



# Infections in immunocompromised patients

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**Goloshchapov O.V.**

**2019**

**САНКТ-ПЕТЕРБУРГ**



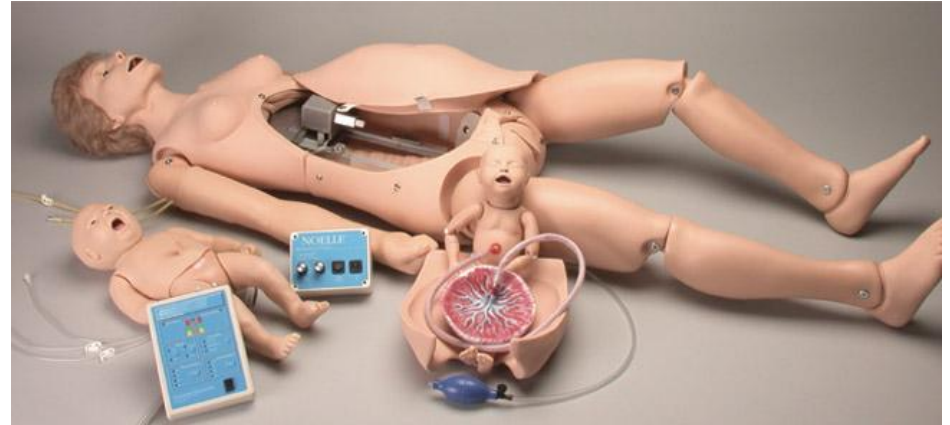
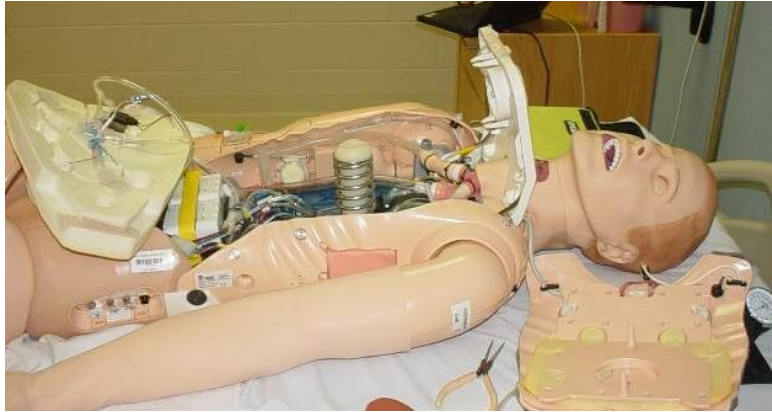
**05 июня, среда**

**12:00 – 12:40**

# Model of an immunocompromised patient?

Secondary Immunodeficiency - Immunocompromised Patient

HOW TO CREATE? How do you look? HOW TO TRAIN?



# Immunocompromised patient. WHERE IS HE?

## Causes of immunological failure

Allergic reactions

High microbial load

Eating disorder

- BEN
- Hypovitaminosis
- Micronutrient deficiency
- Obesity

Anatomical defects

Chronic diseases

- sakh. diabetes
- CRF
- metabolic disorders
- tumors

Iatrogenic factors

- extensive operations

Defects in the immune system

- Leukozy
- Lymphomas
- HIV

Poisoning

Burns

# PREMORBID CONDITION - the state of the organism preceding the development of the disease = Condition before HSCT

Numerous infectious episodes

History of invasive mycoses (aspergillosis)  
Transferred BMI, pneumonia, sinusitis

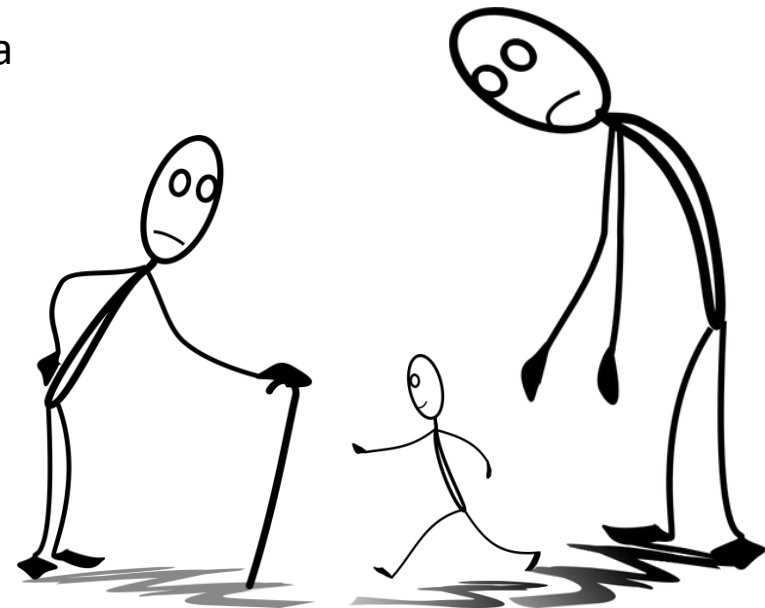
Virus infection - herpes group, polyomavirus

Eating disorders - low BMI, high BMI, cachexia

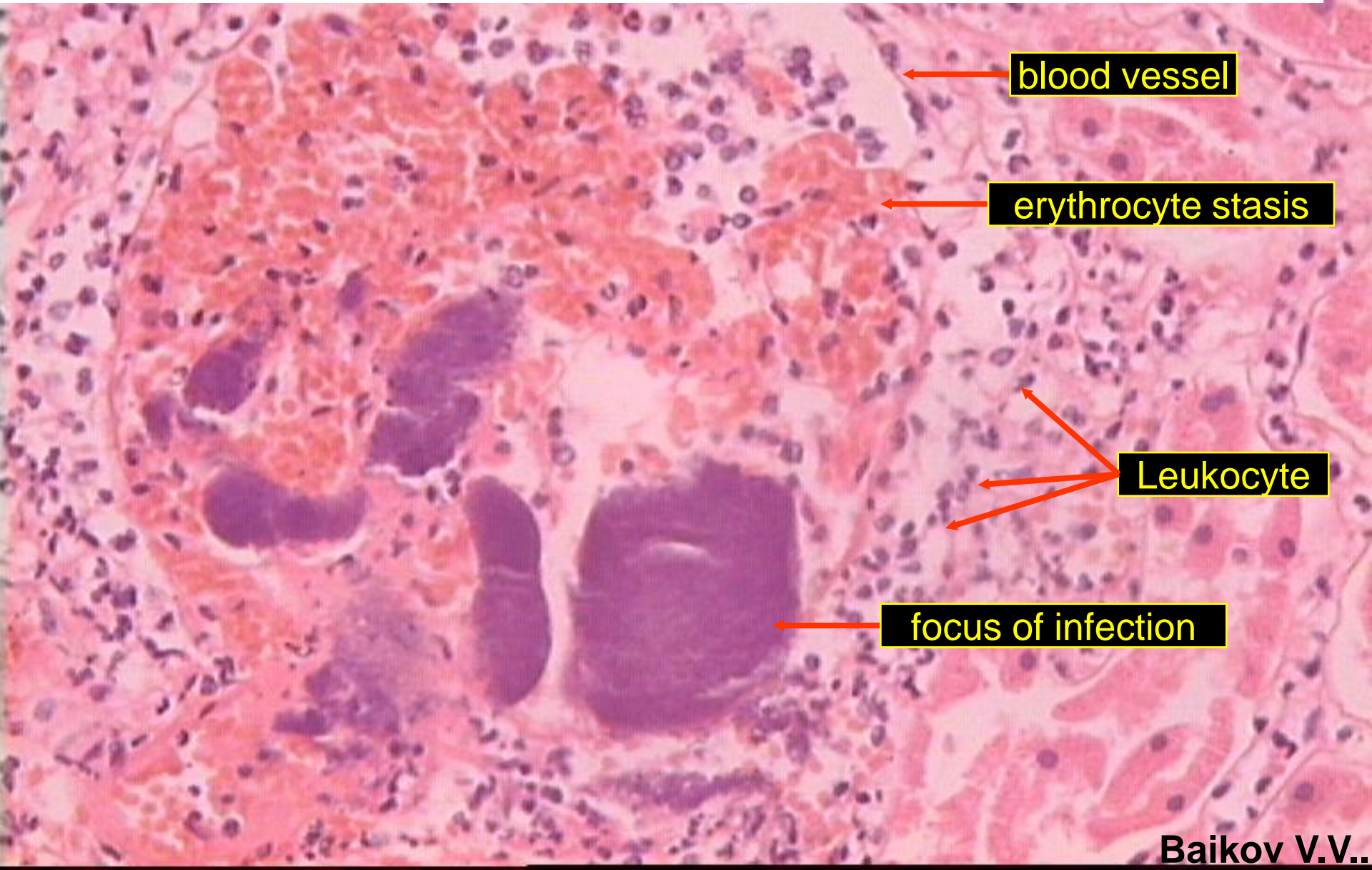
Genetic diseases - a violation of the metabolism of drugs, a  
violation of enzyme systems.  
Change in PD, PK drugs.

Relapse therapy (PCT, monoclonal a / t)

Age from 0 to 90

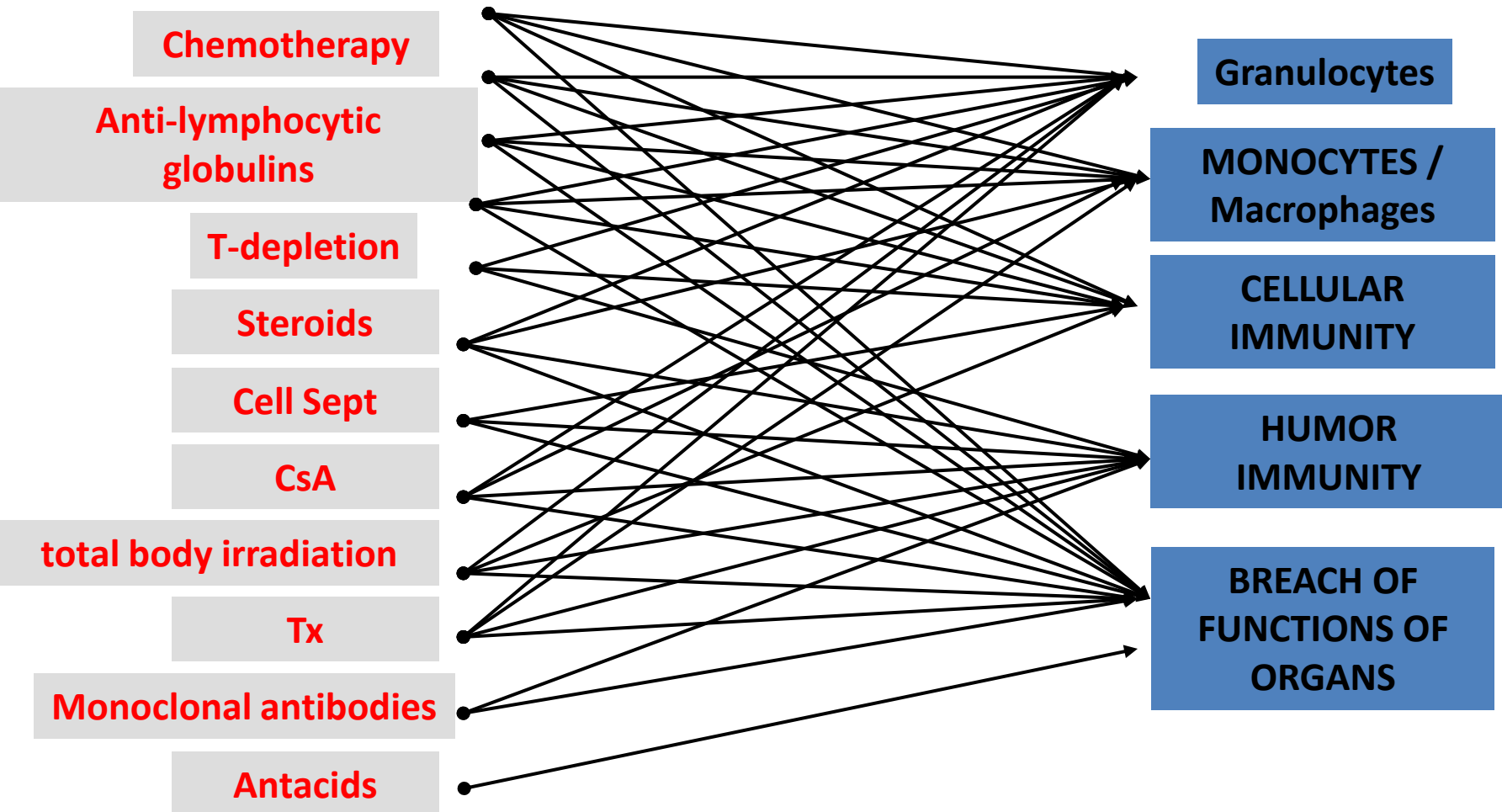


# Alternative exudative path tissue damage



# Risk factors for developing an oncohematological patient

## Patient model after BMT



HOW TO CREATE? - WE ALREADY CREATED (((

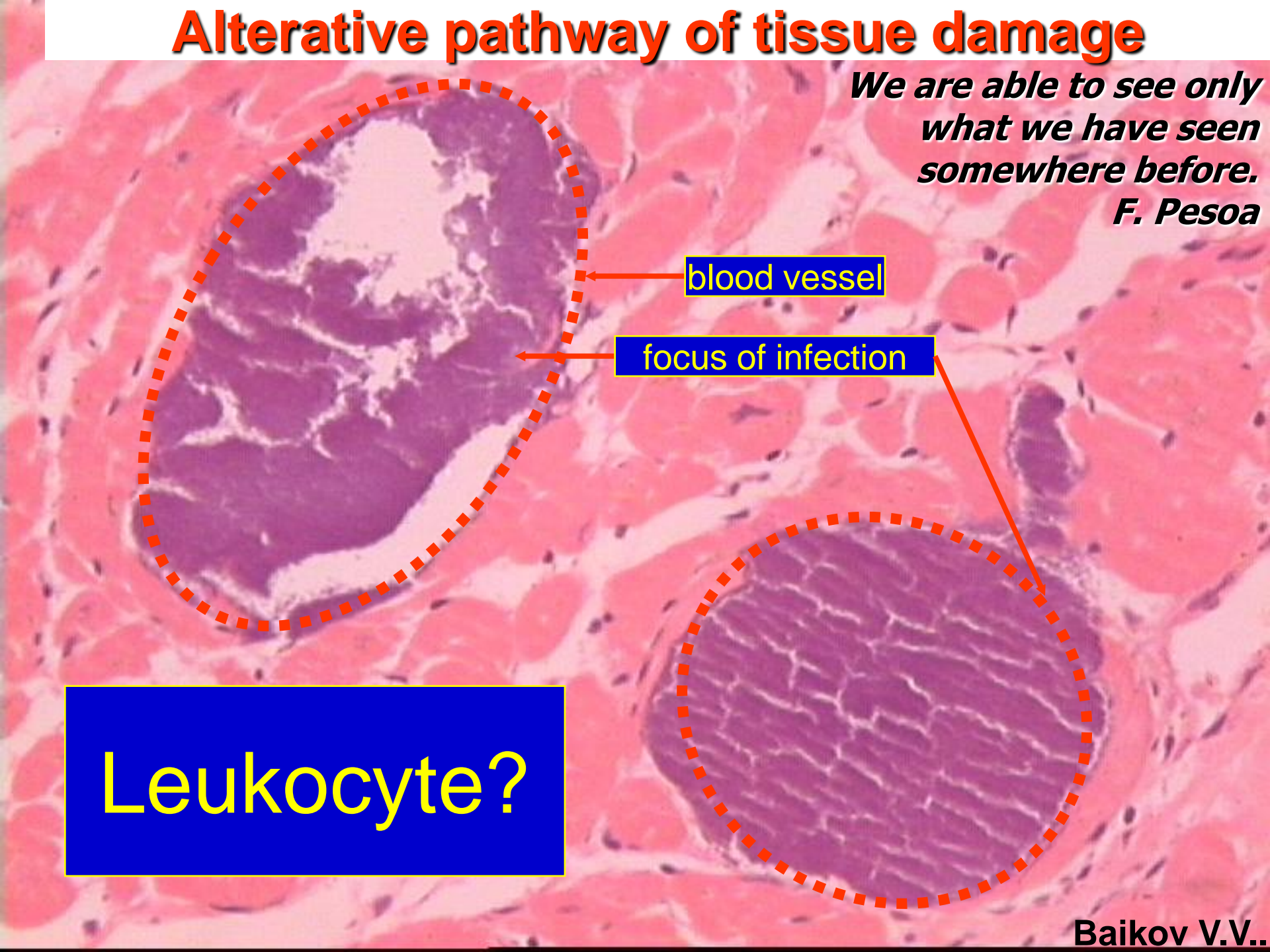
# Alterative pathway of tissue damage

*We are able to see only  
what we have seen  
somewhere before.  
F. Pessoa*

blood vessel

focus of infection

Leukocyte?



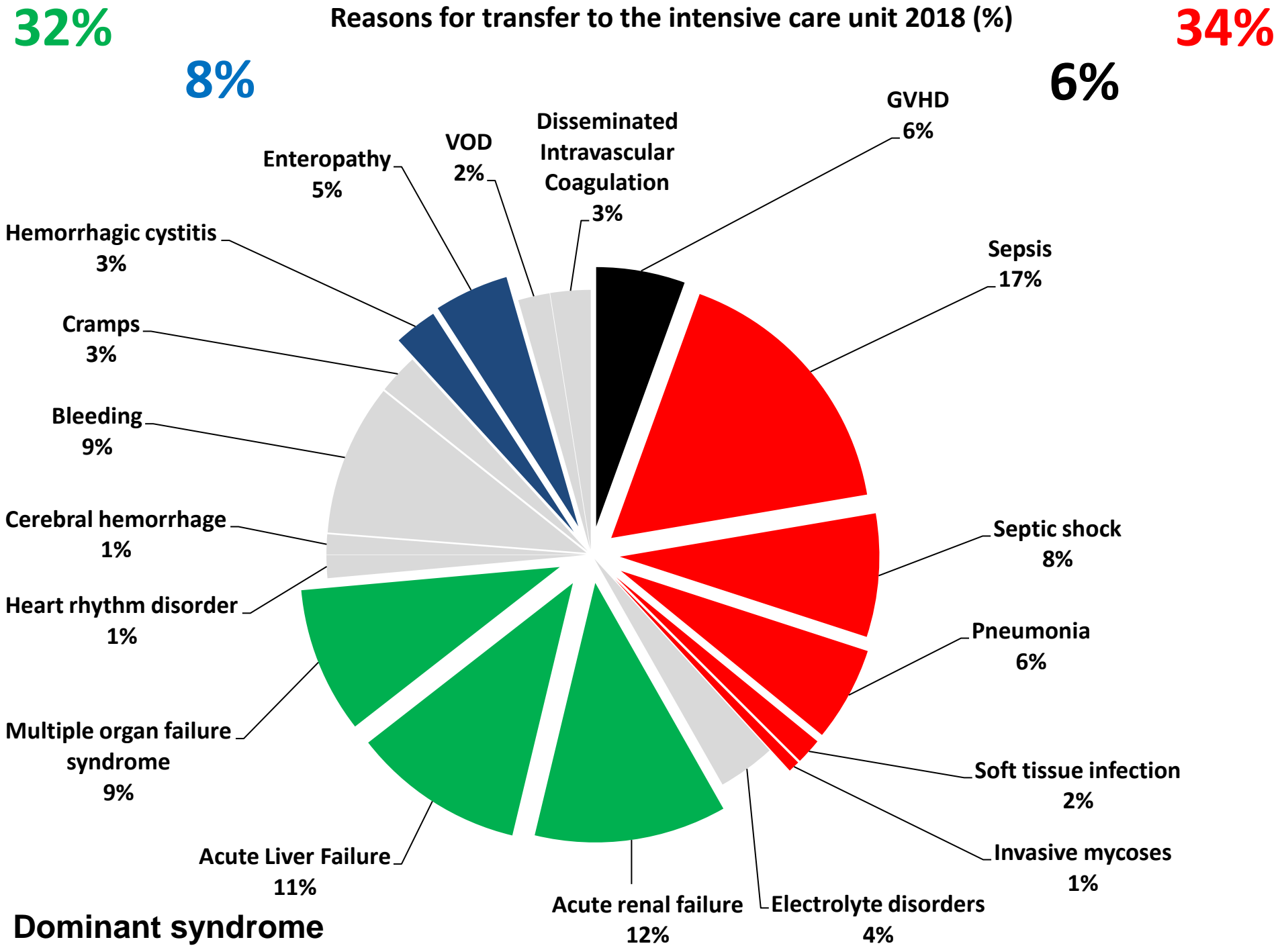
*intensive care unit - 2019*

Bruegel - 1668

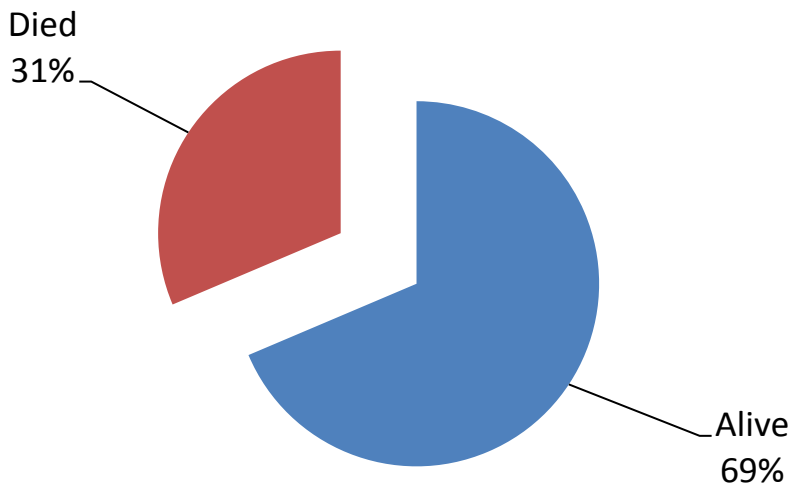




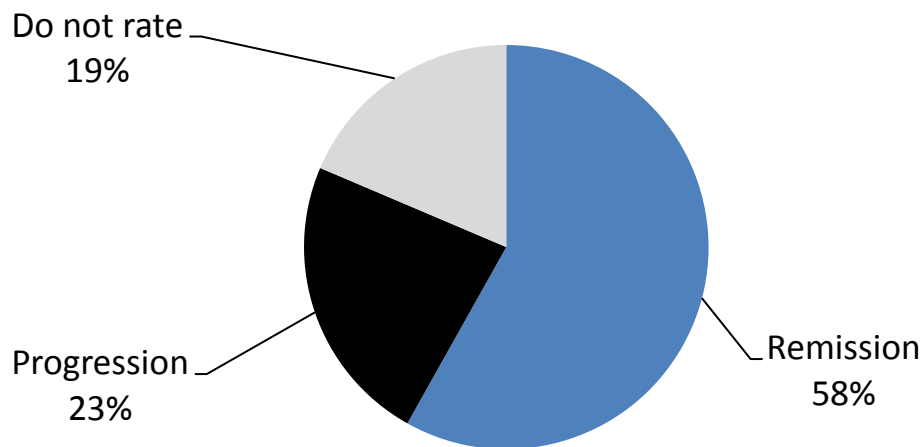
# Reasons for transfer to the intensive care unit 2018 (%)



