sepsis
  - Positive quantitative culture of extracted catheter
  - Positive haemoculture
  - Sepsis without response to ATB therapy, positive response to the catheter extraction

# Haemoculture sampling

- Patient with suspicion of bacterial infection
  - CRP > 60 mg/l
  - Fever in anamnesis
  - (Inserted catheters)
- Aseptic sampling
- 2-3 haemoculture bottles
- 30-60 min. intervals
- **Before** ATB treatment
- If treated, sample **prior to next** ATB dose

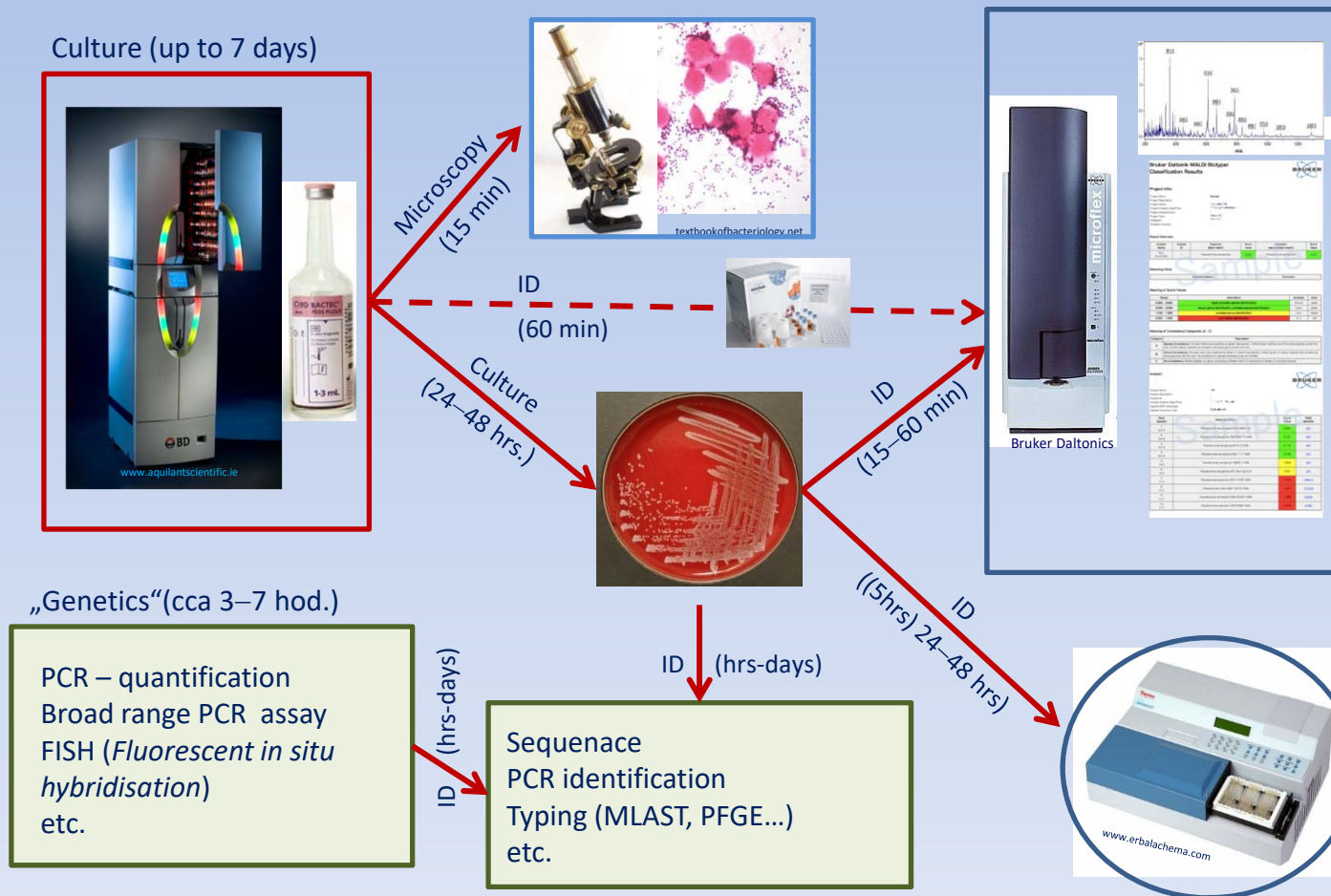
# Haemoculture sampling

- Skin disinfection
  - 0,5% chlorhexidine in 70% alcohol
  - Polyvinylpyrolidon w. 10% of iodine
  - Iodine tincture
  - 70% alcohol
- Change of needle
- Disinfection of bottle end-seal



# Haemoculture examination

**Rapidity + sensitivity + specificity**



# Haemoculture examination

- Positivity
- Length of culture
  - HACEK
  - Fungaemia
- TTD
- No of anaerobic BSI very low

# Other possibilities of sepsis diagnostic

- Serology
- Biochemistry
- MALDI from sample

# Proof of catheter colonisation

## A) Catheter *in situ*

- Quantification of haemocultures
  - Quantity of microbes in catheter sample
  - Comparison of microbial quantity in samples from periphery and from catheter
- Difference in TTD in haemocultures from periphery and from catheter
- Intraluminal brush
- AOLC (Acridine Orange Leukocyte Cytospin)