**Mortality of patients with sepsis 2018 (%)**

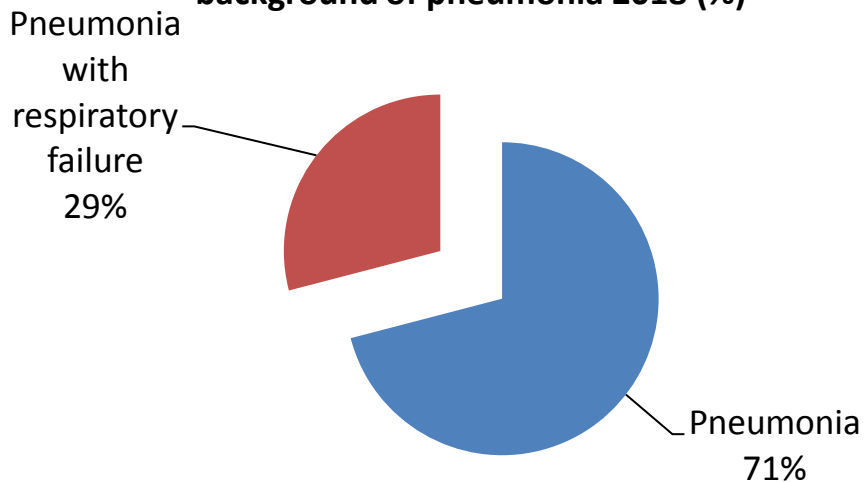


**The frequency of progress of the underlying disease 2018 (%)**

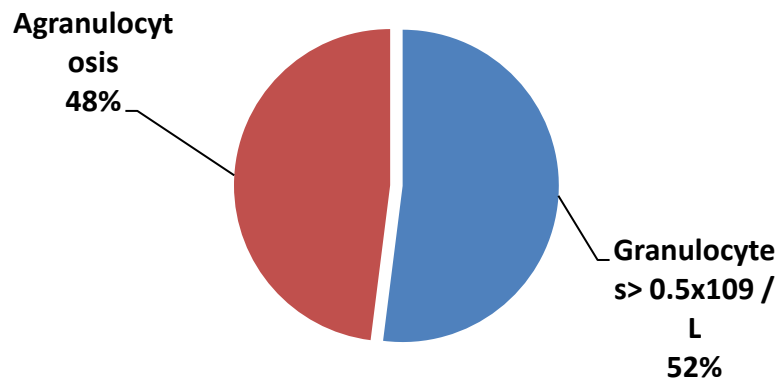


**Mortality rate from sepsis after BMT 55.1% (Kumar G.et.al 2015)**

**The frequency of respiratory failure on the background of pneumonia 2018 (%)**

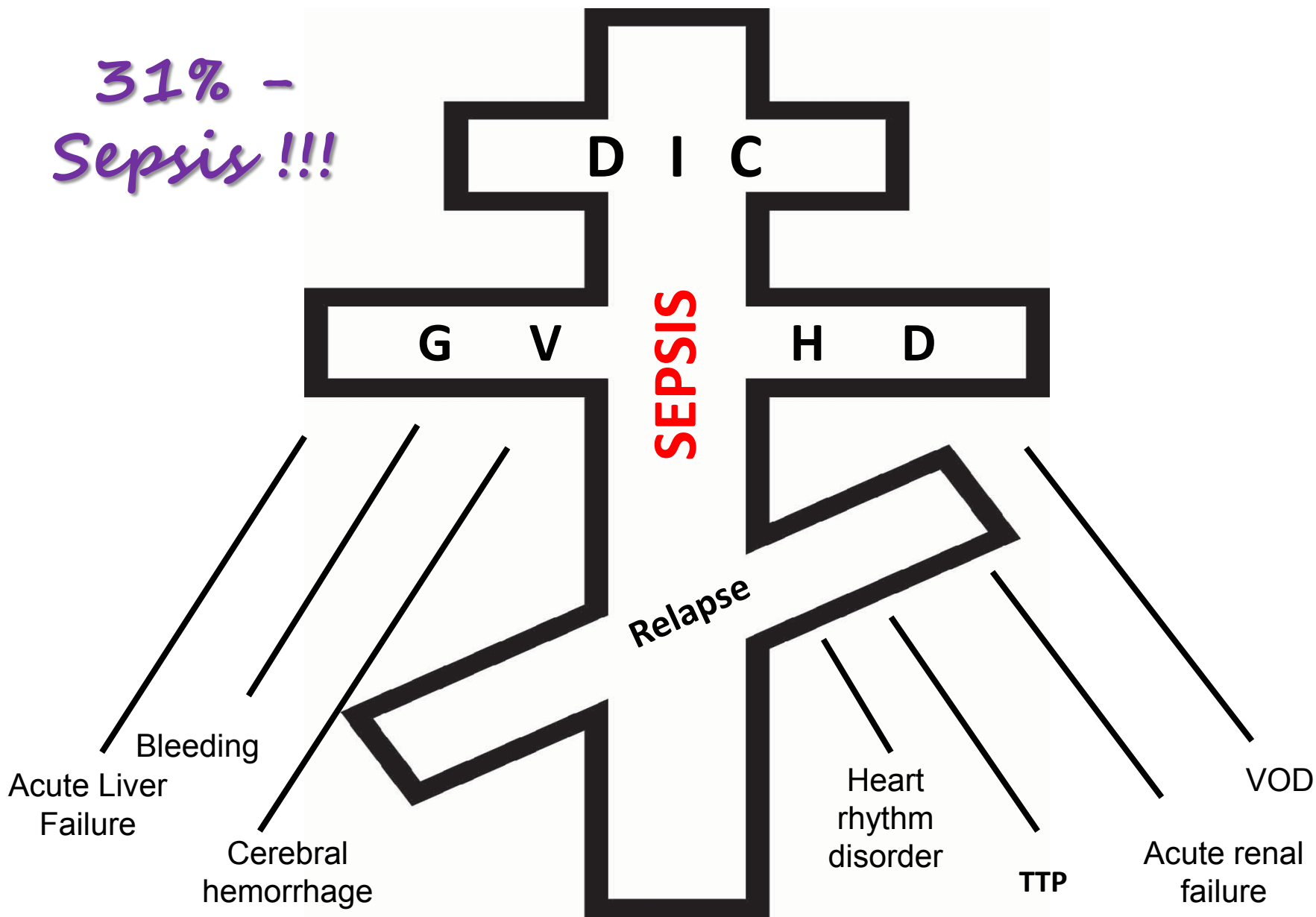


**The frequency of patients with agranulocytosis 2018 (%)**

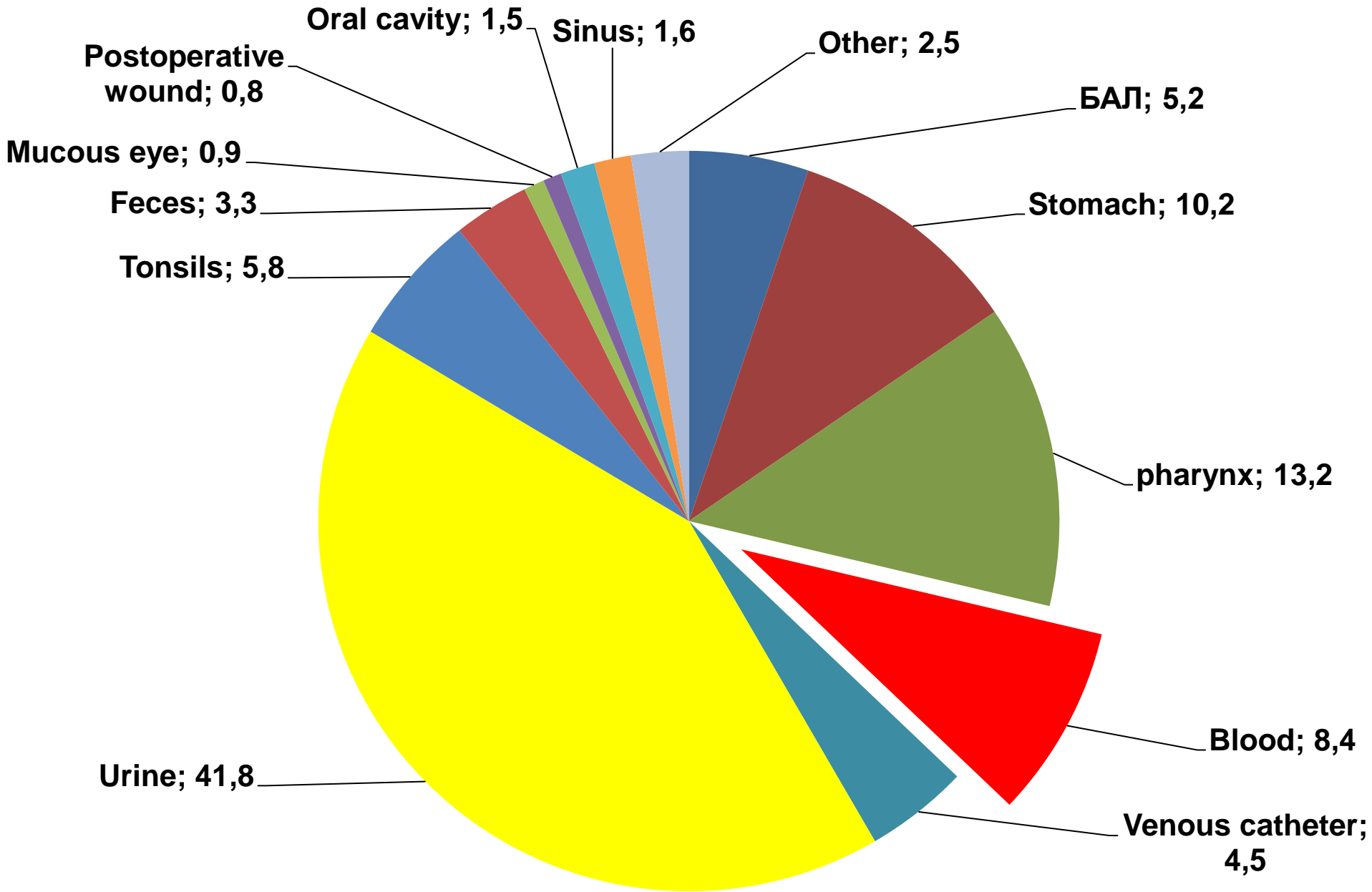


# CROSS - HEMATOLOGIST

31% -  
Sepsis !!!



# Structure of biological material from which microorganisms were isolated (%) 2018

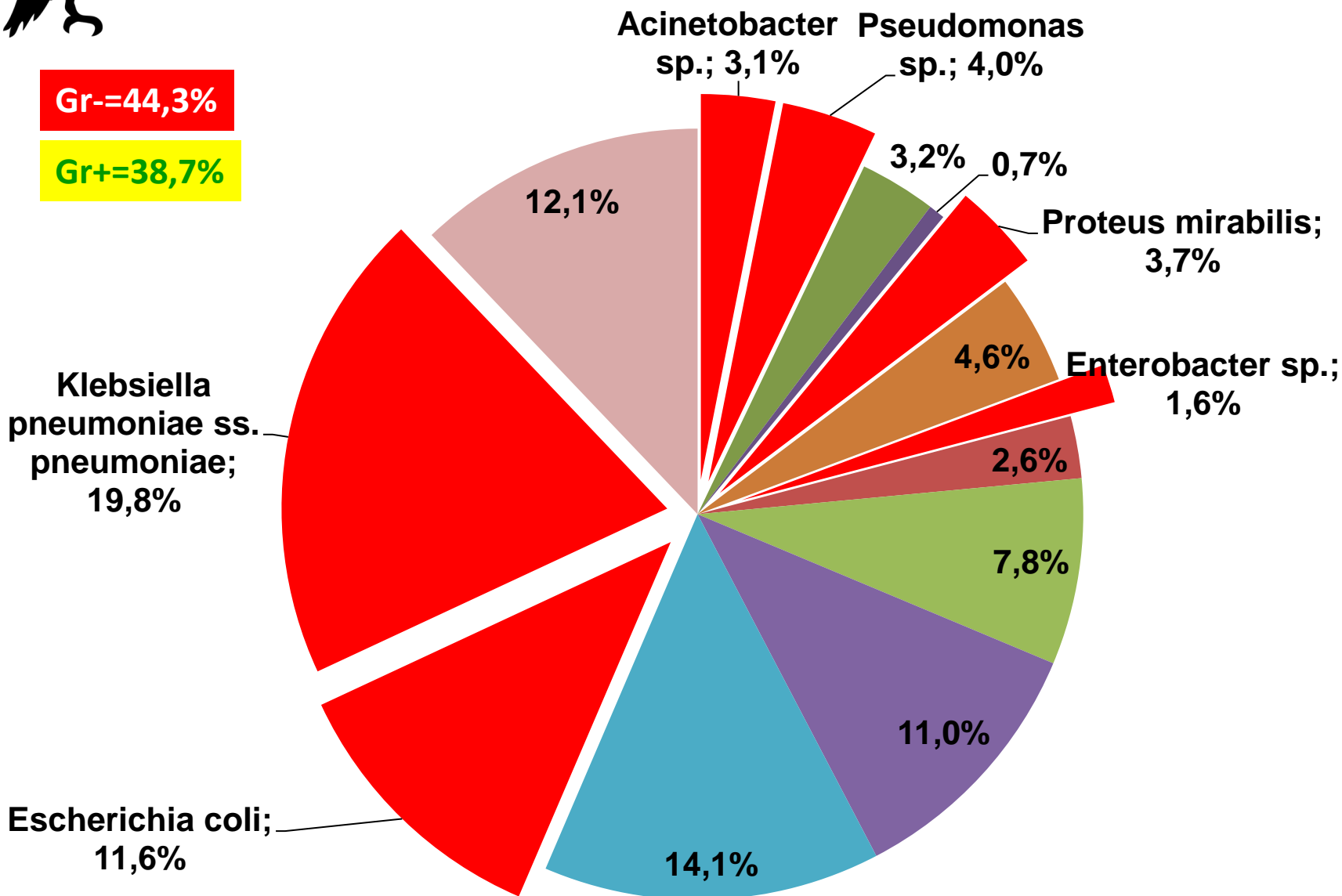




# The structure of microorganisms isolated from biological material (%) 2018

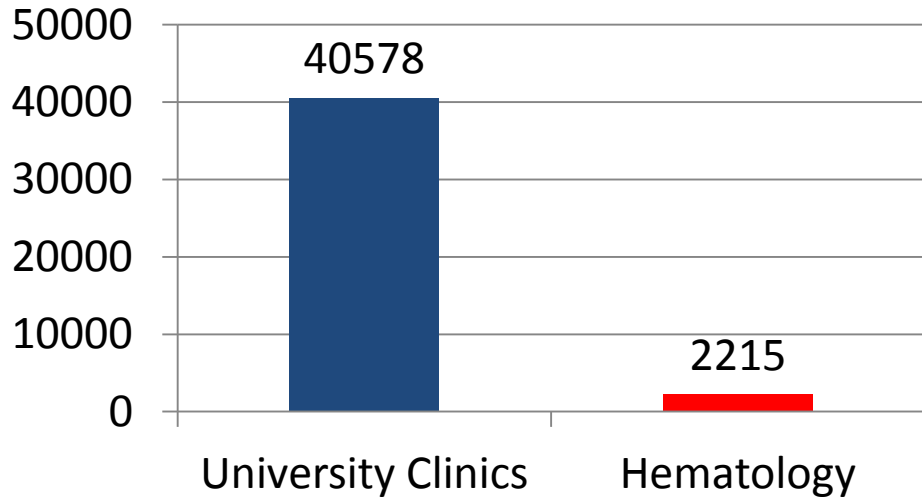
Gr-=44,3%

Gr+=38,7%

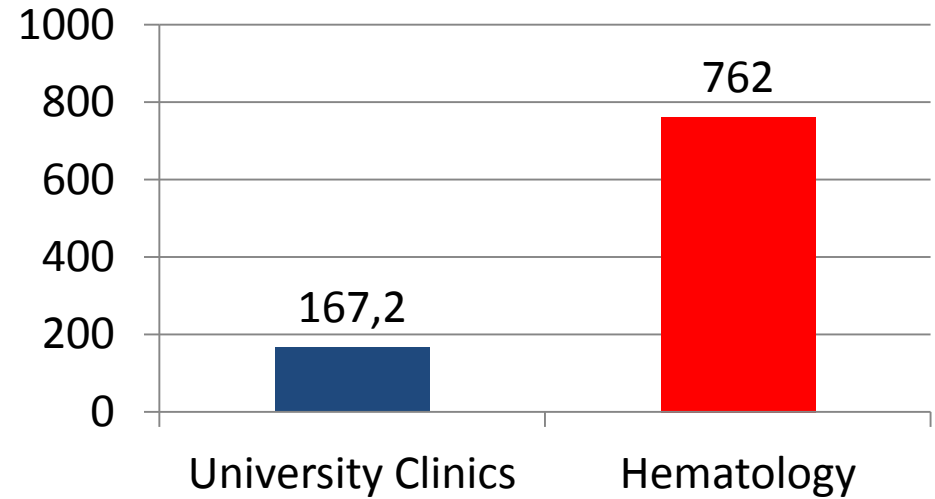


# Bacteriological studies 2 times a week

## Total received



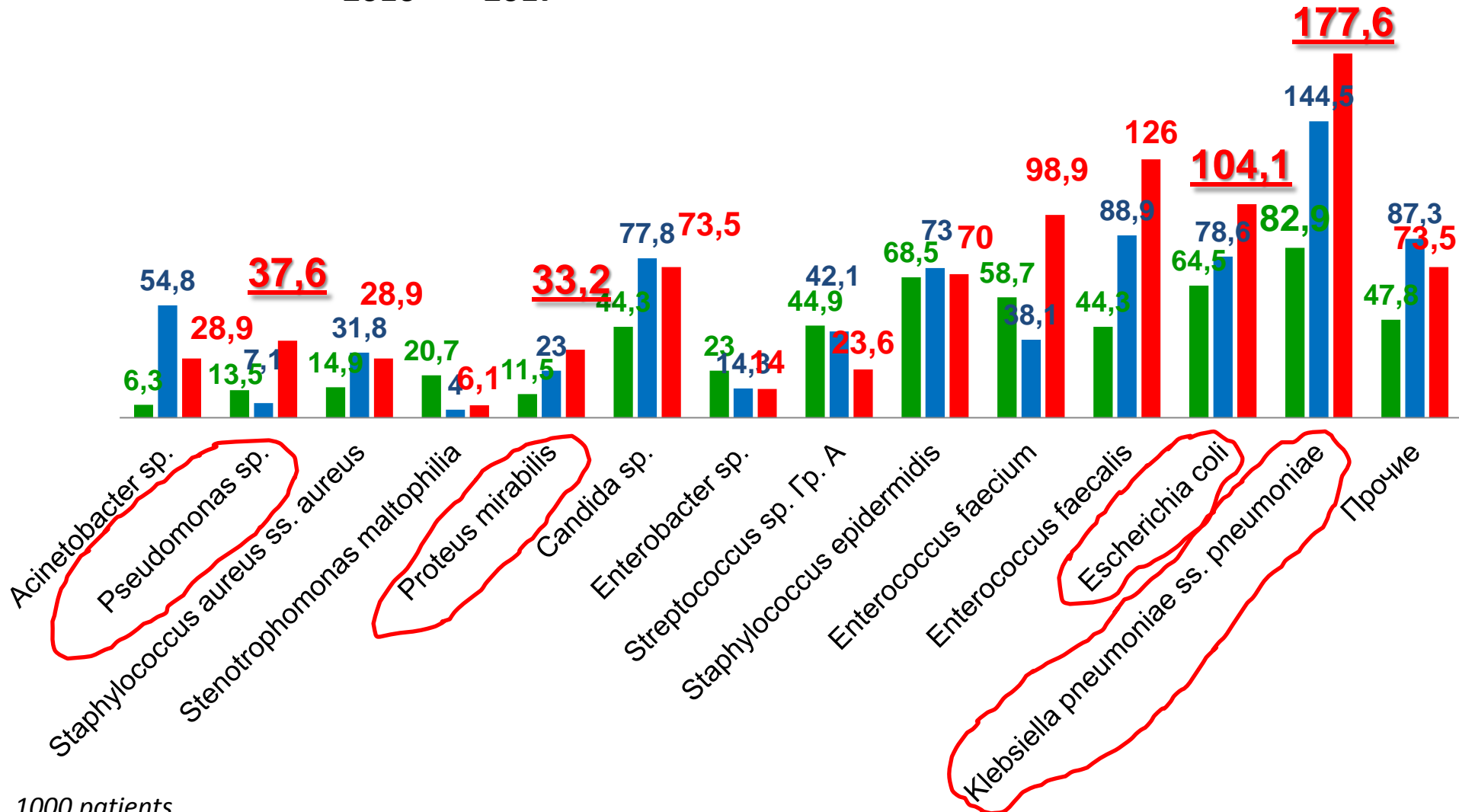
## Cases of microbial isolation



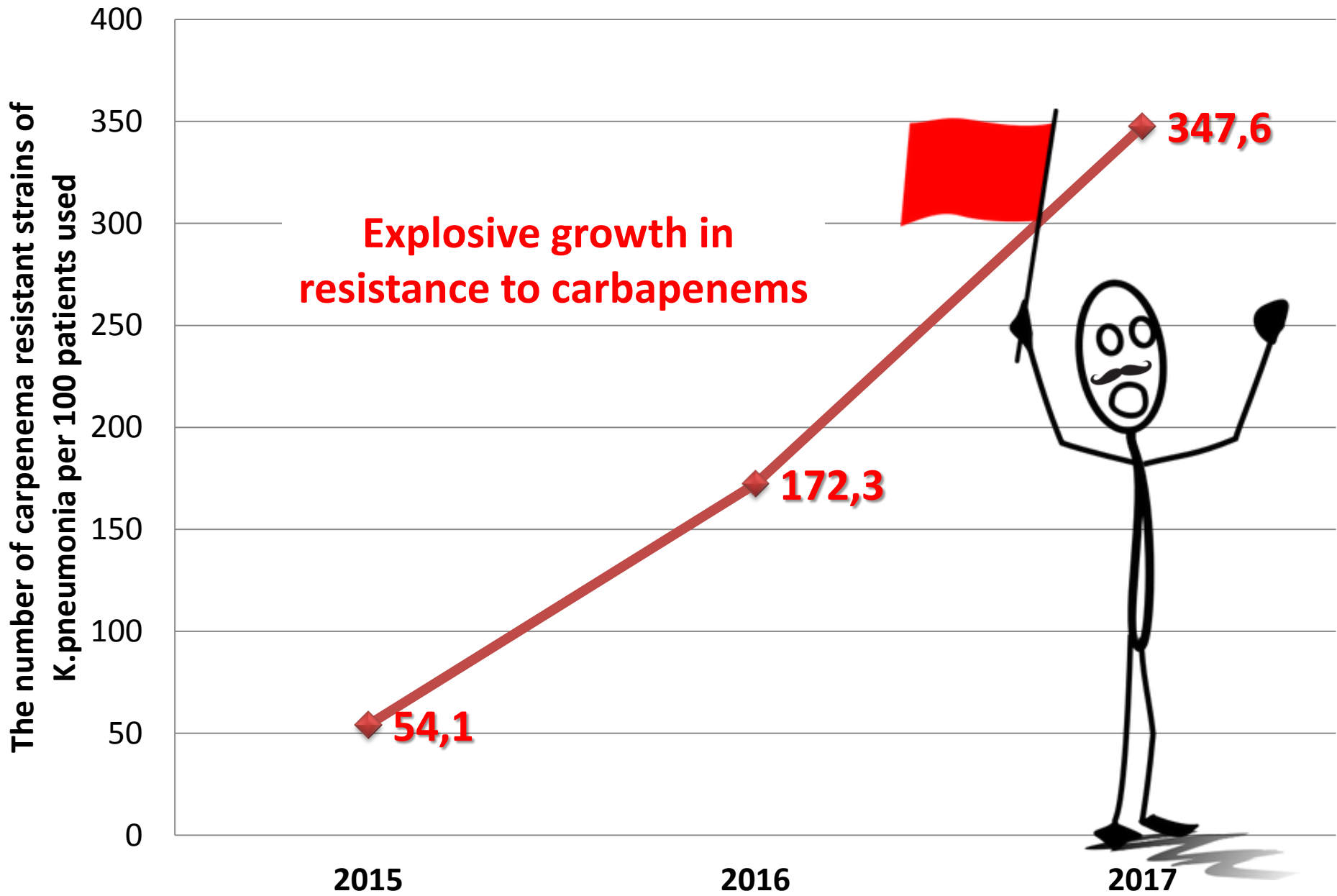
rate per 1000 received

# Long-term dynamics of changes in the structure of microorganisms isolated from all types of biological material ( 2015-2017)

■ 2015 ■ 2016 ■ 2017

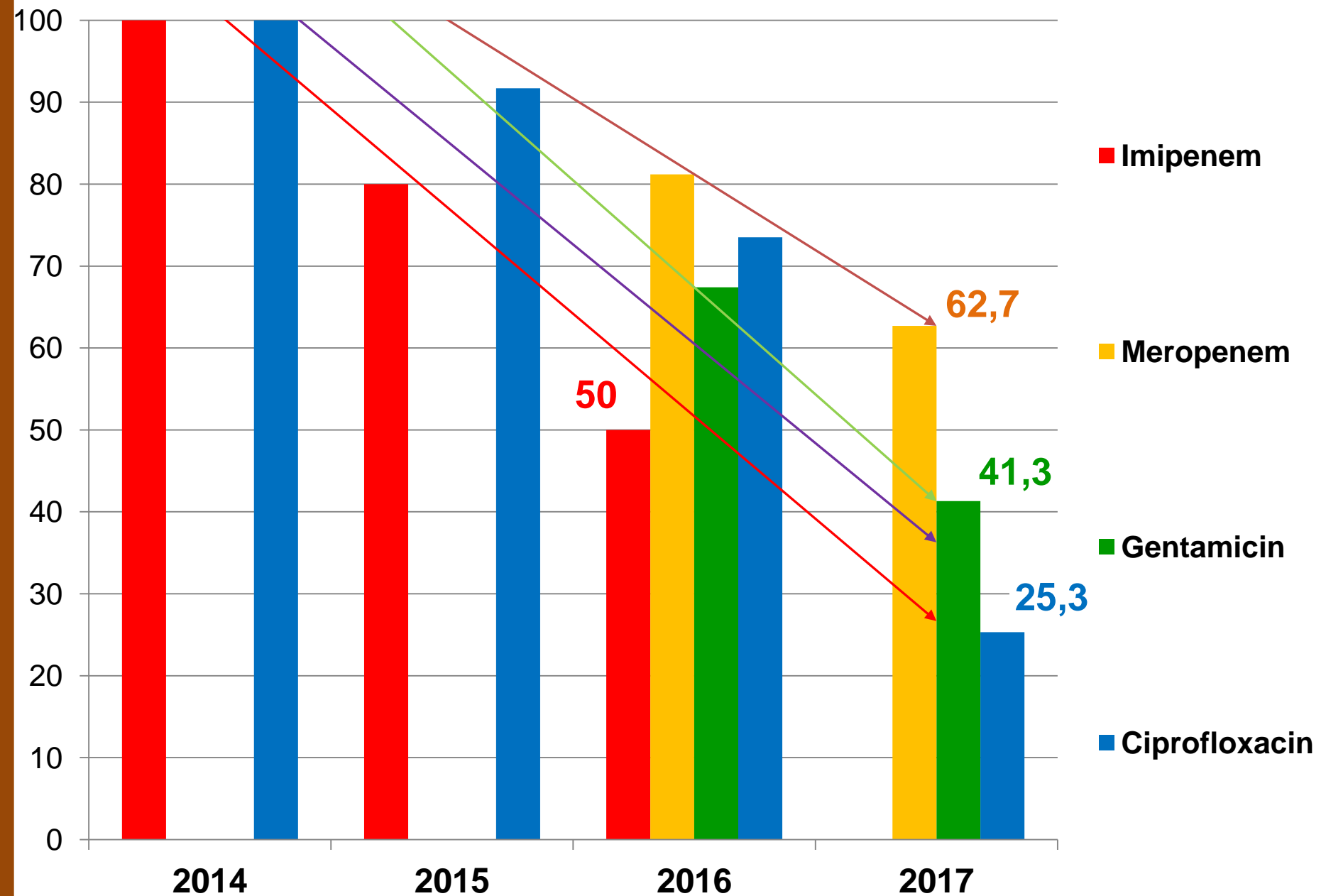


# Changes in the resistance of K.pneumonia strains isolated from patients (2015-2017)

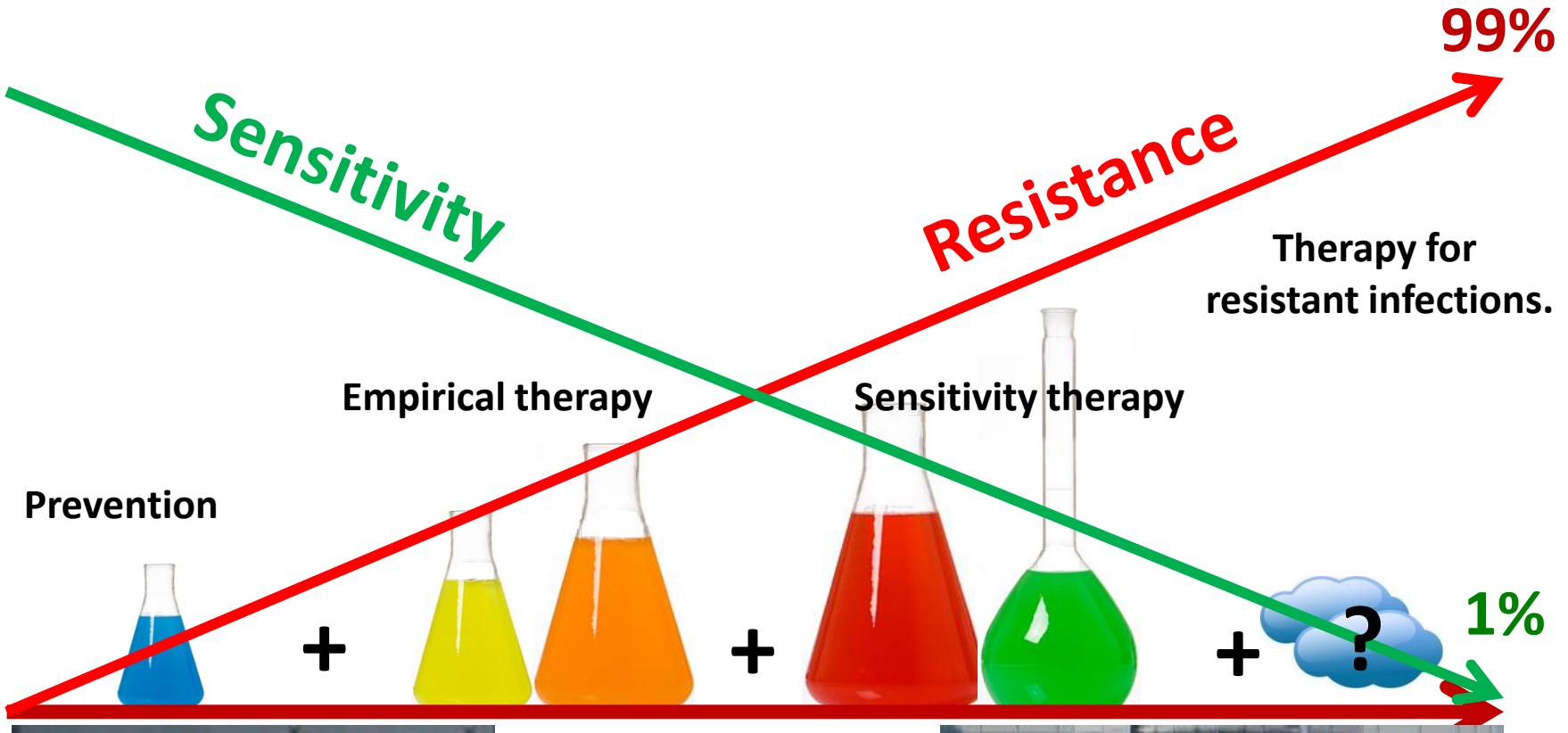




# Sensitivity of *Klebsiella pneumoniae* strains isolated from stool against CARBA, GENTA, CIPRO 2014-2017



DEPARTMENT WITH ABSOLUTE RESISTANCE



Time



## Patient characteristics

### Colonization of *Klebsiella pneumoniae* after BMT

n=12

<b>Возраст</b>	36(22/62)	
Диагноз	n	%
ОЛЛ	3	25
ХМЛ	3	25
НХЛ	1	8
ОМЛ	5	42
<b>Вид ТГСК</b>		
а.н.	10	83
а.р.	1	8
гапло	1	8
<b>Кондиционирование</b>		
Флюдарабин+Бусульфан	12	100
<b>Профилактика РТПХ</b>		
Такролимус+ММФ	2	17
Бендомустин+Сиролимус+ Руксолитиниб	1	8
Циклофосфан+Такролимус	1	8
Циклофосфан	1	8
Циклофосфан+Такролимус+М МФ	7	58

### Inclusion criteria

> 18 years old

- HSCT

*Study days*

1- Day of admission to the clinic

2-D-0-

3-D + 10

4-D + 20

5-D + 30

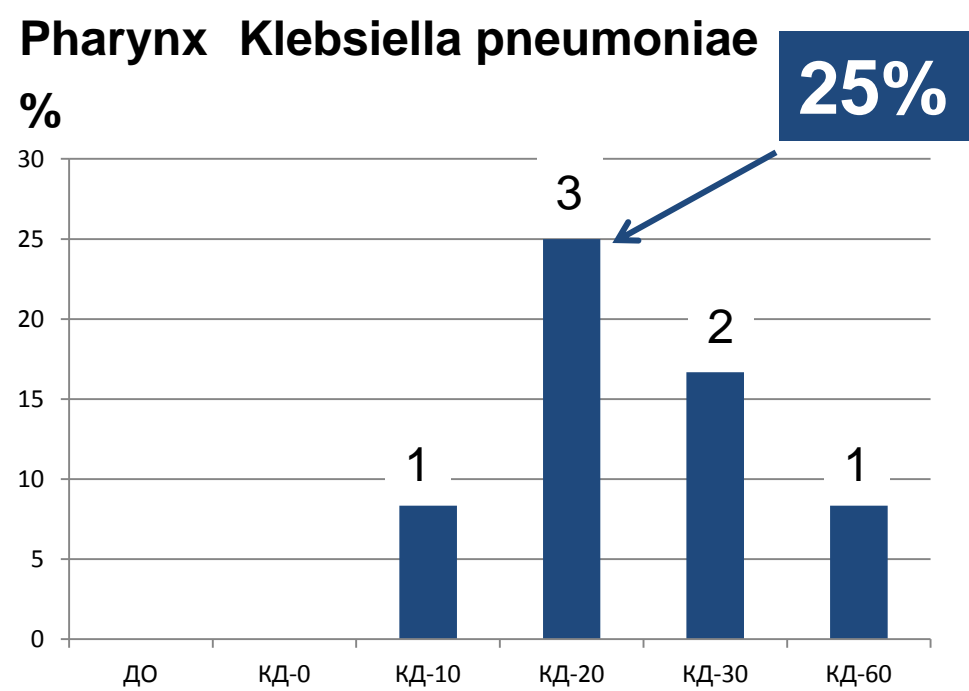
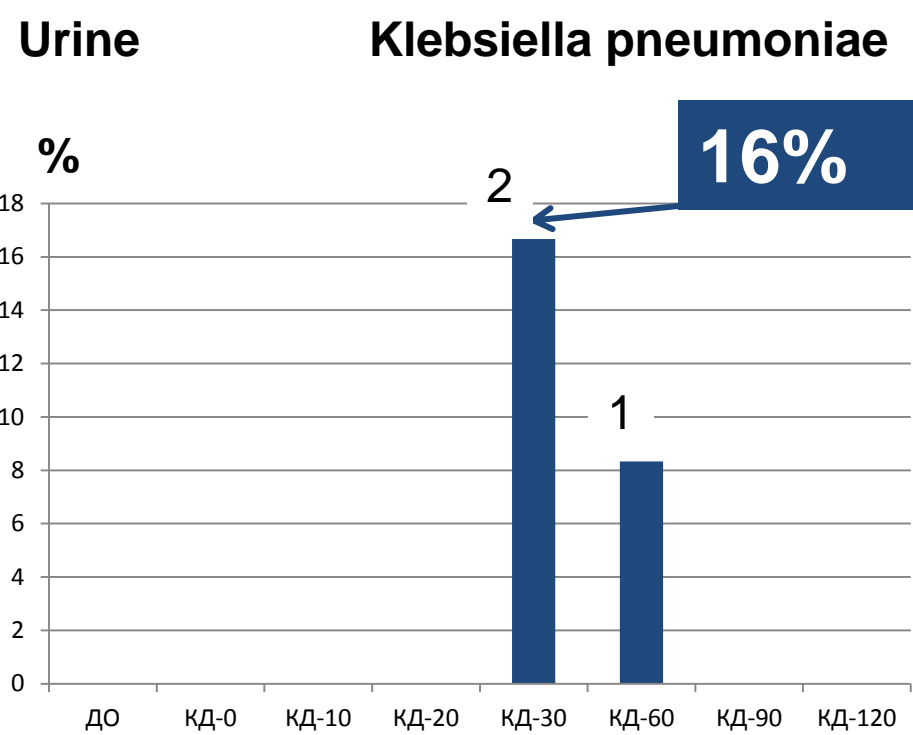
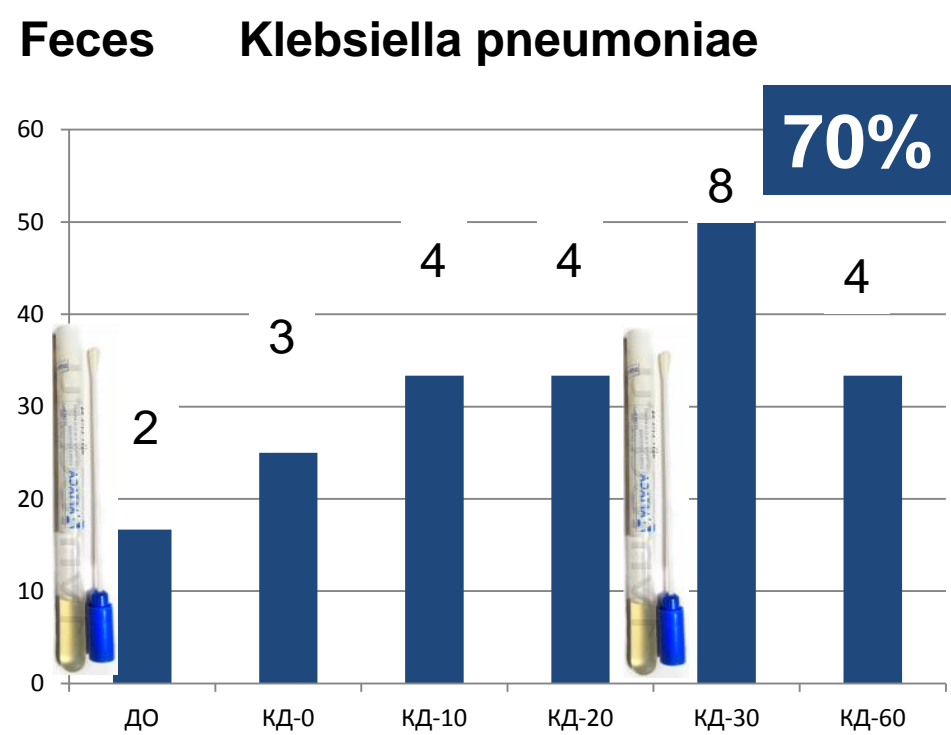
6-D + 60

### Research methods

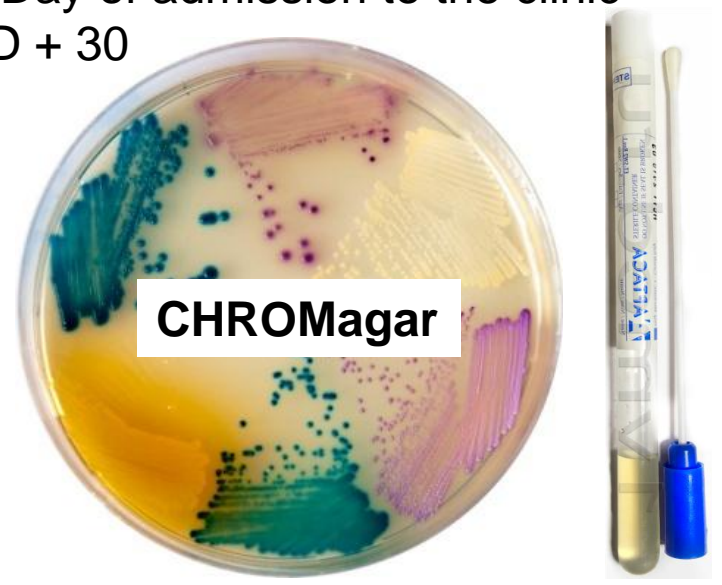
1-Microbiological method

2-sensitivity to a/b

3-Detection of ESBL CES,  
Carbapenem KEC, ESBL E. coli,  
Carbapenem E. coli, VRE using  
chromogenic media CHROMagar



1- Day of admission to the clinic  
2-D + 30

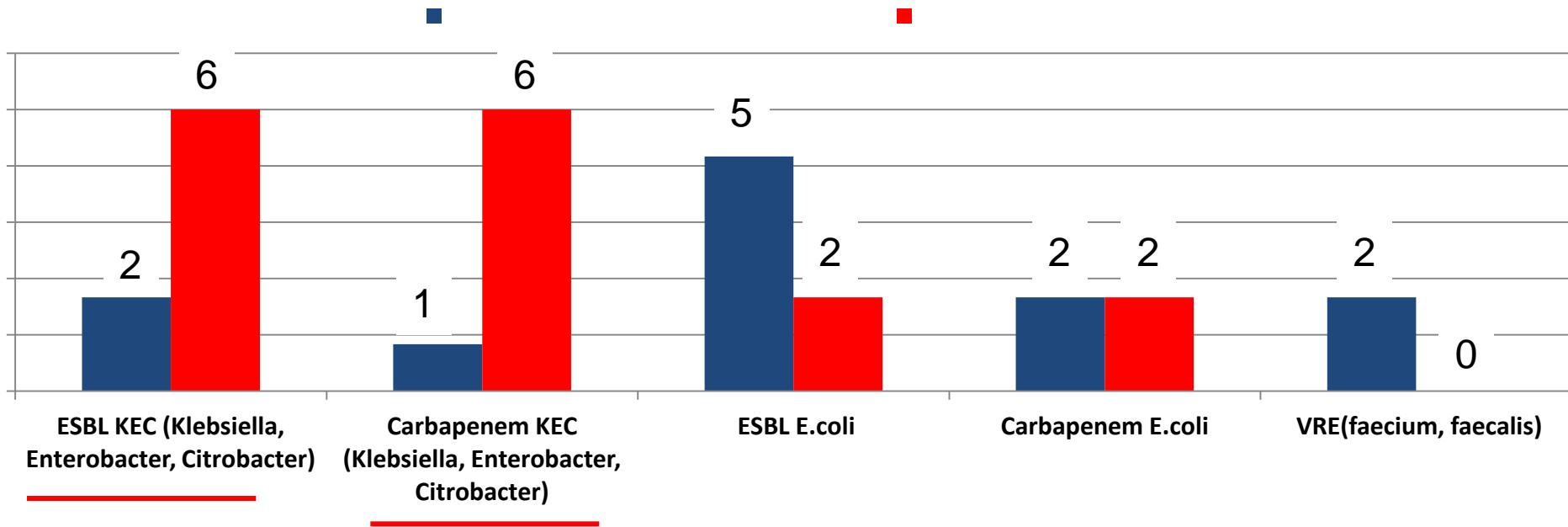
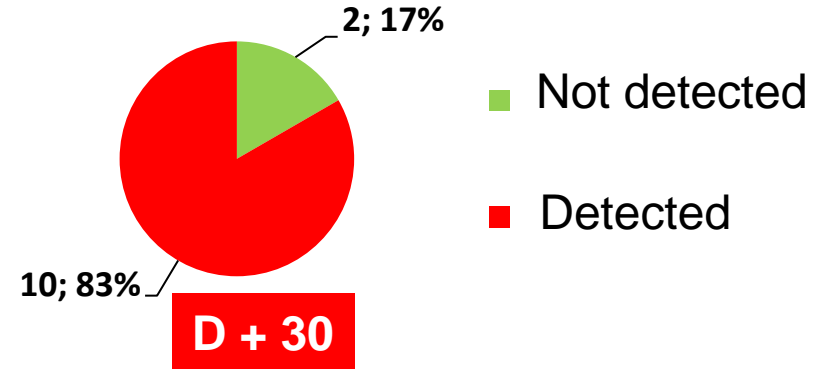
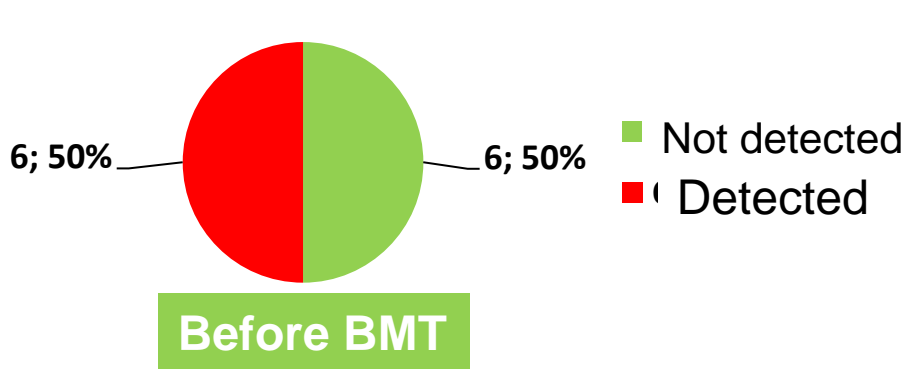


# Chromogenic environment CHROMagar to identify

ESBL KEC, Carbapenem KEC, ESBL E.coli,  
Carbapenem E.coli, VRE (faecium, faecalis)