# Proof of catheter colonisation

## B) Extracted catheter

- Sonication, vortexing
- Semiquantitative method
- Intraluminal flush
- Subculture + subsequent inoculation
- Catheter staining

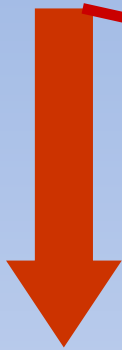
# Interpretation of positive results

- 80% of primary bacteraemia CVCs
- CoNS
- STAU
- ECSP & CASP
- Catheter infection
  - Extraluminal
  - Haematogenic infection
  - Endoluminal

# Interpretation of positive results

- Depends on the species of isolated microbe
- Obligate pathogens
- Typical nosocomial pathogens of BSI
- Saprophytic microbes

# Therapy of CRBSI



**Elimination  
of focus**

+  
ATB

**Retaining of infected catheter**

Less serious CRBSI

Stabilised patient

Reaction on ATB therapy



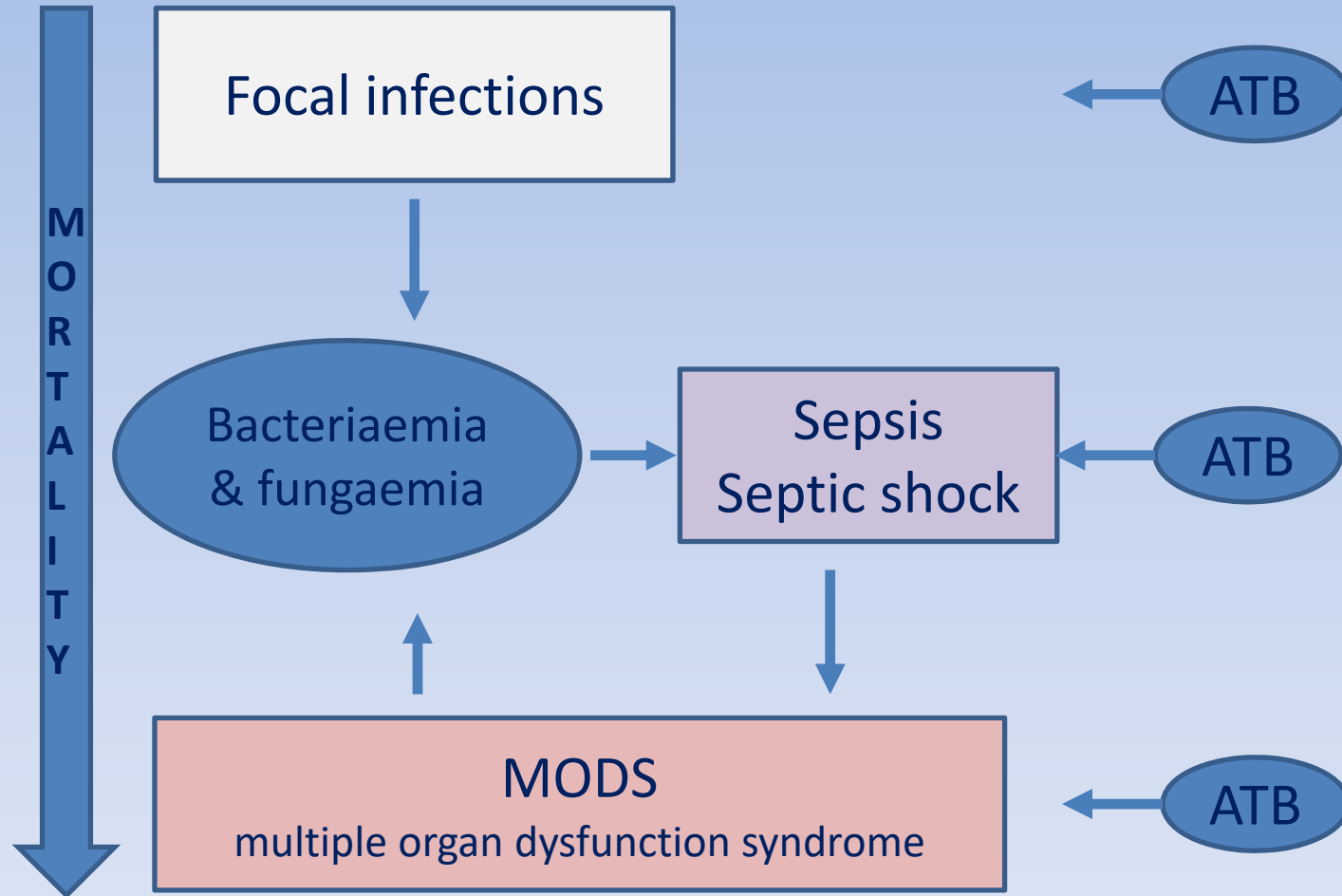
**Attempt at eradication of biofilm**



# ATB therapy of CRBSI

- Systemic ATB treatment
  - × **Fails in eradication of biofilm layer**
- ATB with higher anti-biofilm effect
- Advantage to combine ATBs
- Antimicrobial lock

# Chance of ATBs to affect infectious process



# Treatment of the sepsis

- **Control the infection**
  - Elimination of CA
  - Finding the focus and surgical intervention
  - Removal of cause of septic state
- **Symptomatic therapy**
  - Breathing support
  - Adjustment of haemodynamic
  - Support for failing organs
  - Continuous veno-venous hemodiafiltration
  - In DIC (disseminated intravascular coagulation)