Before BMT

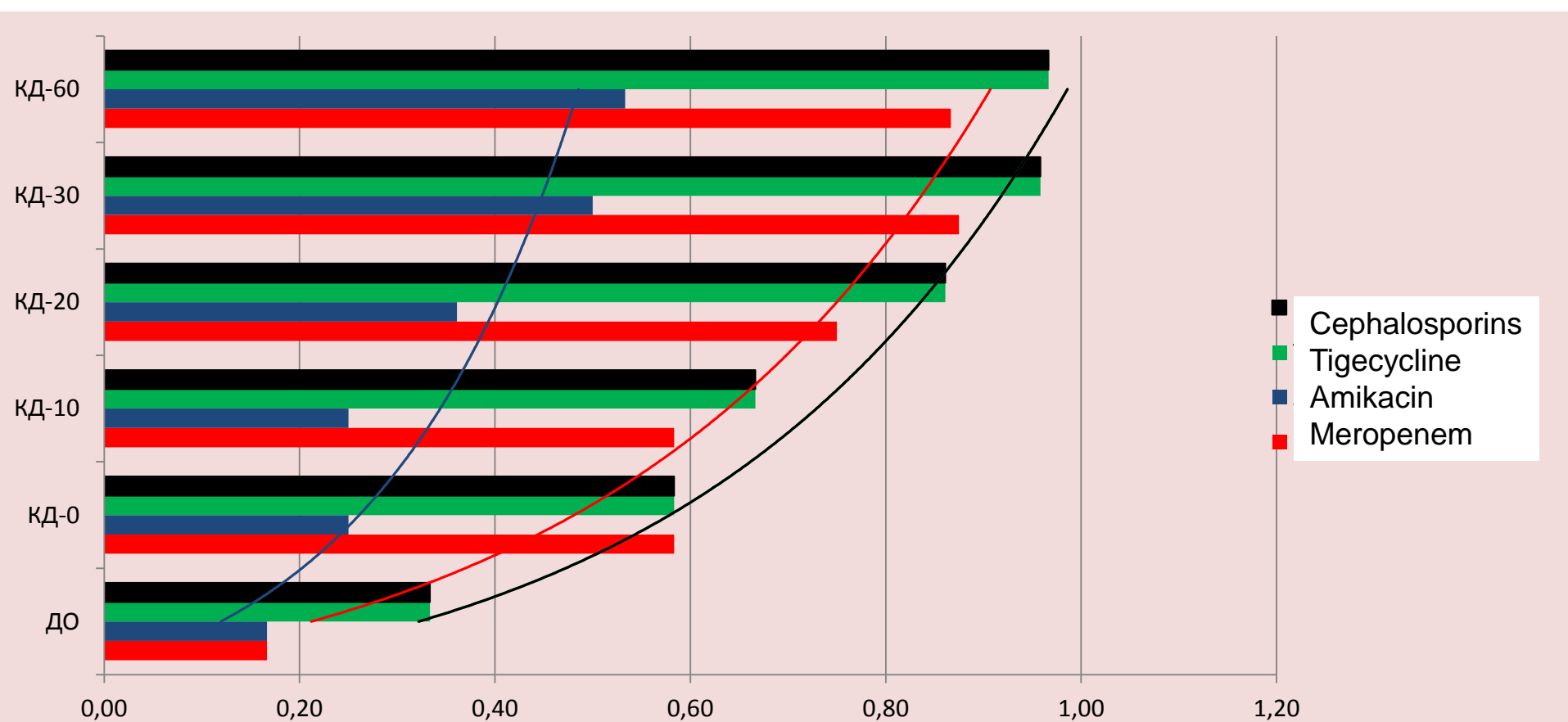
After BMT D + 30





# Feces Increased colonization, increased antibiotic resistance

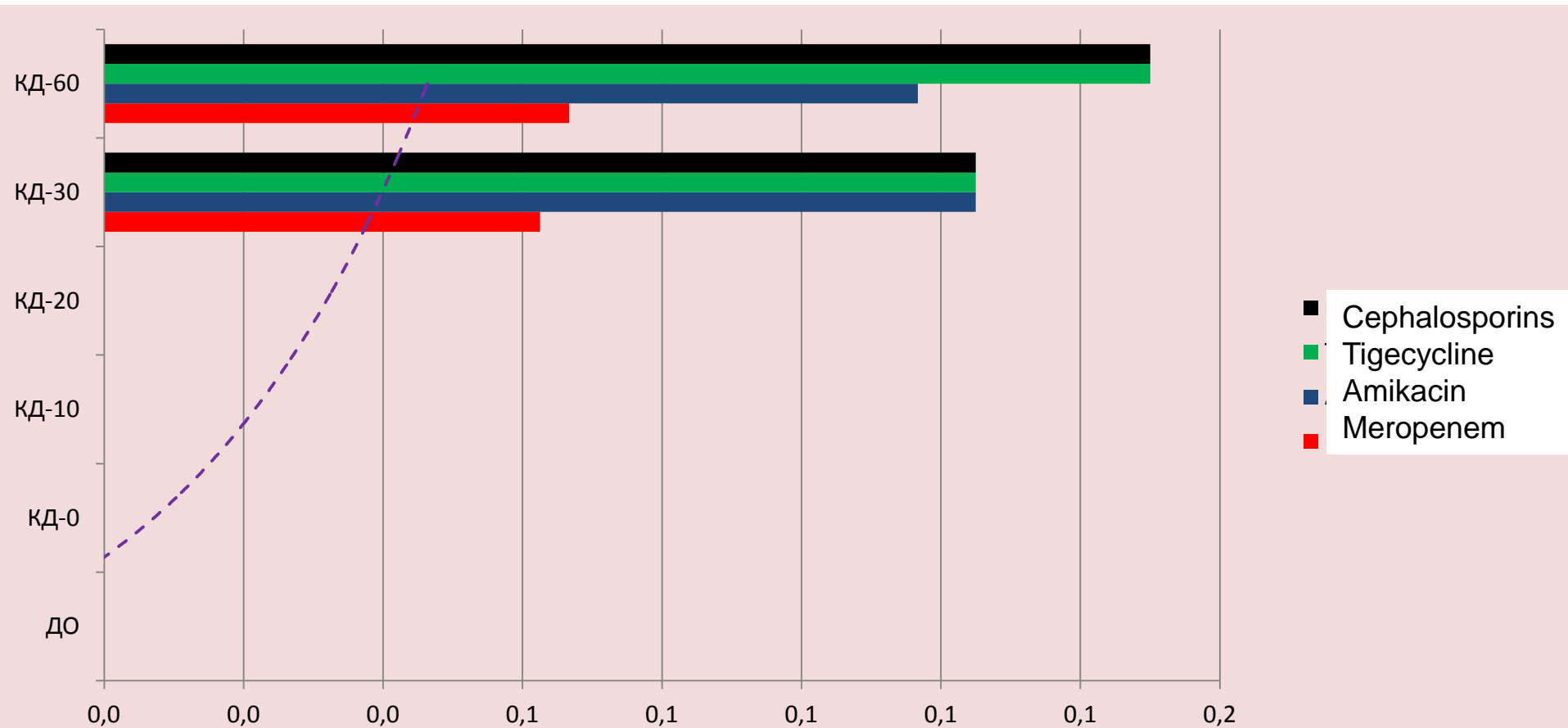
**n=12 patients after BMT**



Urine

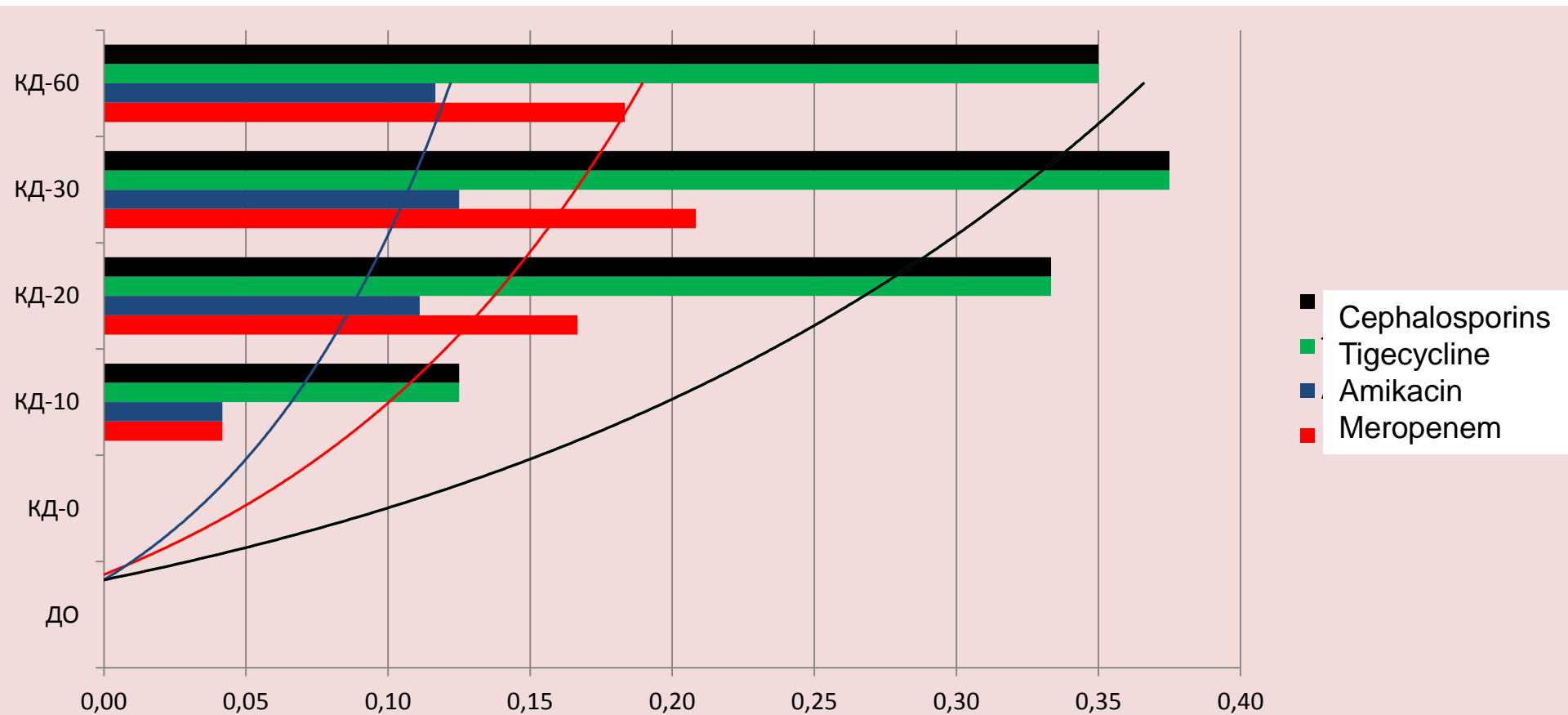
Increased colonization, increased antibiotic resistance

n=12 patients after BMT





n=12 patients after BMT



# Resistance *Acinetobacter* spp. in the hematology department (HD) intensive care unit (ICU)

55 isolates	HD/ICU	HD/ICU	HD/ICU
	S%	I%	R%
<b>Cefoperazone/Sulbactam</b> ★	<b>82/54</b>	<b>9/0</b>	<b>9/46</b>
☹️☹️ Ciprofloxacin	<b>10/8</b>	<b>14/0</b>	<b>76/92</b>
☹️ Imipenem	<b>26/8</b>	<b>15/0</b>	<b>59/92</b>
☹️ Meropenem	<b>32/0</b>	<b>17/18</b>	<b>51/82</b>
☹️ Netilmicin	<b>34/0</b>	<b>5/0</b>	<b>61/100</b>
<b>Tigecycline</b> ★★	<b>98/100</b>	<b>2/0</b>	<b>0/0</b>

Recommendations for starting therapy in the hematology department (HD)

Cefoperazone/Sulbactam

Recommendations for starting therapy in the intensive care unit (ICU)

Tigecycline

# Resistance *Klebsiella* spp. in the hematology department (HD) intensive care unit (ICU)

825 isolates		HD/ICU	HD/ICU	HD/ICU
		S%	I%	R%
Amikacin	☹️	36/15	19/11	66/53
Aztreonam	☹️	7/2	0/1	93/97
Cefoperazone/Sulbactam	★	63/27 ☹️	2/2	35/71
Ciprofloxacin	☹️☹️	9/5	2/6	89/89
Colistin	★★	98/93	0/0	2/7
Imipenem		★76/37 ☹️	1/4	23/59
Meropenem		★63/36 ☹️	3/8	34/56
Netilmicin	☹️	33/13	6/0	61/87
Tigecycline	★★	95/93	3/2	2/3

Meropenem

Imipenem

Tigecycline

Colistin

Recommendations for starting therapy in the hematology department (HD)

Recommendations for starting therapy in the intensive care unit (ICU)

# Resistance Enterobacter spp. in the hematology department (HD) intensive care unit (ICU)

515 isolates	HD/ICU	HD/ICU	HD/ICU
	S%	I%	R%
<b>Amikacin</b> ★	<b>94/79</b>	<b>1/8</b>	<b>5/13</b>
<b>Aztreonam</b> 😞	<b>30/12</b>	<b>0/3</b>	<b>70/85</b>
<b>Cefoperazone/Sulbactam</b> ★	<b>97/74</b>	<b>1/10</b>	<b>2/16</b>
<b>Ciprofloxacin</b> 😞😞	<b>17/25</b>	<b>6/25</b>	<b>77/50</b>
<b>Colistin</b> ★★	<b>94/100</b>	<b>0/0</b>	<b>6/0</b>
<b>Imipenem</b> ★★	<b>99/95</b>	<b>0/0</b>	<b>1/5</b>
<b>Meropenem</b> ★★	<b>92/100</b>	<b>0/8</b>	<b>8/0</b>
<b>Netilmicin</b> 😞	<b>59/13</b>	<b>8/0</b>	<b>33/87</b>
<b>Tigecycline</b> ★★	<b>100/100</b>	<b>0/0</b>	<b>0/0</b>

Cefoperazone/Sulbactam  
Amikacin  
Meropenem

Tigecycline    Colistin

Recommendations for starting therapy in the hematology department (HD)

Recommendations for starting therapy in the intensive care unit (ICU)

# Resistance **E. Faecalis** / **E. Faecium**

in the hematology department (HD) intensive care unit (ICU)

515 isolates	HD/ICU	HD/ICU	HD/ICU
<b>E. faecalis</b>	S%	I%	R%
Ampicillin	★ 85/85	1/4	14/11
Ampicillin/Sulbactam	★ 95/96	0/0	5/4
Linezolid	★ 100/100	0/0	0/0
Tigecycline	★ 100/96	0/0	0/4
Vancomycin	★ 100/96	0/0	0/4
<b>E. faecium</b>	S%	I%	R%
Ampicillin	☹ 0/0	0/0	100/100
Ampicillin/Sulb.	☹ 0/0	0/0	100/100
Linezolid	★ 100/100	0/0	0/0
Tigecycline	★ 100/100	0/0	0/0
Vancomycin	★ 92/75	0/0	8/25
Clindamycin	☹ 0/0	0/0	100/100

	HD/ICU	HD/ICU	HD/ICU
<b>Staphylococcus</b>	S%	I%	R%
Daptomycin	★100/100	0/0	0/0.
Ampicillin/Sulbactam	☹️ 18/17	0/0	82/83
Linezolid	★ 99/97	0/0	1/3.
Tigecycline	★ 99/100	0/0	1/0.
Vancomycin	★100/100	0/0	0/0.
Clindamycin	☹️ 56/45	7/9	37/46
Oxacillin	☹️ 24/10	0/0	76/90
<b>Streptococcus spp.</b>	S%	I%	R%
Levofloxacin	☹️ 63/60	5/10	32/30
Ampicillin/Sulb.	67/50	3/5	30/45
Ceftriaxone	☹️ 35/36	18/11	47/53
Tigecycline ★	★ 100	0	0.
Vancomycin ★	★ 90	0/0	10.
Clindamycin	☹️ 52/20	3/10	45/70
Erythromycin	☹️ 18/10	10/0	72/90

**The problem is drug combinations.**

**Mono or combination therapy?**

**Have you asked a clinical pharmacologist?**

**Who is prescribing more than two antibiotics?**

**Too many antibiotics!**

**Too expensive!**

**Well, who treats like that?**

# Resistant therapy *Klebsiella* spp.

Bacteremia *Klebsiella pneumoniae* KPC+  
- effect only from the combined ABT

n=41

78% -внутрибольничная инфекция

## 1) 28-day mortality

- Mono: 57,8%
- Combo: 13,3% p=0.01

## 2) Multivariate analysis:

Combined ABT was significantly associated with patient survival,  
OR = 0.07 (95% CI 0.009-0.71, p = 0.02)

**The most effective combinations:**

**Tigecyclin + Carbapenem**

**Colistin + Carbapenem**

carbapenem-  
resistant  
strains



# Mortality

## Combination therapy

Колистин

+

Carbapenems

Tigecyclin

Fluoroquinolones

13%

Tigecyclin

+

Carbapenems

Aminoglycosides

## Monotherapy

Colistin

Tigecyclin

Carbapenems

Gentamicin

Ampicillin-sulbactam

Piperacillin-Tazobactam

57,8%

In Vitro – OK!!!



# Effect of combination therapy

## KPC Klebsiella spp. – with bloodstream infections

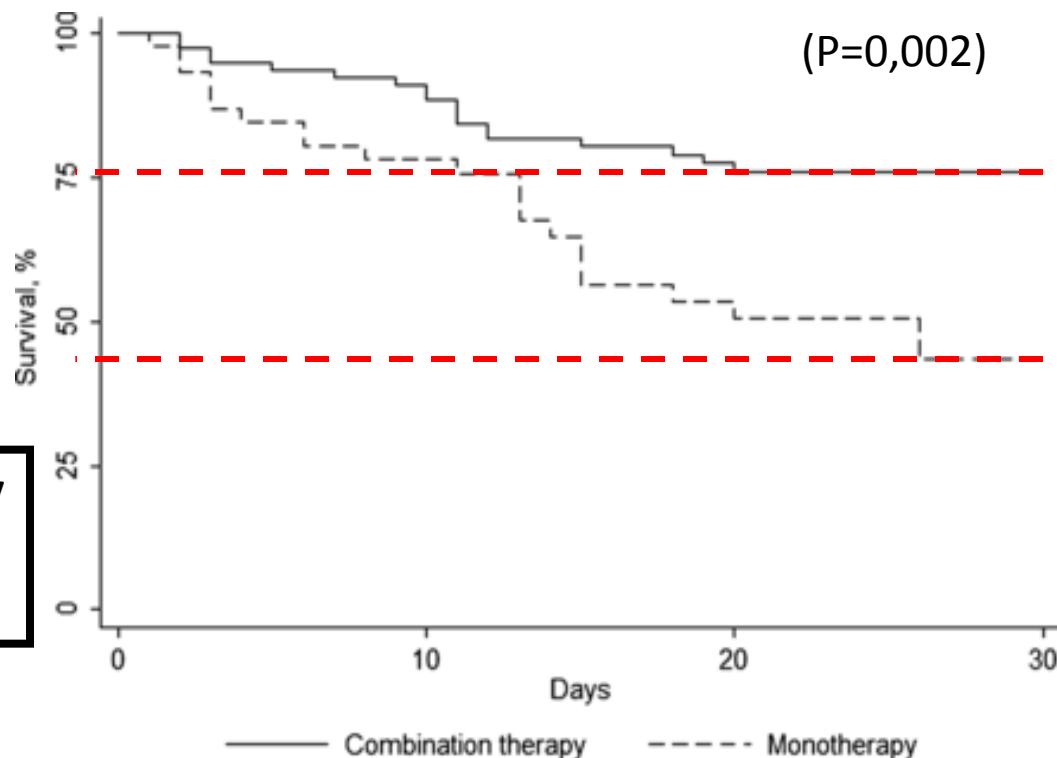
n=125

### Mortality %

Mono - 54,3

2 AB - 41,1

3 AB - 17,4



Inadequate initial antimicrobial therapy  
- cause of death  
(P = 0,003)

**Tigecyclin + Carbapenems + Colistin**

P = 0,01

**Tigecyclin + Carbapenems + Gentamicin**

**Colistin + Carbapenems + Gentamicin**

# Resistant therapy Klebsiella spp.

N=250

## Mortality %

Mono: 44,4%

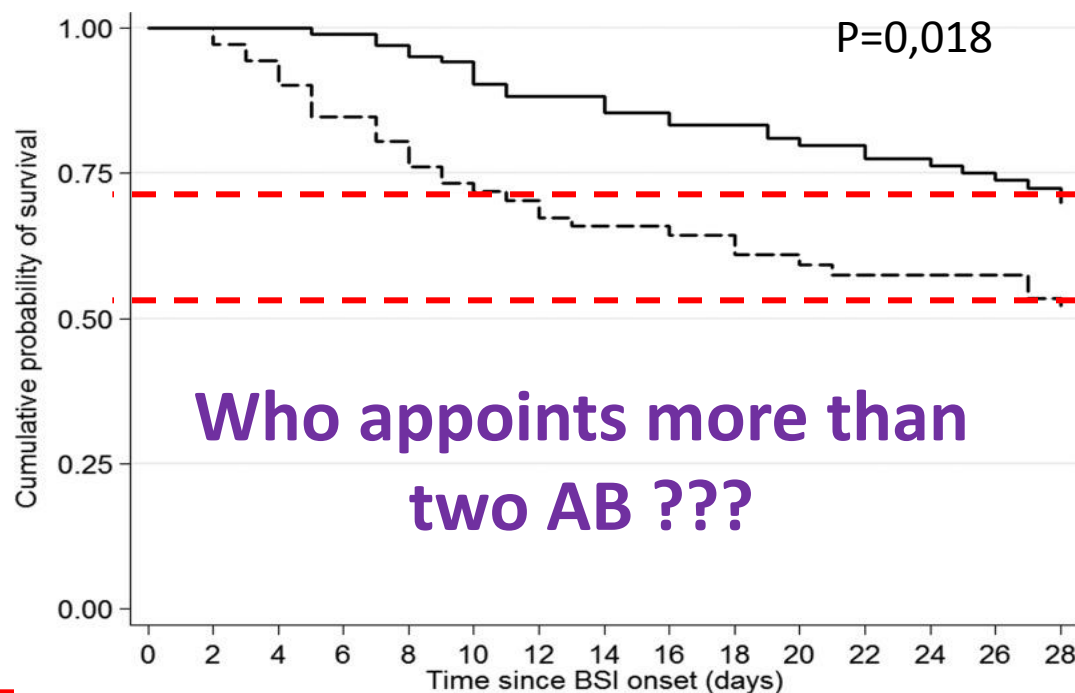
Combo: 27,2%

### Monotherapy - Mortality %

Tigecyclin 40.4

Colistin 54.5

Carbapenem 58.0



### Combination Therapy

- Carbapenem + Tigecyclin + AH or Colistin
- Tigecyclin + Colistin + AG
- Tigecyclin + Colistin

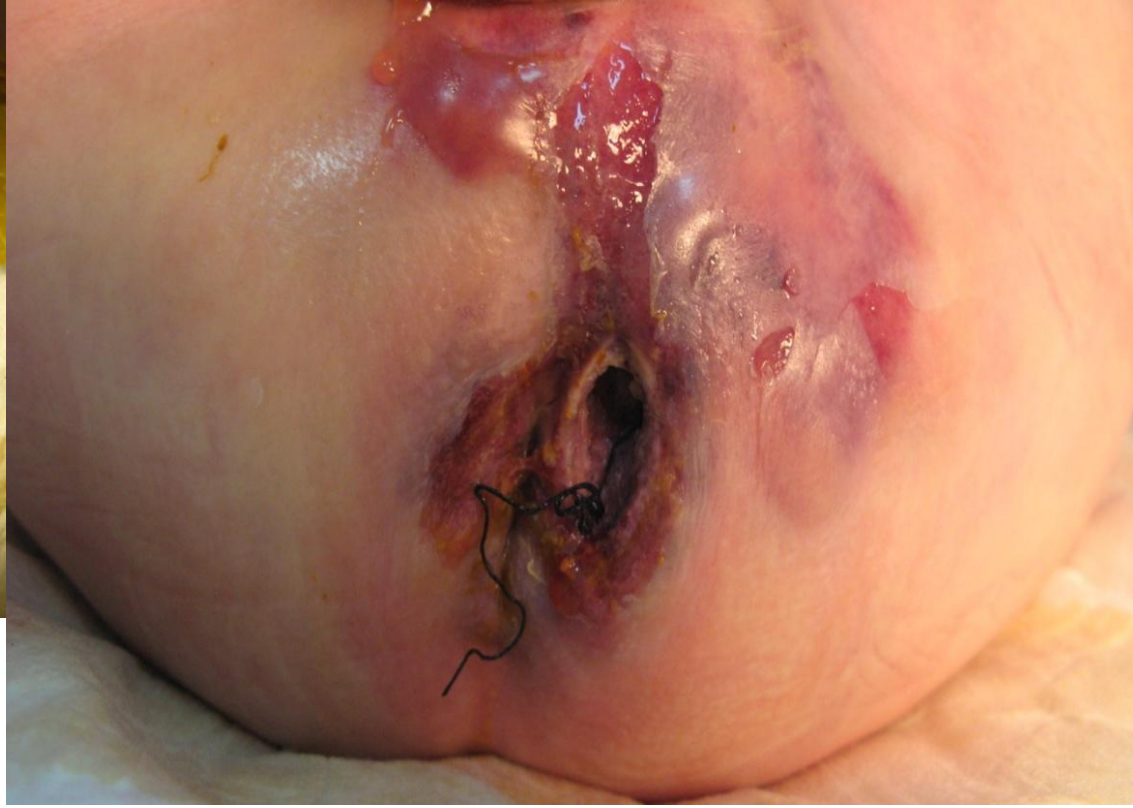
### - Mortality (%)

0%

27.3%

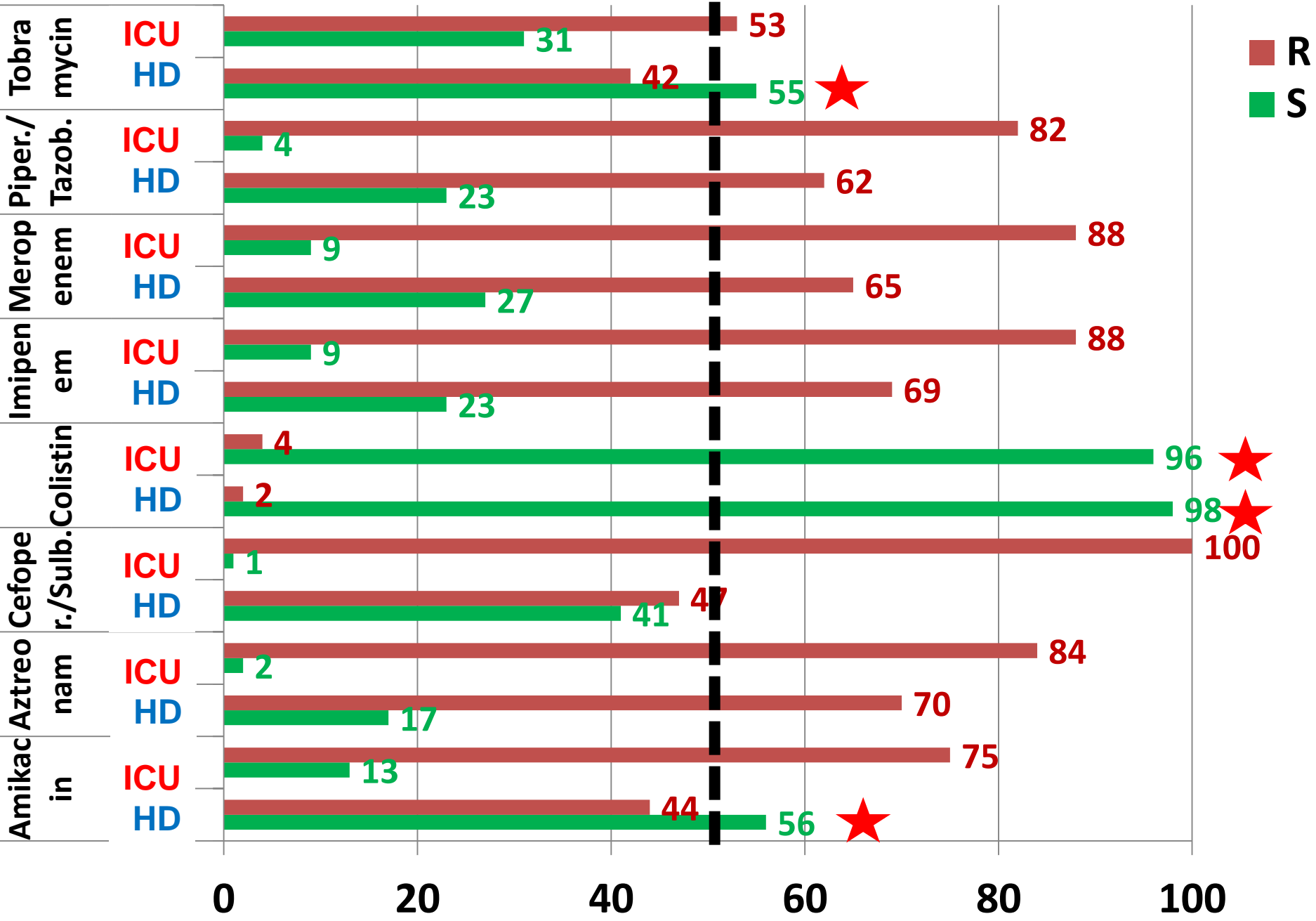
23.8%

# Pseudomonas spp.



# Pseudomonas aeruginosa

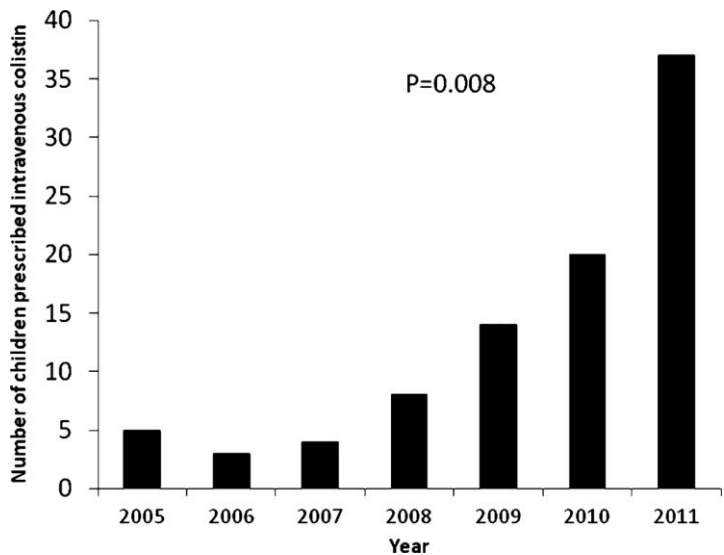
264 isolates



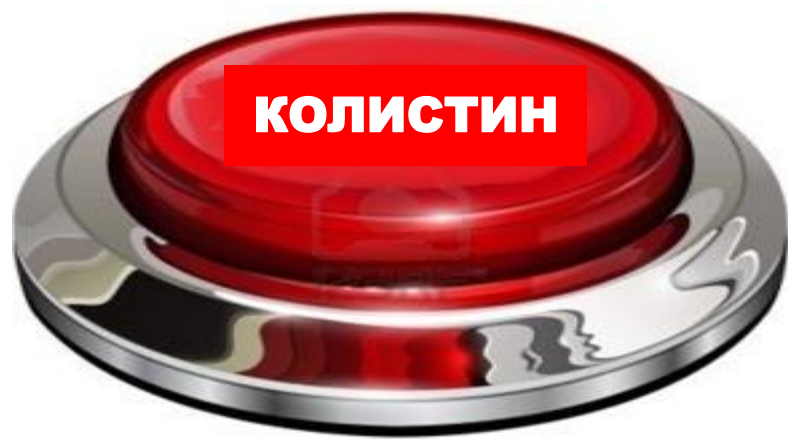
1950

# COLISTINE =

colistin A (polymyxin E1) +  
colistin B (polymyxin E2)



[Pediatr Infect Dis J. 2013 Jan; 32\(1\): 17–22. Pranita D. Tamma](#)  
The Use of Intravenous Colistin Among Children in the United States

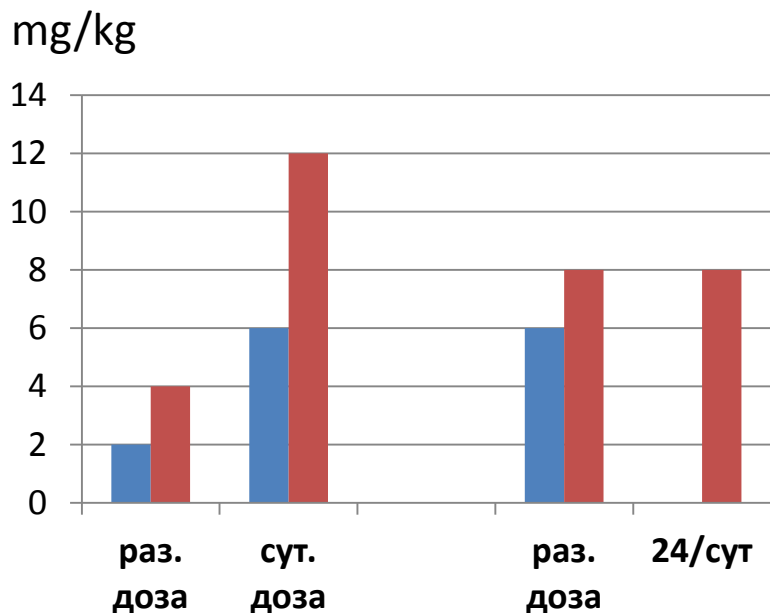


## Colistin problems

- 1-resistance
- 2 is not applicable in monotherapy
- 3-limit nephrotoxicity



**Colistin 9.000.000 Ui ev,  
then 4.500.000 x 2 ev**



*4 medicines left ???*

**TIENAM**

**+ TIGACYCLINE**

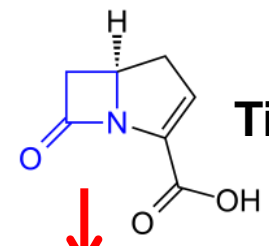
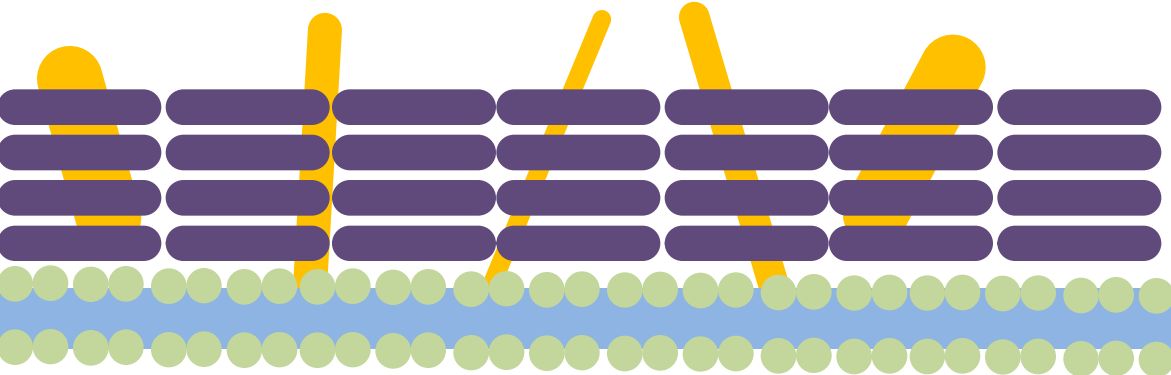
**+ COLISTINE**



**+ AMEN**

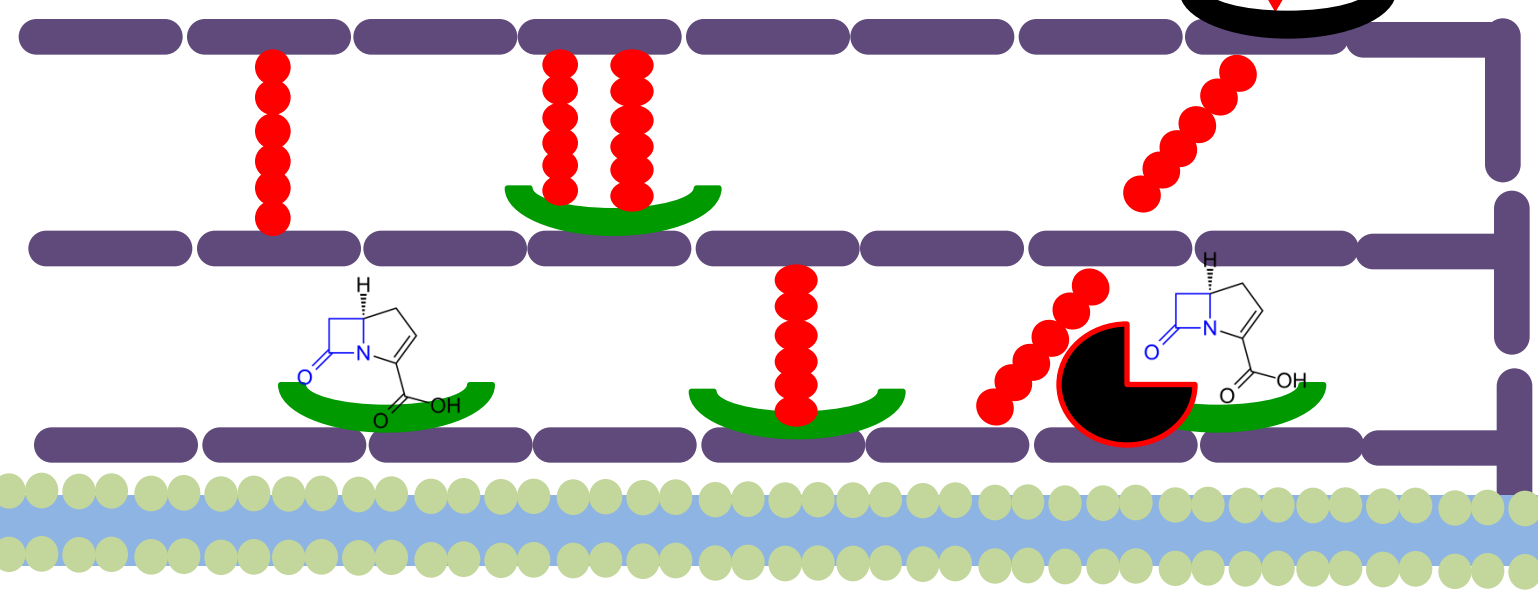
# Mechanisms of resistance to carbapenems

Teichoic Acids  
Peptidoglycans  
Cytoplasmic membrane

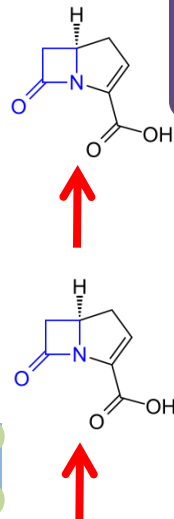


**Tightness**

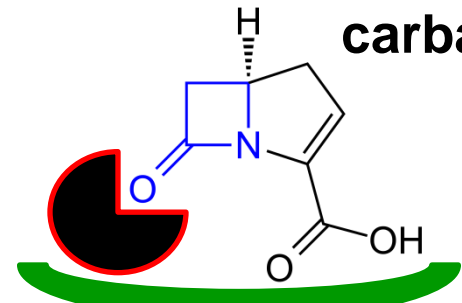
**Transpeptidase**



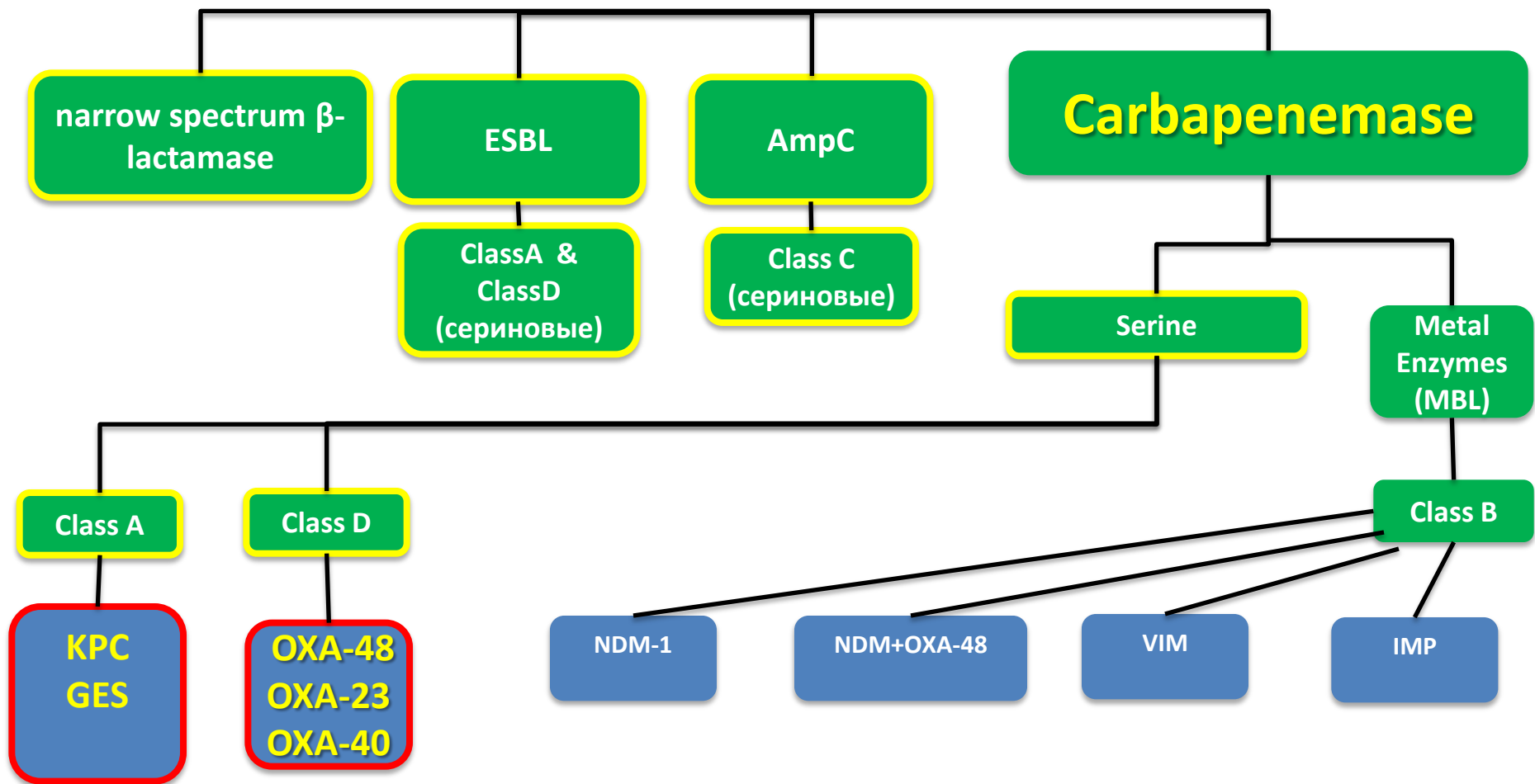
**Removal**



**carbapenemase**



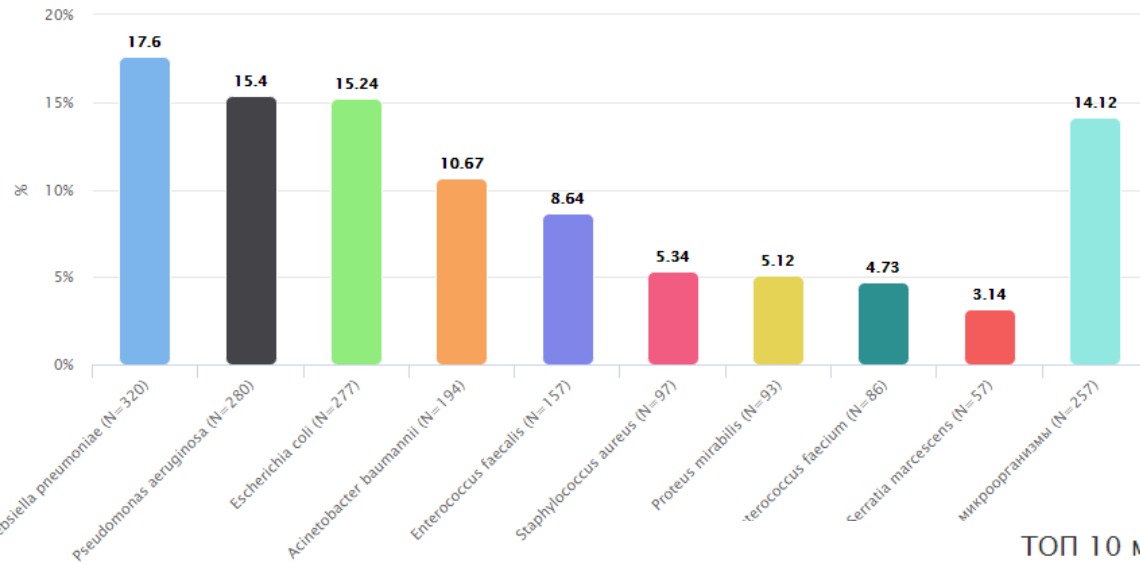




# St. Petersburg

## Klebsiella spp

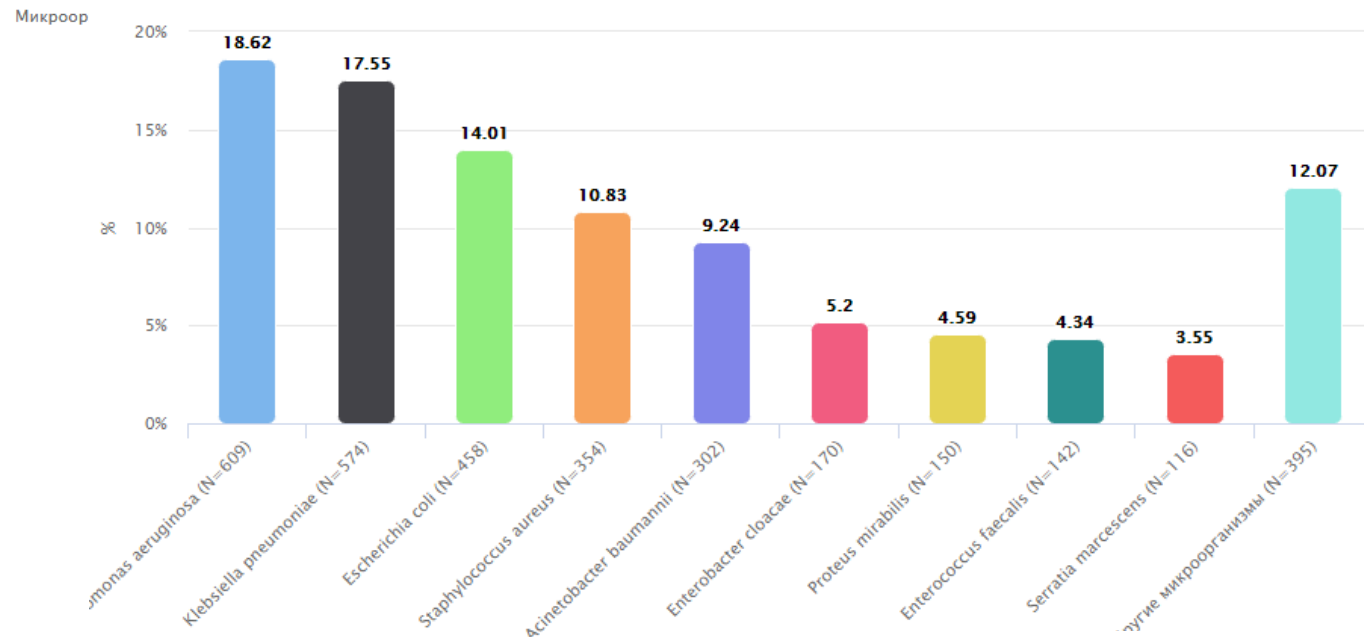
ТОП 10 микроорганизмов (N=1818)



# Moscow

## Pseudomonas spp.

ТОП 10 микроорганизмов (N=3270)

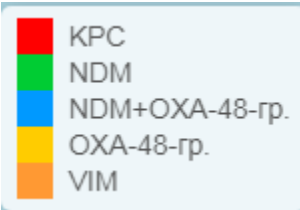


Микроорганизмы

МАКМА

16.11.2018

# Carbapenemase - Klebsiella pneumoniae



## St. Petersburg

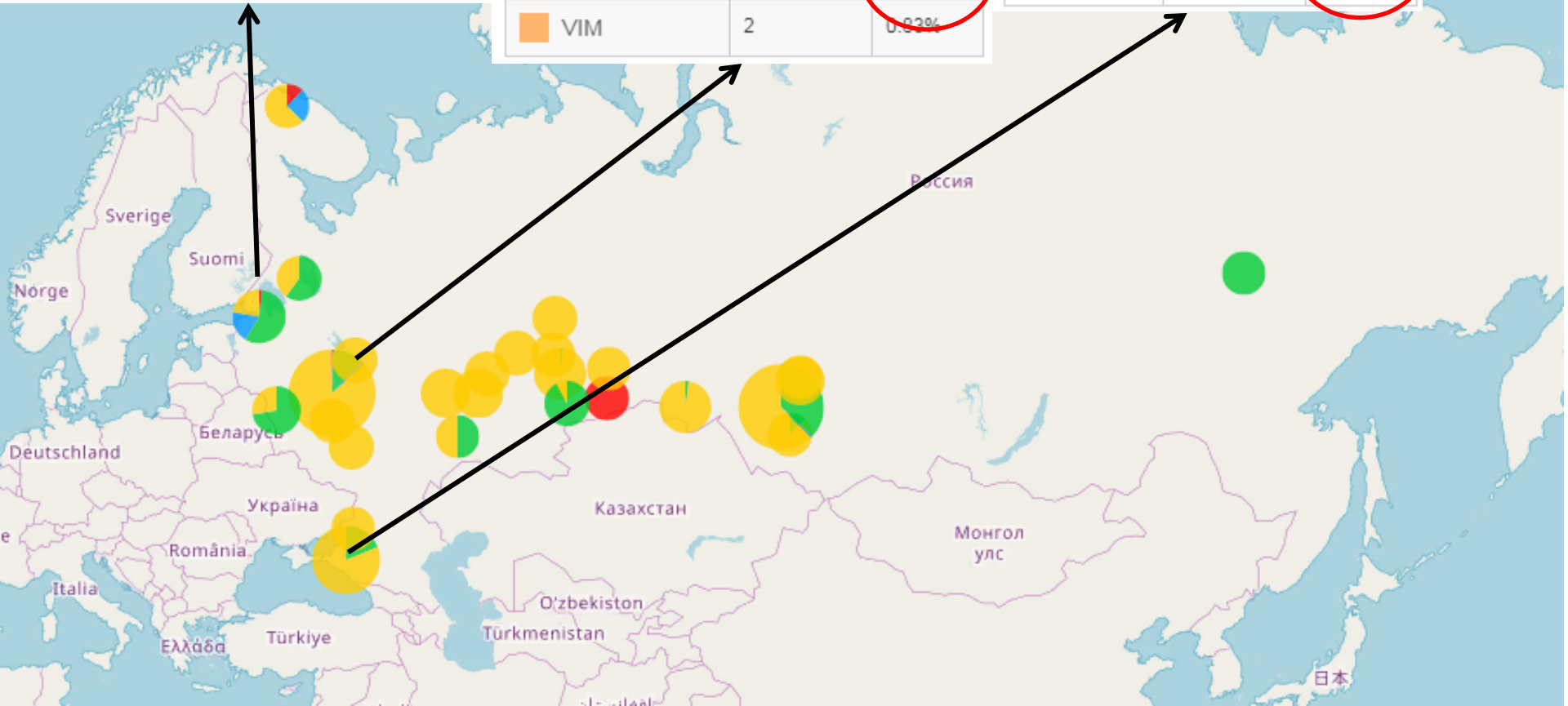
Категория	Количество	Процент
KPC	1	1.72%
NDM	33	56.9%
NDM+OXA-48-гр.	11	18.97%
OXA-48-гр.	13	22.41%

## Moscow

Категория	Количество	Процент
KPC	1	0.42%
NDM	27	11.25%
NDM+OXA-48-гр.	4	1.67%
OXA-48-гр.	206	85.83%
VIM	2	0.83%

## Krasnodar

Категория	Количество	Процент
NDM	26	18.84%
OXA-48-гр.	112	81.16%



# Genetic markers of antibiotic resistance



1	4751803
2	4811833
3	4877268
4	4842587
5	4811458
6	4811694
7	4812047
8	4900878
9	4798614
10	4812183
11	4877702
12	4812183
13	4812184
14	4707690
15	4707665
16	4713974
17	4713251
18	4713086
19	4712994
20	4697973
21	4616198
22	4697983
23	4707798
24	4707924
25	4707916
26	4643601
27	4643603
28	4643513
29	4646196

12.03.2018	моча	KL.pneumoniae	12.03.2018
03.04.2018	ЦВК	Acinet. Sp	03.04.2018
28.04.2018	кал	E.coli	28.04.2018
14.04.2018	моча	KL.pneumoniae	14.04.2018
06.04.2018	кал	KL.pneumoniae	06.04.2018
10.04.2018	катетер	Pseud. sp	10.04.2018
04.04.2018	кал	E.coli	04.04.2018
10.05.2018	мочевой катетер	KL.pneumoniae	10.05.2018
03.04.2018	БАЛ	KL.pneumoniae	03.04.2018
04.04.2018	миндалины	KL.pneumoniae	04.04.2018
25.04.2018	промывные воды бр	Ps.sp	25.04.2018
04.04.2018	миндалины	Ps.sp	04.04.2018
04.04.2018	кал	KL.pneumoniae	04.04.2018
12.02.2018	миндалины	KL.pneumoniae	12.02.2018
12.02.2018	ЦВК	KL.pneumoniae	12.02.2018
19.02.2018	моча	KL.pneumoniae	19.02.2018
16.02.2018	ЦВК	KL.pneumoniae	16.02.2018
15.02.2018	зев	KL.pneumoniae	15.02.2018
15.02.2018	кровь	KL.pneumoniae	15.02.2018
12.02.2018	моча	KL.pneumoniae	12.02.2018
27.12.2017	кал	KL.pneumoniae	27.12.2017
12.02.2018	кровь	KL.pneumoniae	12.02.2018
12.02.2018	пром. Воды бронхов	KL.pneumoniae	12.02.2018
13.02.2018	БАЛ	KL.pneumoniae	13.02.2018
13.02.2018	моча	KL.pneumoniae	13.02.2018
12.01.2018	кал	KL.pneumoniae	12.01.2018
12.01.2018	моча	KL.pneumoniae	12.01.2018
11.01.2018	половые органы	KL.pneumoniae	11.01.2018
29.12.2017	зев	KL.pneumoniae	29.12.2017

Carbapenemas e+/-	Multiplex PCR(NDM,OXA- 48,KPC)_Carbap enemase type
NDM+OXA-48	NDM+OXA-48
отр	отр
отр	отр
отр	отр
отр	отр
отр	отр
NDM	NDM
KPC	KPC
KPC	KPC
NDM+OXA-48	NDM+OXA-48
отр	отр
KPC	KPC
KPC	KPC
KPC	KPC
KPC+NDM	KPC+NDM
KPC+NDM	KPC+NDM
отр	отр
OXA-48	OXA--48
NDM+OXA-48	NDM+OXA-48
отр	отр
KPC	KPC
NDM	NDM
NDM	NDM
KPC+NDM	KPC+NDM
NDM	NDM
отр	отр
отр	отр
NDM	NDM
NDM	NDM
отр	отр

# Carbapenemase-Producing *Enterobacteriaceae* and Nonfermentative Bacteria, the Philippines, 2013–2016

John Mark Velasco, Maria Theresa Valderama, Trent Peacock,<sup>1</sup> Nirdnoy Warawadee, Kathyleen Nogrado, Fatima Claire Navarro, Domingo Chua, Jr., Srijan Apichai, Ruekit Sirigade, Louis R. Macareo, Brett Swierczewski

Technical Appendix Table. Molecular resistance mechanisms of carbapenem-resistant clinical (n = 45) and environmental isolates (n = 3) from a tertiary-care military hospital in Manila, the Philippines, August 2013–April 2016\*

Identification	Source	Organism	Carba NP	Carba			Month	Year	Imipenem		Meropenem		Sex	Hospital ward
				<i>bla</i> <sub>NDM</sub>	<i>bla</i> <sub>KPC</sub>	<i>bla</i> <sub>VIM</sub>			MIC (μg/mL)	MIC (μg/mL)				
Patient isolates														
PH-0138–14	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Nov	2013	>8	>8		M	Neonatal ICU	
PH-0542–14	Soft tissue	<i>E. coli</i>	Pos	Pos	Neg	ND	Jun	2014	>8	>8		M	Pediatric	
PH-0630–14	Wound	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jul	2014	>8	>8		F	Female Medical	
PH-0631–14	Blood	<i>C. freundii</i>	Pos	Pos	Neg	ND	Jul	2014	>8	>8		M	Neurosurgery	
PH-0756–14	Catheter	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Aug	2014	>8	>8		F	Medical ICU	
PH-0787–14	Endotracheal tip	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Aug	2014	>8	>8		M	Medical ICU	
PH-0837–14	Catheter	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Sep	2014	>8	>8		F	Female Surgical	
PH-0846–14	Catheter	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Sep	2014	>8	>8		M	Male Medical Oncology	
PH-0850–14	Urine	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Sep	2014	>8	>8		F	Female Medical	
PH-0873–14	Urine	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Oct	2014	>8	>8		M	Surgical ICU	
PH-0874–14	Wound	<i>Klebsiella sp.</i>	Pos	Pos	Neg	ND	Oct	2014	>8	>8		M	Female Medical	
PH-0901–14	Wound	<i>C. freundii</i>	Pos	Pos	Neg	ND	Oct	2014	>8	>8		F	Female Surgical	
PH-1037–14	Catheter	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Dec	2014	>8	>8		F	Female Medical	
PH-1076–14	Urine	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Dec	2014	>8	>8		M	Medical ICU	
PH-1078–14	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Dec	2014	>8	>8		F	Female Medical	
PH-1088–14	Endotracheal tip	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		F	Medical ICU	
PH-1093–14	Tracheal aspirate	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Dec	2014	>8	>8		F	Female Medical	
PH-1099–14	Endotracheal tip	<i>Acinetobacter sp.</i>	Pos	Pos	Neg	ND	Dec	2014	*	>8		M	Surgical ICU	
PH-1115–14	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Dec	2014	>8	>8		F	Female Medical	
PH-1142–15	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		F	Female Medical	
PH-1143–15	Wound	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		M	Neurology	
PH-1150–15	Catheter	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		M	Neurosurgery	
PH-1159–15	Catheter	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		M	Neurology	
PH-1165–15	Urine	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		M	Pulmonary Disease	
PH-1166–15	Urine	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Feb	2015	>8	>8		M	Surgical ICU	
PH-1261–15	Blood	<i>C. freundii</i>	Pos	Pos	Neg	ND	Jul	2015	8	>8		M	Nephrology	
PH-1263–15	Blood	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Jul	2015	>8	>8		F	Neonatal ICU	
PH-1265–15	Blood	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Jul	2015	8	8		F	Neonatal ICU	
PH-1266–15	Blood	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Jul	2015	>8	>8		F	Neonatal ICU	
PH-1270–15	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		F	Female Medical	
PH-1280–15	Urine	<i>C. freundii</i>	Pos	Pos	Neg	ND	Jan	2015	>8	>8		M	Neurology	
PH-1363–15	Wound	<i>P. aeruginosa</i>	Pos	Pos	Neg	ND	Sep	2015	>8	>8		M	Surgical ICU	
PH-1379–15	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Sep	2015	>8	>8		M	Medical ICU	
PH-1384–15	Blood	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		F	Medical ICU	
PH-1394–15	Wound	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		M	Surgical ICU	
PH-1419–15	Urine	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		F	Female Medical	
PH-1477–15	Wound	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		F	Medical ICU	
PH-1478–15	Wound	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		F	Female Medical	
PH-1482–15	Wound	<i>K. pneumoniae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		F	Medical ICU	
PH-1499–15	Wound	<i>E. cloacae</i>	Pos	Pos	Neg	ND	Oct	2015	>8	>8		F	Medical ICU	

**Initial empirical therapy**

The choice depends on:  
Localization and conditions of infection  
The presence of risk factors for MDR flora  
Severity of the condition  
Local Epidemiology

There is an effect:  
AB continuation

**48-72 hours  
Evaluation of the effectiveness  
of AB**

**No effect:  
neobhod AB correction**

**No results:  
empirical therapy**

**There are results  
microbiologist. research**

**Gain starting  
empirical therapy**

**Change AB**

**Targeted therapy**

**Adding AB  
vs MRSA**

**Addition of AB with  
activity against Gr-**

The choice depends on:  
Localization and conditions of infection  
The presence of risk factors for MDR flora  
Severity of the condition  
Local Epidemiology

# MDR RISK FACTORS OF AGENTS

## **ESBL extended-spectrum $\beta$ -lactamase (ESBL)**

Prior therapy with cephalosporins or fluoroquinolones  
Hospitalization in the previous 3 months.  
Being in the ICU  
Long hospitalization

## **CRE Carbapenem-resistant Enterobacteriaceae**

Colon colonization CRE  
Prior Carbapenema Therapy  
CRE high in ICU

## **Acinetobacter baumannii**

Being in the ICU  
Prior therapy with wide-spectrum carbapenems and AB

## **Pseudomonas aeruginosa**

Mechanical ventilation of the lungs > 4 days  
Preceding broad spectrum AB  
Glucocorticoids  
Sternotomy  
Chronic obstructive pulmonary disease, bronchiectasis, cystic fibrosis

# Nosocomial infection - type IIIB – MRSA, ESBL, CRE, Acinetobacter baumannii, Pseudomonas aeruginosa

**MRSA**



**Telavancin  
Linezolid**

**ESBL**



**Carbapenems  
Cefipim / Sulbactam  
Cefoperazone / Sulbactam  
Tigecyclin**

**CRE**



**Ceftazidim /  
avibaktam  
= Zavicefta  
  
+/- Aztreonam**

**Acinetobacter  
baumannii**



**Tigecyclin  
+ Polymyxin**

**Pseudomonas  
aeruginosa**

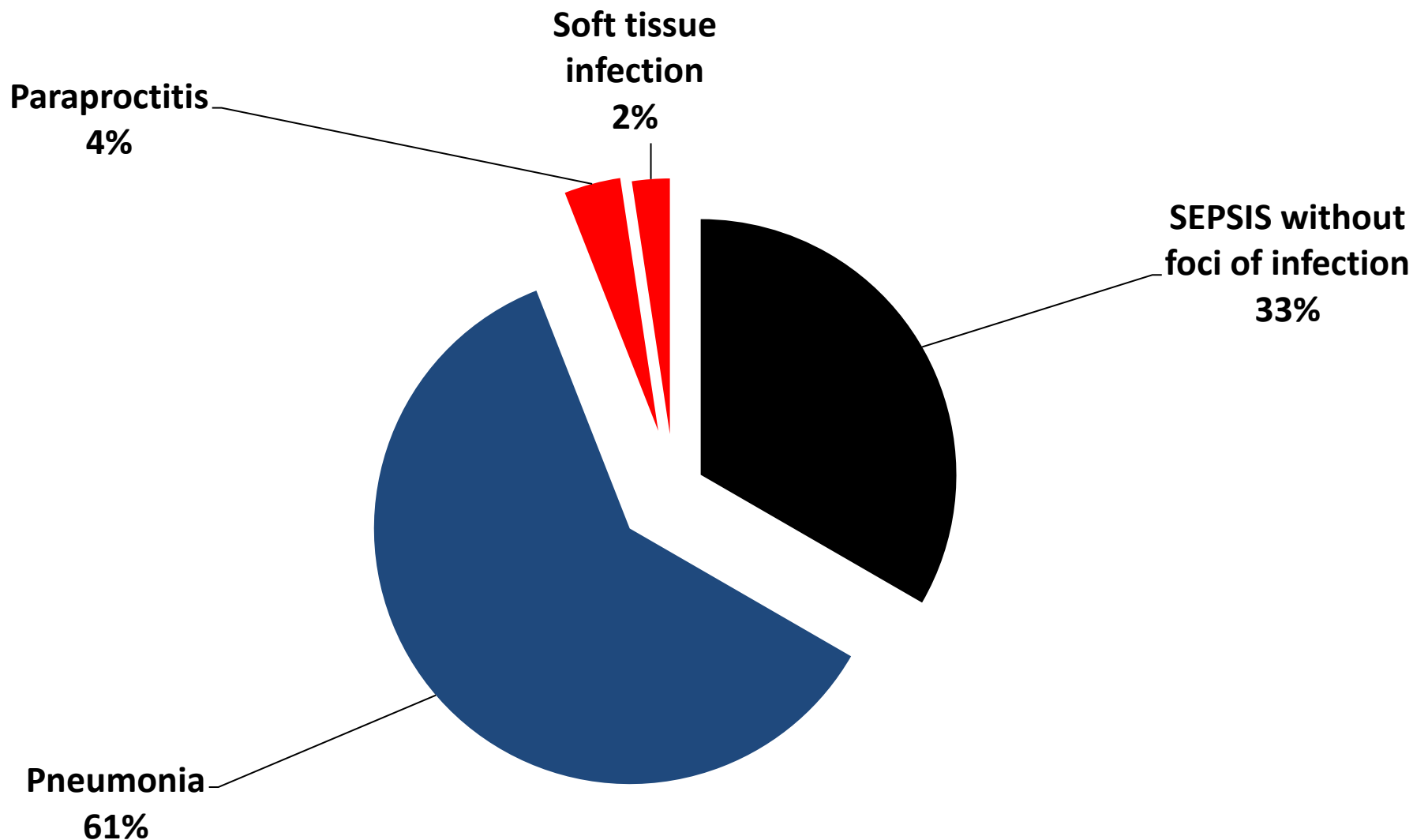


**Zeftolosan /  
tazobactam  
= ZERBAXA**



# Focus of infection

Infectious complications. Source of infection. 2018 (%)



# Soft tissue infection



**Antibiotics**

**Infusion therapy**

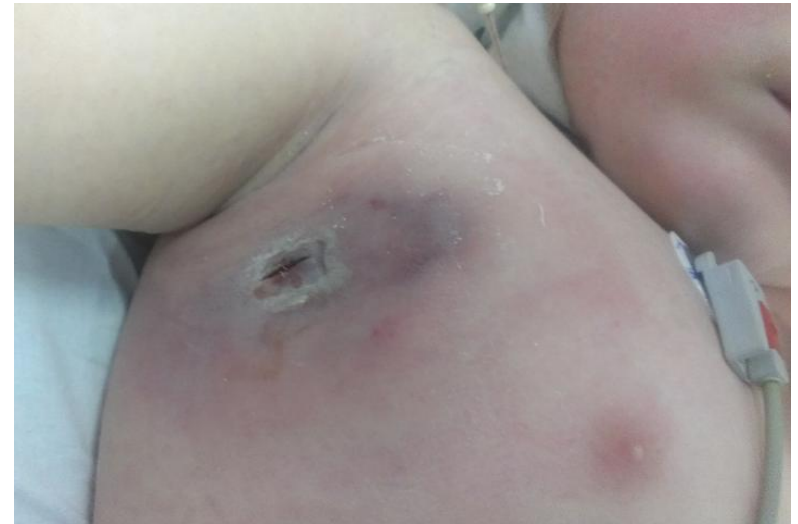
**Intravenous  
immunoglobulins**

**Biopsy**

**Ultrasound**

**Surgeon observation**

# Soft tissue infection



**Central catheter - Bacteremia *Klebsiella pneumoniae***

**Biopsy - *Klebsiella pneumoniae***

**Tienam - R  
Tigacyclin - ?  
Colistin - S**

**Infusion therapy  
130%**

**Pentaglobin**

**Artificial nutrition**

**Biopsy - ?**

**Ultrasound**

# Soft tissue infection

**Balance correction**  
**KHS correction**  
**Correction of coagulopathy**  
**Hepatoprotectors**  
**Prevention of gastrointestinal paresis**  
**CRRT, Plasmapheresis**



**Norepinephrine**  
**Dopamine**  
**Hydrocortisone**  
**Cytokinepheresis**  
**LPS-sorption**



# Soft tissue infection - after medical procedures



*Pseudomonas aeruginosa*



# Soft tissue infection - after medical procedures

*Klebsiella pneumoniae*



# ***Klebsiella pneumoniae* KPC+ Bacteremia + Septicemia + Wound infection**

**Diagnosis: AML**

**D + 30, repeated,  
allogeneic, unrelated**

**Pancytopenia**



***Klebsiella pneumoniae* KPC+ -  
chronic carriage in the gastrointestinal tract**

***Klebsiella pneumoniae* KPC+ -  
feces, seeding from the oral mucosa**

# Septicemia



**Septicopyemia screenings in soft tissue - lips**

**Central catheter - Bacteremia**  
*Klebsiella pneumoniae* KPC+

**Bite wound IV finger of the right hand.**



**Antibacterial therapy:**

**Tienam - R**

**Tigacyclin -?**

**Colistin - S**



# Infection of the soft tissues of the external genital organs



*Klebsiella pneumoniae*



# Infection of the soft tissues of the external genital organs



*Pseudomonas aeruginosa*

# Pseudomonas spp.



**Tienam - R**  
**Colistin - S**

# Problem surgery

09.10.2015

11.10.2015





13.10.2015



16.10.2015



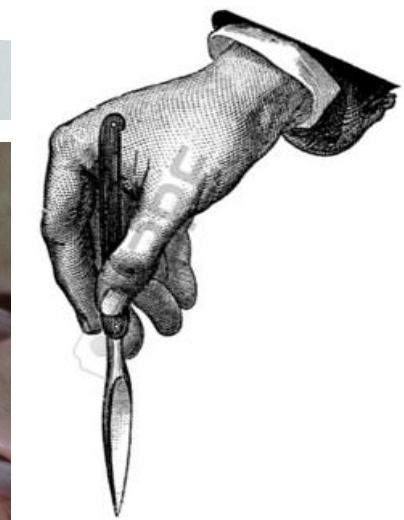


19.10.2015



20.10.2015

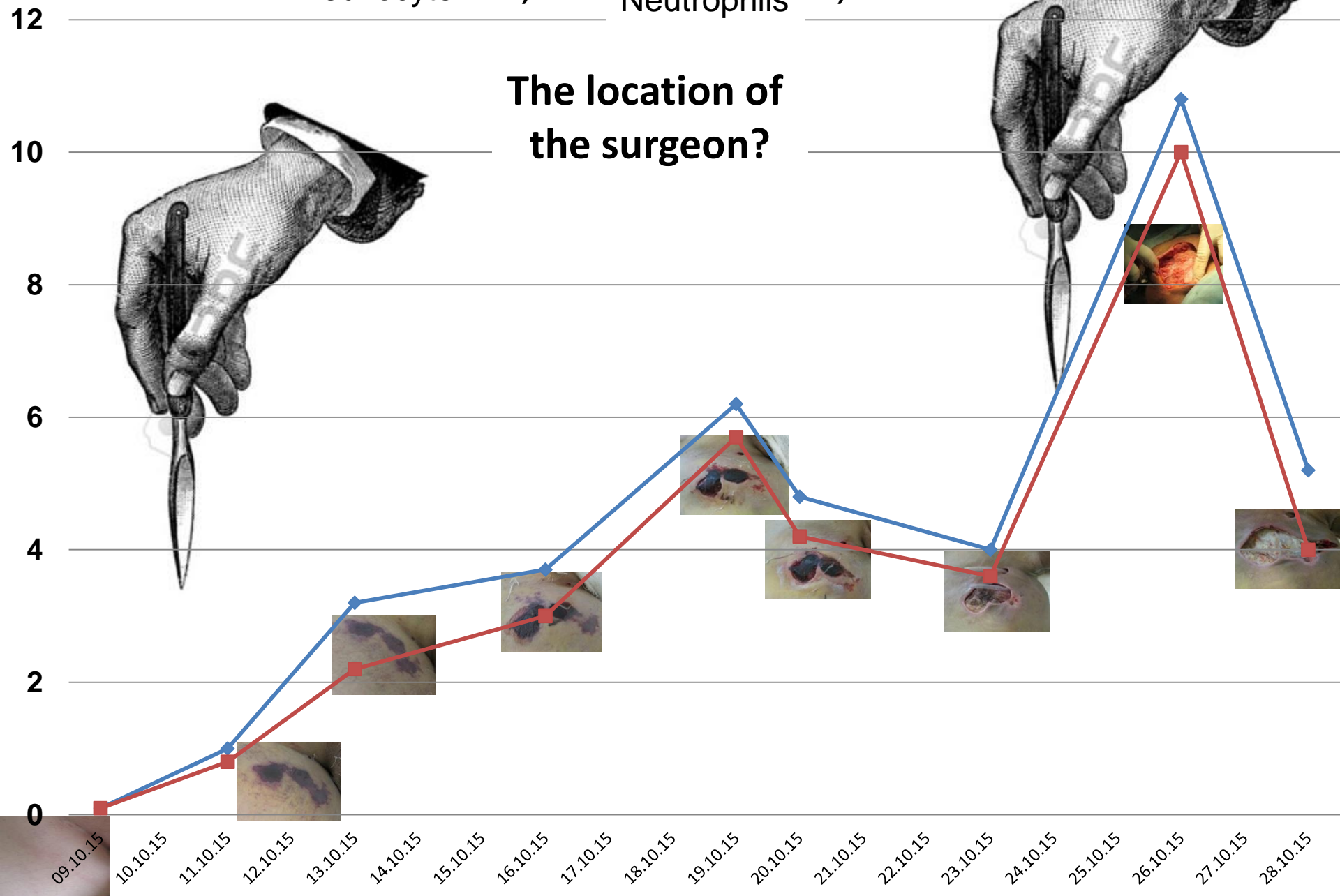




# Hematopoiesis Recovery

—●— leukocyte (WBC) —■— Neutrophils (NE) #

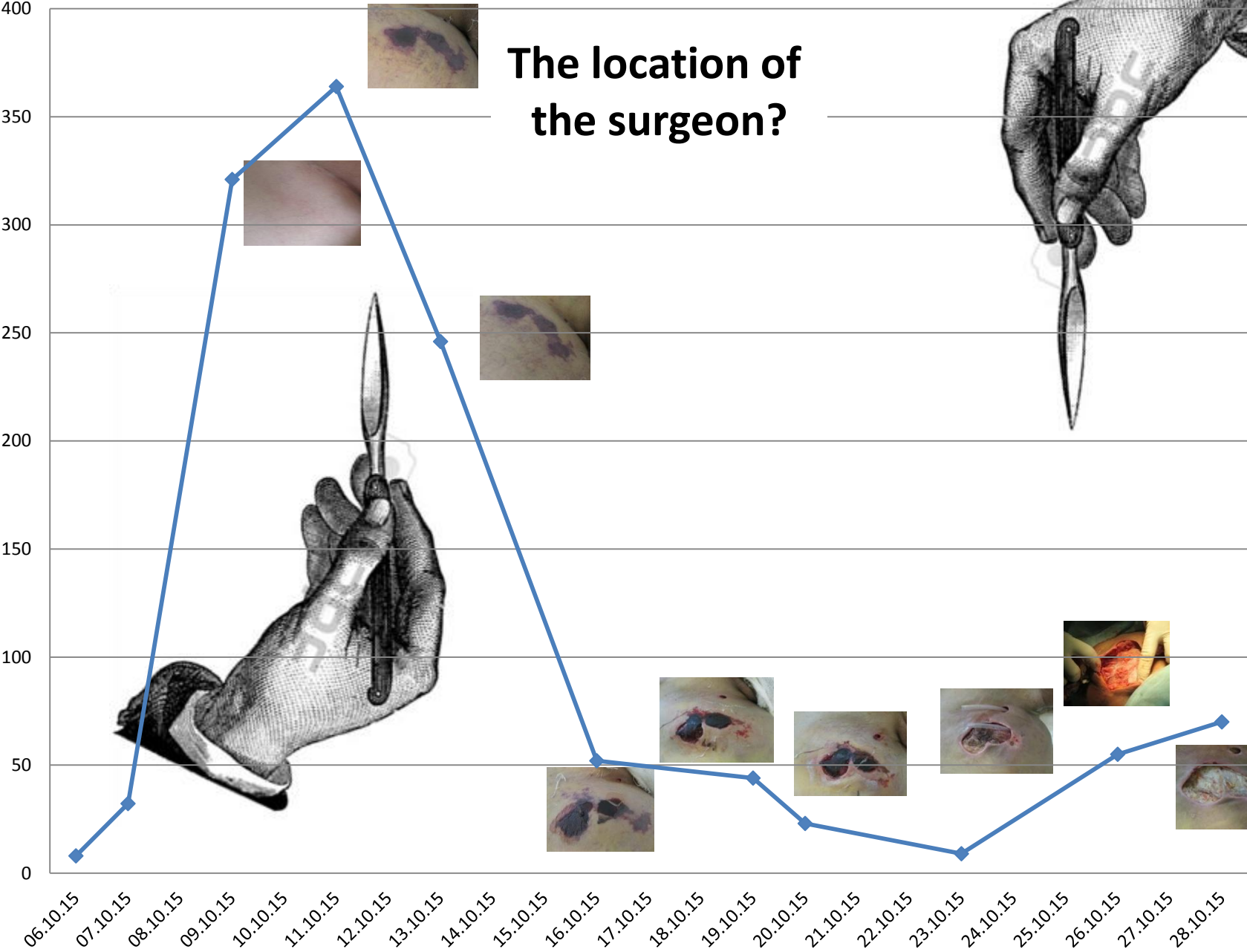
The location of the surgeon?

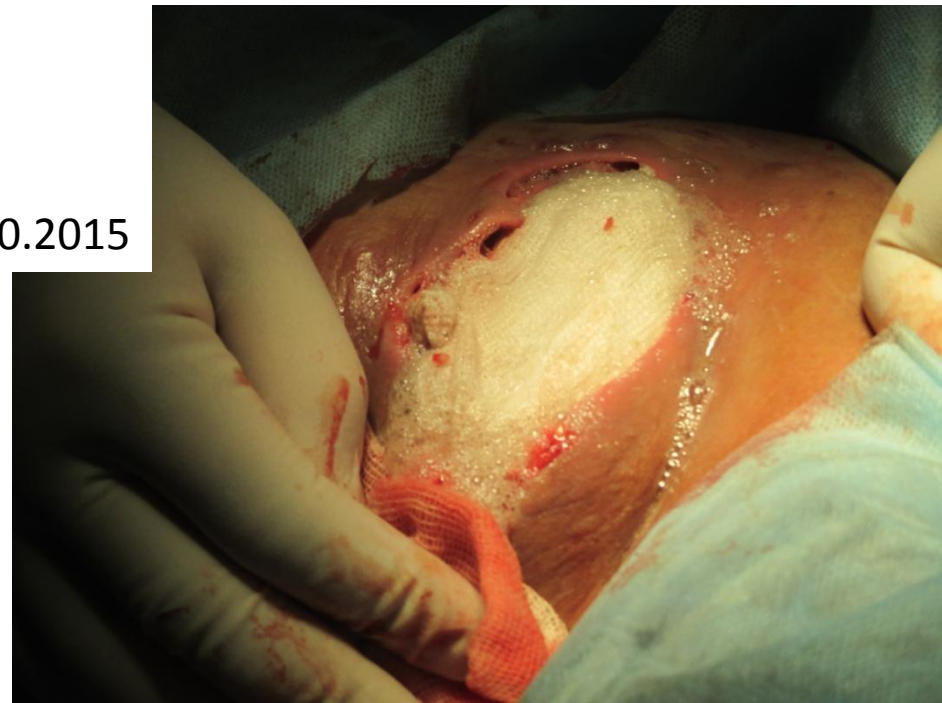
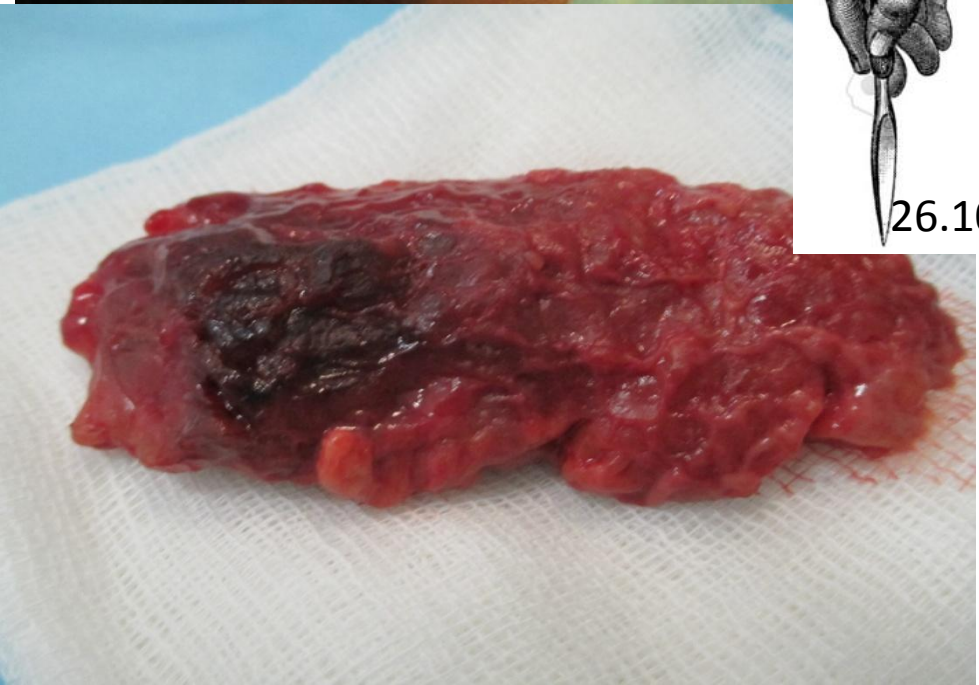
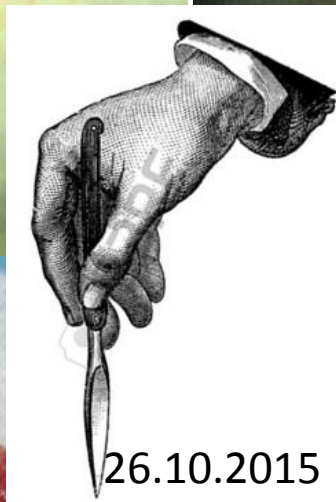
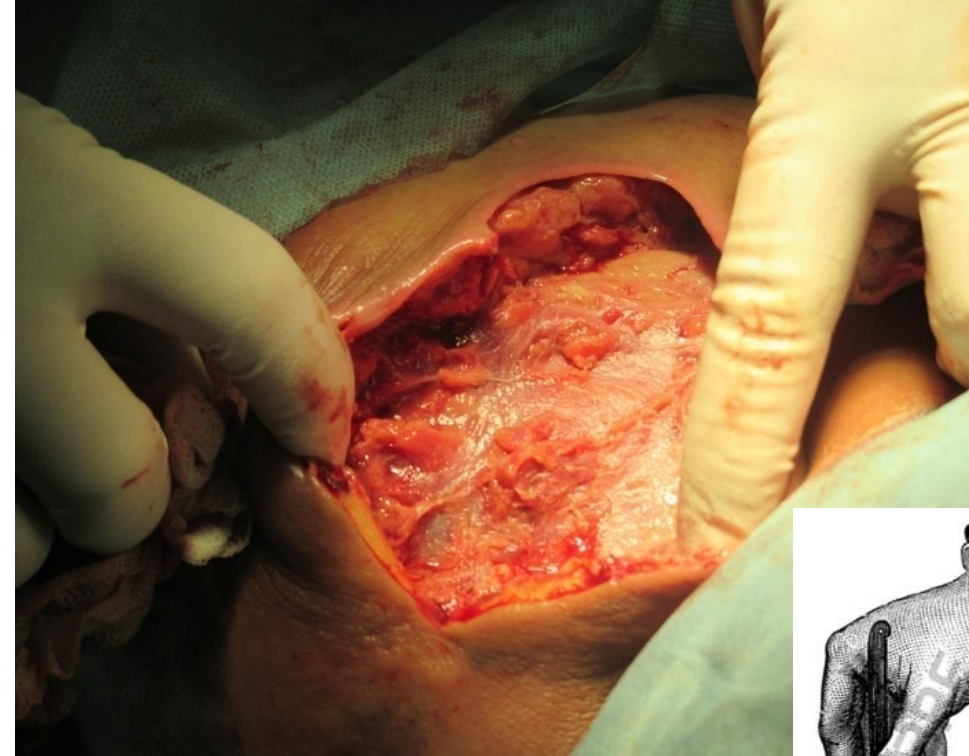


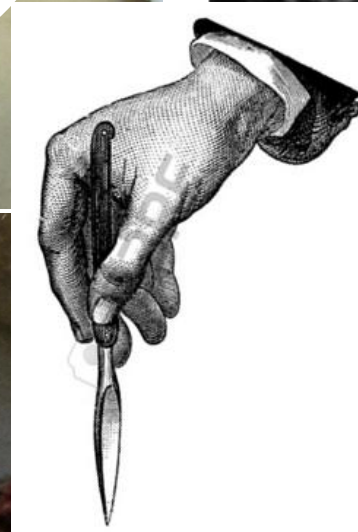


# CRP

CRP







# BMT - as a “rescue” therapy

## Is soft tissue infection a contraindication to HSCT?

18 year old woman

Diagnosis

Acquired idiopathic extra-severe aplastic anemia

Allogeneic related bone marrow transplantation

Soft tissue infection of the left hand - Pseudomonas aeruginosa

Chronic tonsillitis associated with Pseudomonas aeruginosa.

Chronic rhinosinusitis associated with Pseudomonas aeruginosa.

Therapy 1

Imipenem + Cilastatin 500 mg №4

Fosfomycin 3 gr №4

T>38

CRP>100

PCT>2

Therapy 2

Imipenem + Cilastatin 500 mg №4

Colistin 80 mg №2

Before BMT



$L=0,2 \times 10^9 / l$

D+25

Before BMT



$L=0,1 \times 10^9 / l$

D+35

D+15



$L=0,1 \times 10^9 / l$

D+60



$L=0,5 \times 10^9 / l$



$L=1,1 \times 10^9 / l$



$L=2,2 \times 10^9 / l$

Hemorrhagic stomatitis

2 days



**Stenotrophomonas maltophilia**

**+ SIRS)**

2 days

**Cough**

**+**

**Hemoptysis**



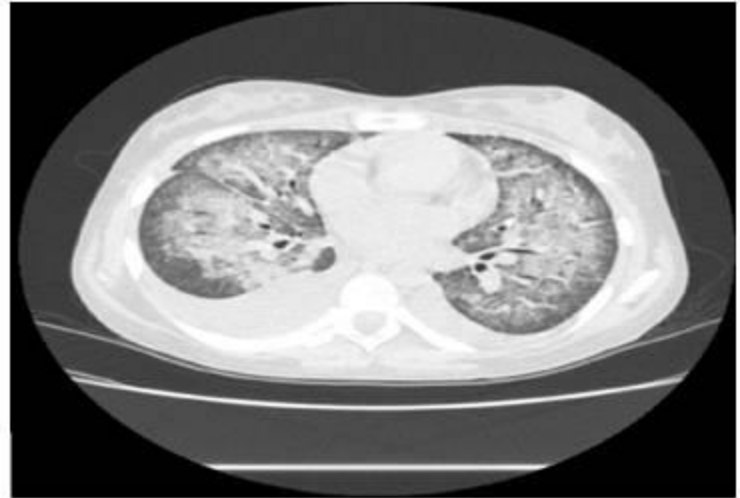
)

**Respiratory insufficiency**

1 days



**+**

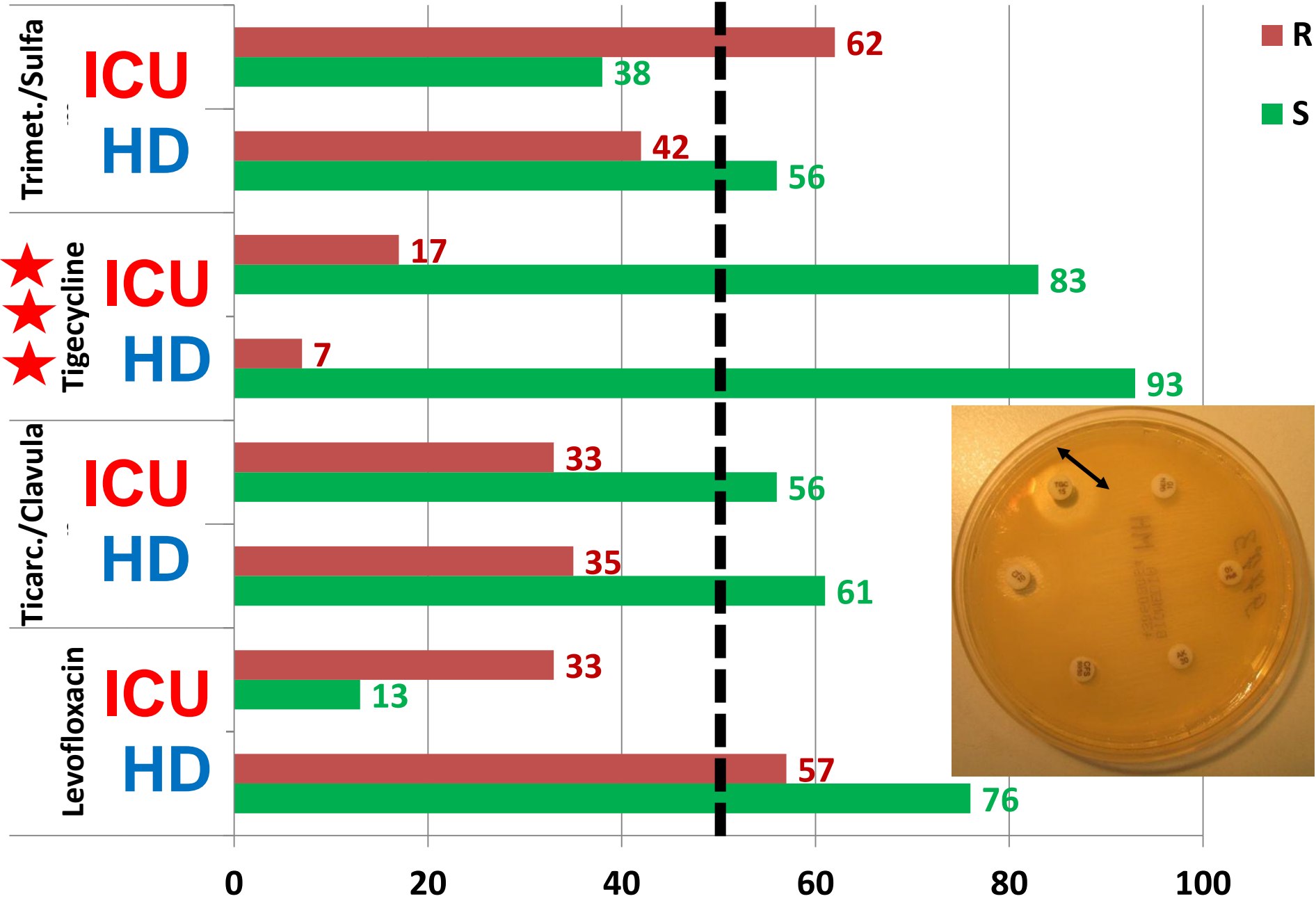


)

**= Stenotrophomonas maltophilia**

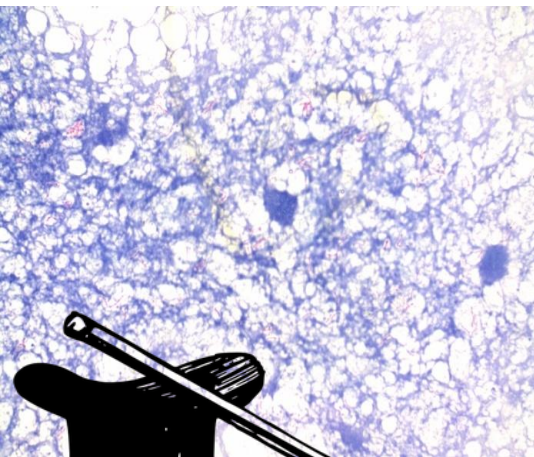
125 isolates

# Stenotrophomonas maltophilia

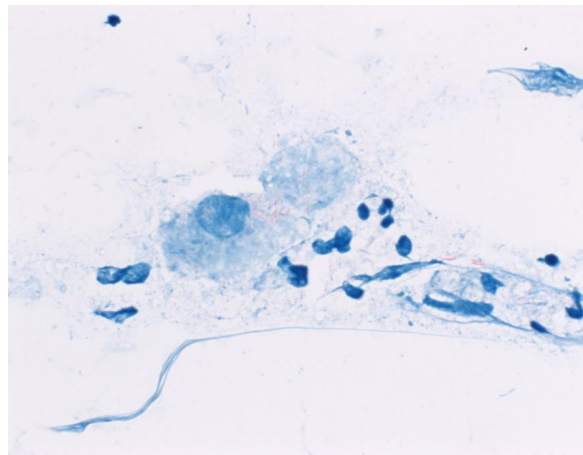


# EXOTIC? DO NOT THINK! JUST NEED TO BE EXCLUDED

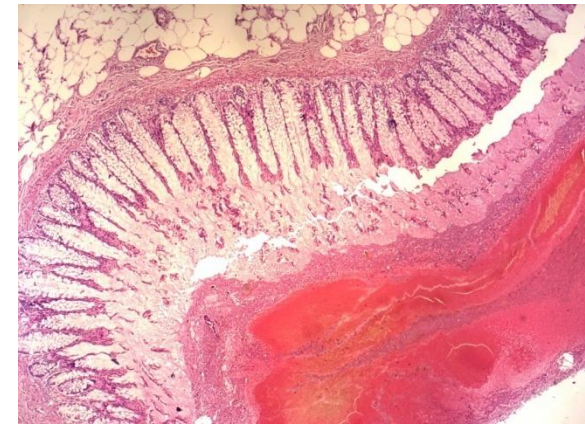
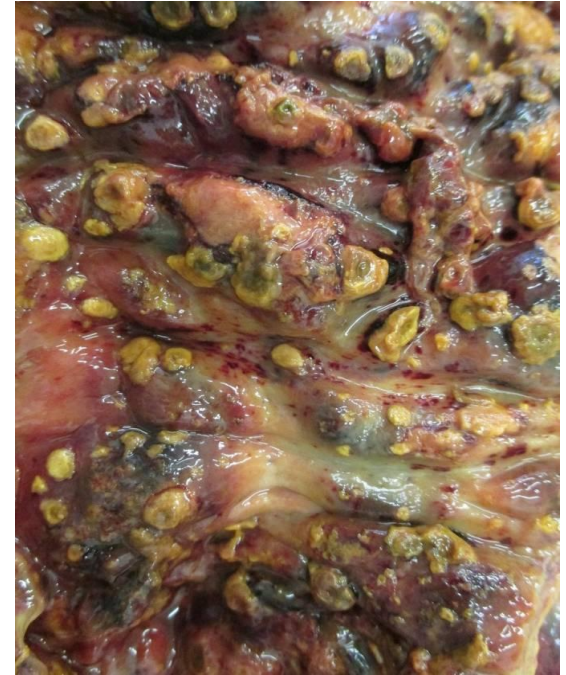
## Tuberculosis



## Mycobacteriosis



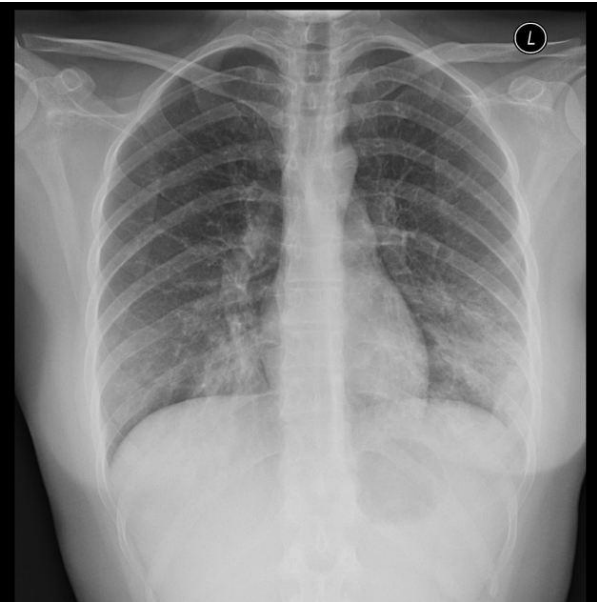
## Pseudomembranous colitis



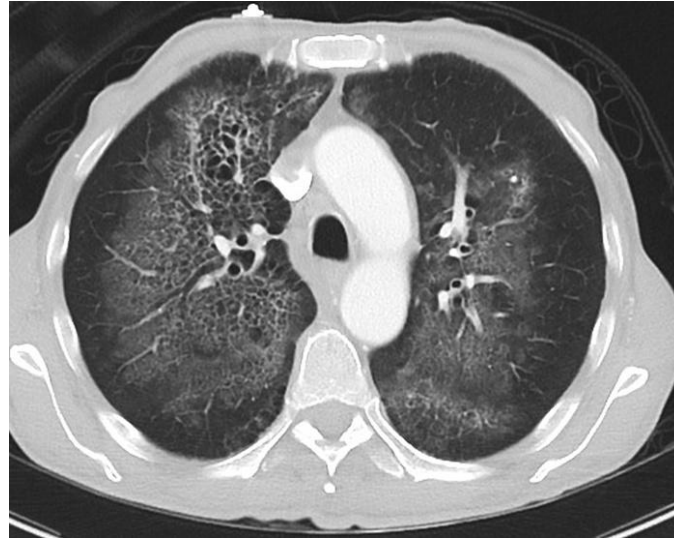


# EXOTIC? DO NOT THINK! JUST NEED TO BE EXCLUDED

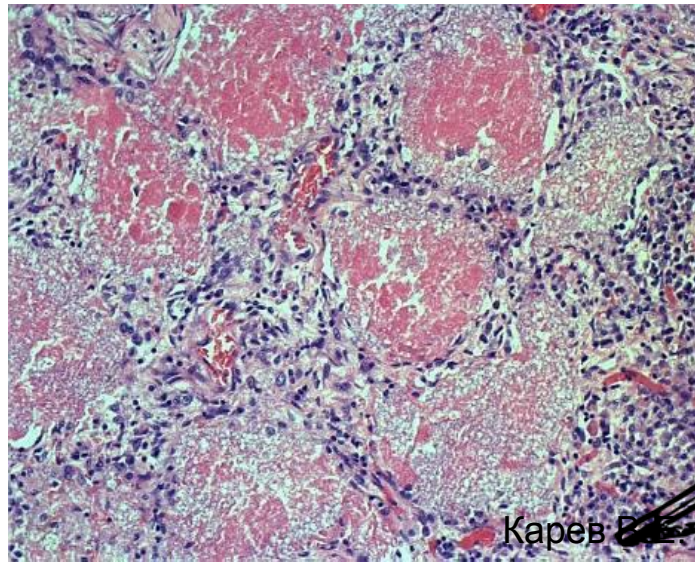
**Mycoplasma pneumoniae pneumonia**



**Pneumocystis pneumonia**



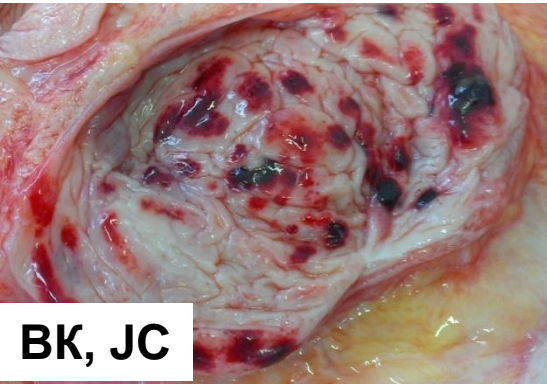
**Chlamydia pneumoniae pneumonia**



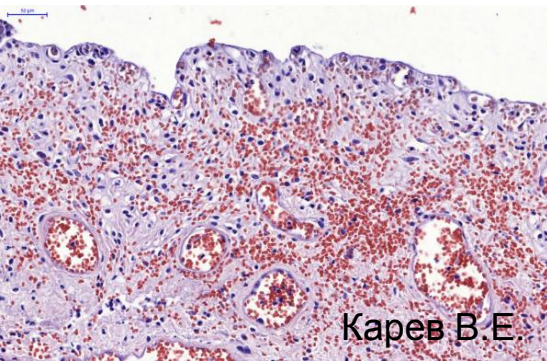
Карев В



Hemorrhagic cystitis 14-17%%



**BK, JC**



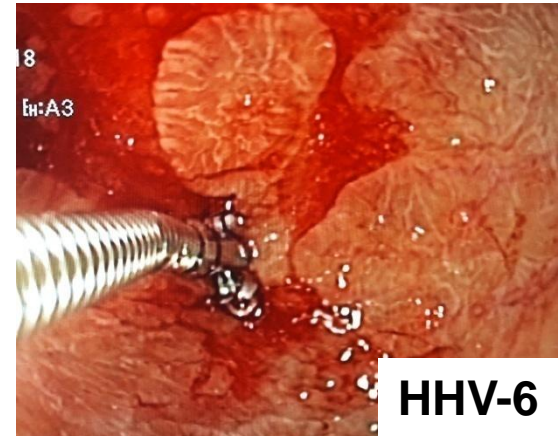
Kapev B.E

Desquamative hemorrhagic cystitis with the formation of ulcers

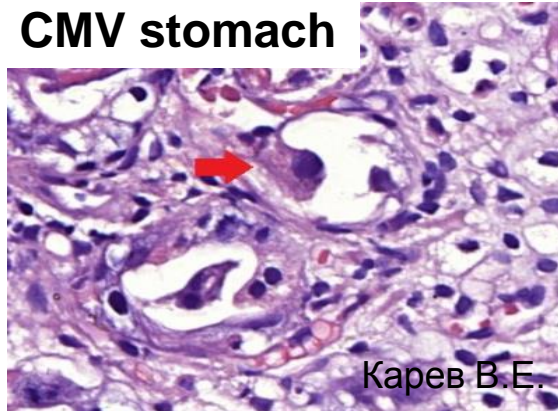


**HSV 1-2**

Hemorrhagic enteritis, colitis



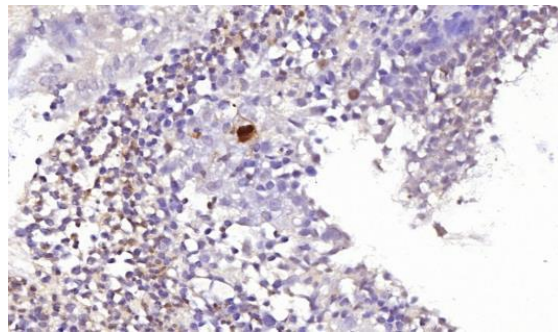
**HHV-6**



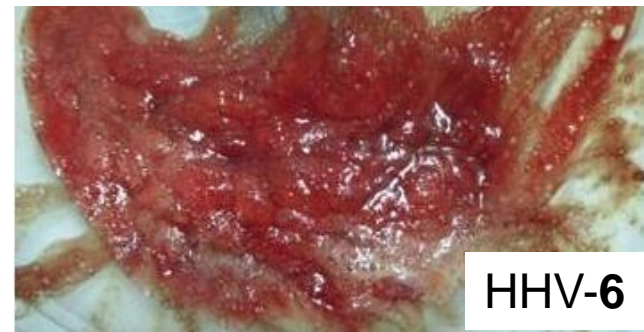
**CMV stomach**

Kapev B.E.

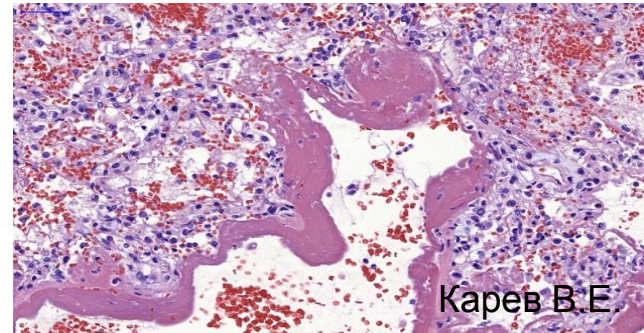
**Adeno colon**



Diffuse alveolar bleeding



**HHV-6**



Kapev B.E

Interstitial lesions, hyaline membranes, alterative changes in the epithelium



**VZV**



# BIOPSY





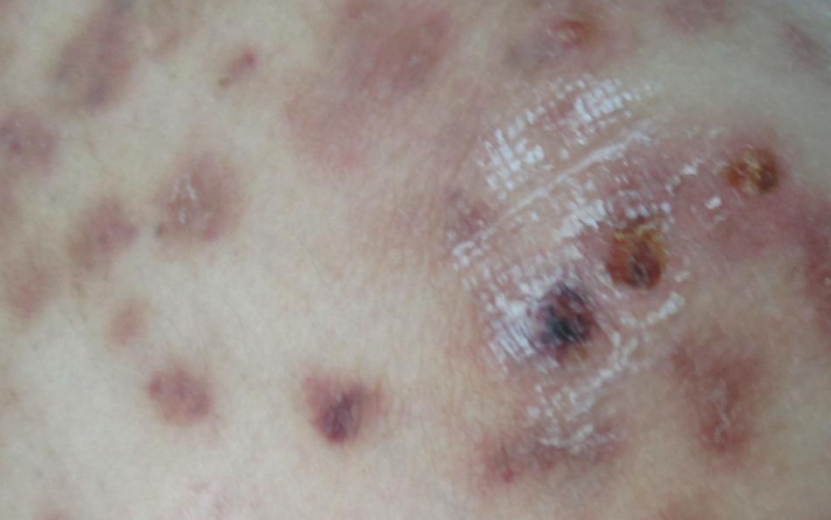
**Sepsis**

**Sepsis markers +**

**Microbiology - negative**

**PCR – Vir - negative**

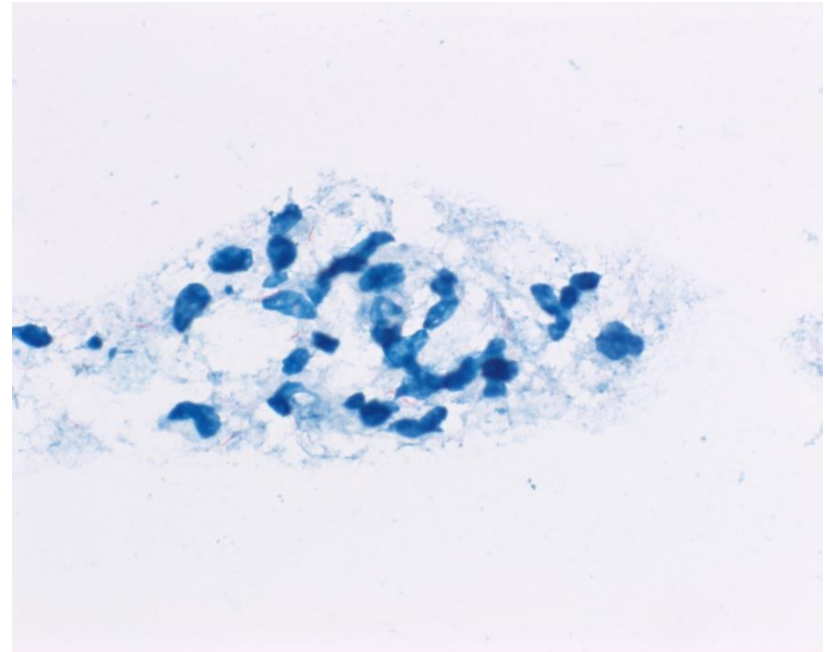
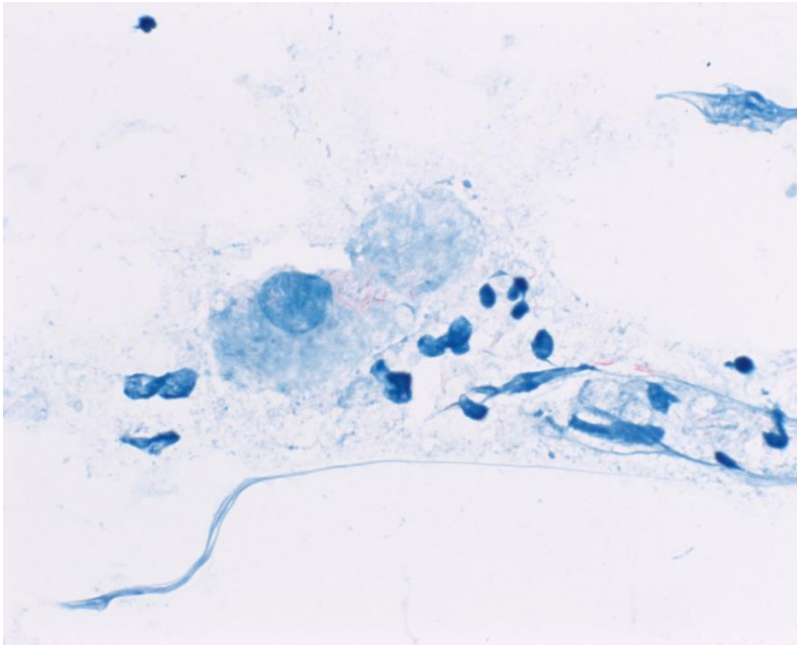
**Mycology - negative**



**There is pus - no pathogen?**



# Mycobacteriosis



**Microscopic method - Coloring according to Zill-Nielsen**

Meropenem - S

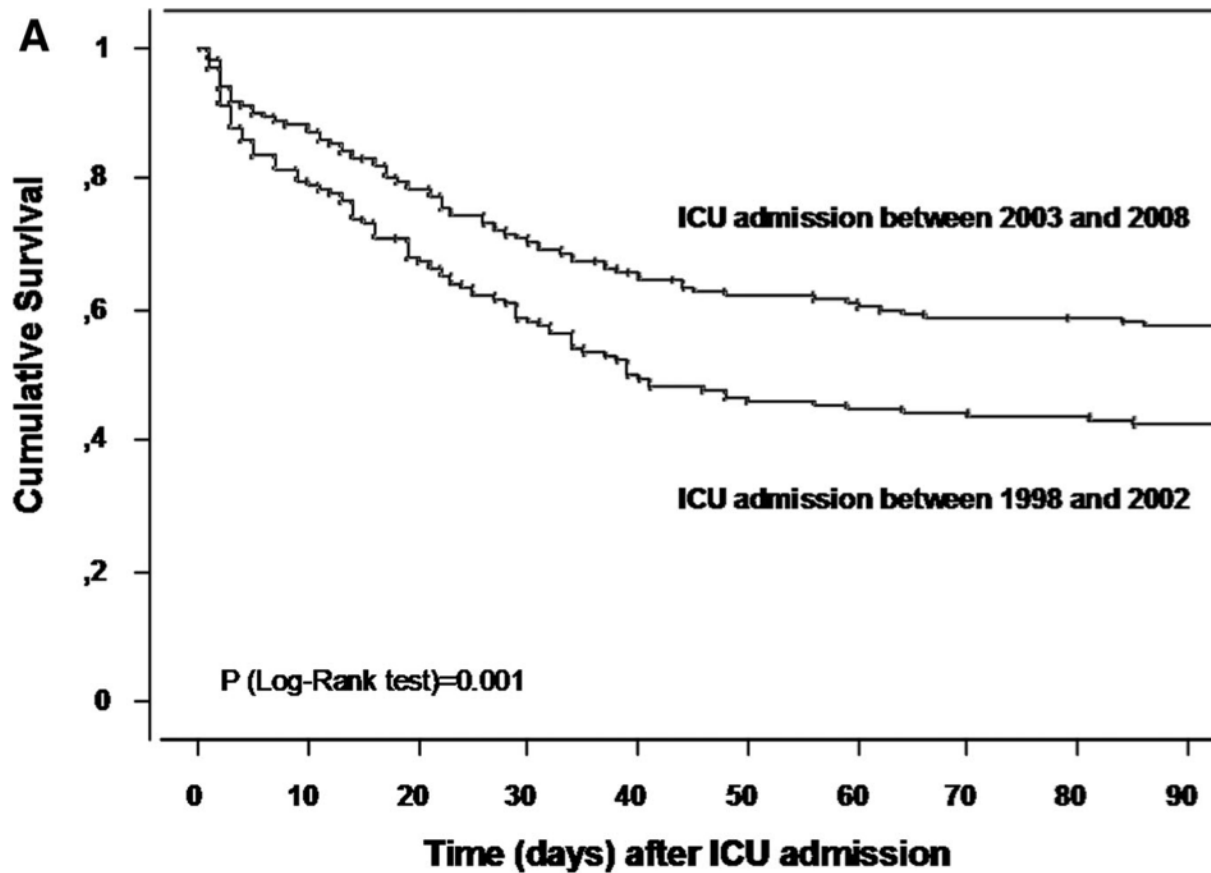
Linezolid - S

Levofloxacin - S

# Survival in neutropenic patients with severe sepsis or septic shock

Legrand et al, Crit care med 2012;40:43

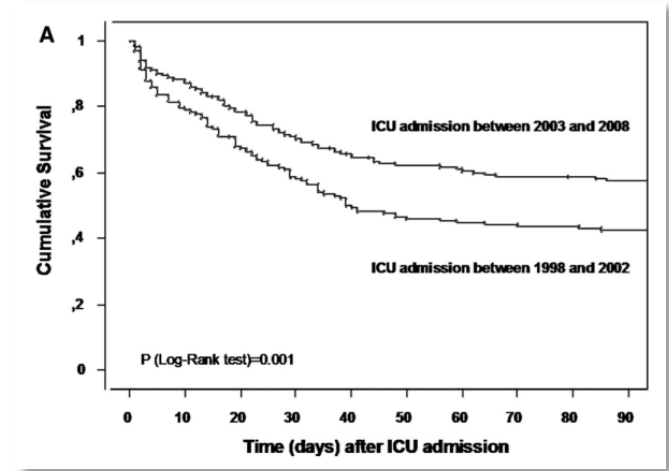
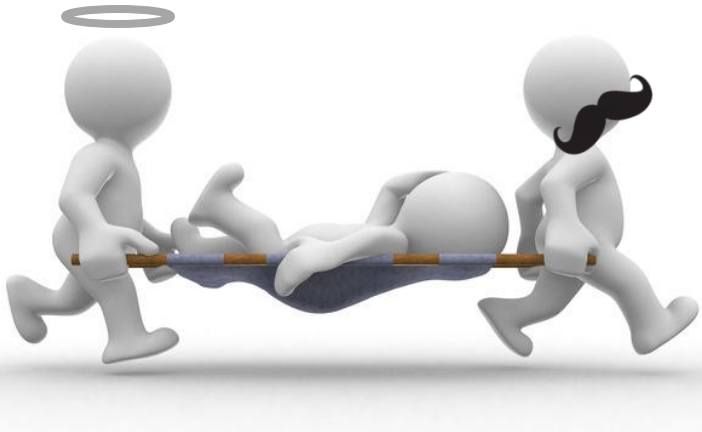
*What happened after 2003?*



# Survival in neutropenic patients with severe sepsis or septic shock

Legrand et al, Crit care med 2012;40:43

*Nothing special...*



**1 - Early translation into intensive care with unproved sepsis**

**2- Early combined antibacterial therapy in patients with unproved sepsis**

**3- Early removal of CVV in patients with unproved sepsis**



# TO CHANGE SEPSIS THERAPY? WHY CHOOSE?

Point last  
opportunities!  
ICU



**The wonderful climate of the Philippines!**



**Thank you for the attention!**