Antimikrobiyal Direnç: Bugünü ve Geleceği
- Tedavi Yönetimi: Sorunlar ve Akılcı Yaklaşım

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Enfeksiyon Hastalıkları ve Klinik Mikrobiyoloji Kliniği

Antimikrobiyal Direnç nedir?

- **Kozmosun bir üyesi olan Bakterilerin hayatta kalma mücadelesidir.**
- **Antimikrobiyal direnç direnç hızı ile tanımlanır ve direnç hızının kabul edilebilir seviyenin üzerine çıkması asıl problemi oluşturur.**
- **Antimikrobiyal direnç antibiyogram raporundaki dirençli antibiyotik listesinden ÇOK AMA ÇOK daha fazlasıdır.**

ANTİBİYOTİKLERİN TARİHSEL KRONOLOJİSİ

Figure 1 Developing Antibiotic Resistance: A Timeline of Key Events[5]

ANTIBIOTIC RESISTANCE IDENTIFIED		ANTIBIOTIC INTRODUCED	
Penicillin-R *Staphylococcus*	1940		
		1943	Penicillin
		1950	Tetracycline
		1953	Erythromycin
Tetracycline-R *Shigella*	1959		
		1960	Methicillin
Methicillin-R *Staphylococcus*	1962		
Penicillin-R pneumococcus	1965		
Erythromycin-R *Streptococcus*	1968		
		1967	Gentamicin
		1972	Vancomycin
Gentamicin-R *Enterococcus*	1979		
		1985	Imipenem and ceftazidime
Ceftazidime-R Enterobacteriaceae	1987		
Vancomycin-R *Enterococcus*	1988		
Levofloxacin-R pneumococcus	1996	1996	Levofloxacin
Imipenem-R Enterobacteriaceae	1998		
XDR tuberculosis	2000	2000	Linezolid
Linezolid-R *Staphylococcus*	2001		
Vancomycin-R *Staphylococcus*	2002	2003	Daptomycin
PDR-*Acinetobacter* and *Pseudomonas*	2004/5		
Ceftriaxone-R *Neisseria gonorrhoeae*	2009	2010	Ceftaroline
PDR-Enterobacteriaceae			
Ceftaroline-R *Staphylococcus*	2011		

PDR = pan-drug-resistant; R = resistant; XDR = extensively drug-resistant

Dates are based upon early reports of resistance in the literature. In the case of pan-drug-resistant *Acinetobacter* and *Pseudomonas*, the date is based upon reports of health care transmission or outbreaks. Note: penicillin was in limited use prior to widespread population usage in 1943.

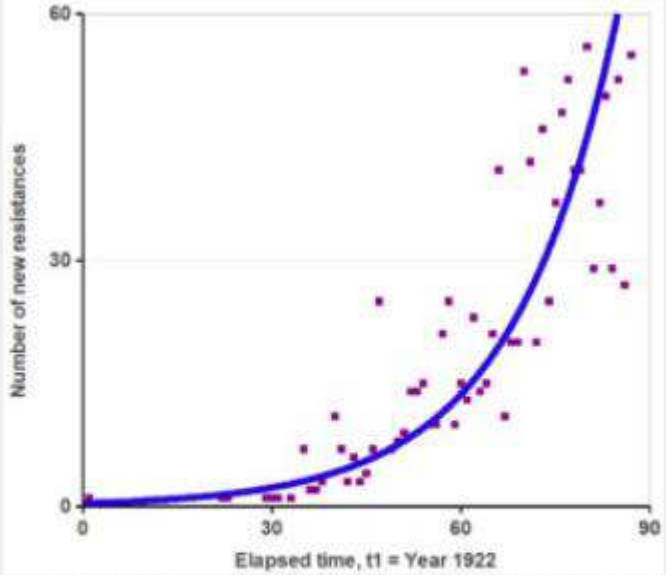


Fig. 1. How fast new cases of antibiotic resistance have been arising around the world.

Very fast rise in the number of cases of antibiotic resistance each year around the world. The trend (as shown by the line) is exponential. First data year is 1922, which corresponds to elapsed time t = 1.

Ventola CL. The Antibiotic Resistance Crisis: Part 1: Causes and Threats. *Pharmacy and Therapeutics*. 2015;40(4):277-283.

BAKTERİLERİN DİRENÇ MEKANİZMALARI YENİ GELİŞEN BİR DURUM MU?

Drug Resistance Updates
Volume 7, Issue 2, April 2004, Pages 111-123

Evolution of the serine β-lactamases: past, present and future

Barry G Hall, Miriam Barlow

Show more

https://doi.org/10.1016/j.drup.2004.02.003

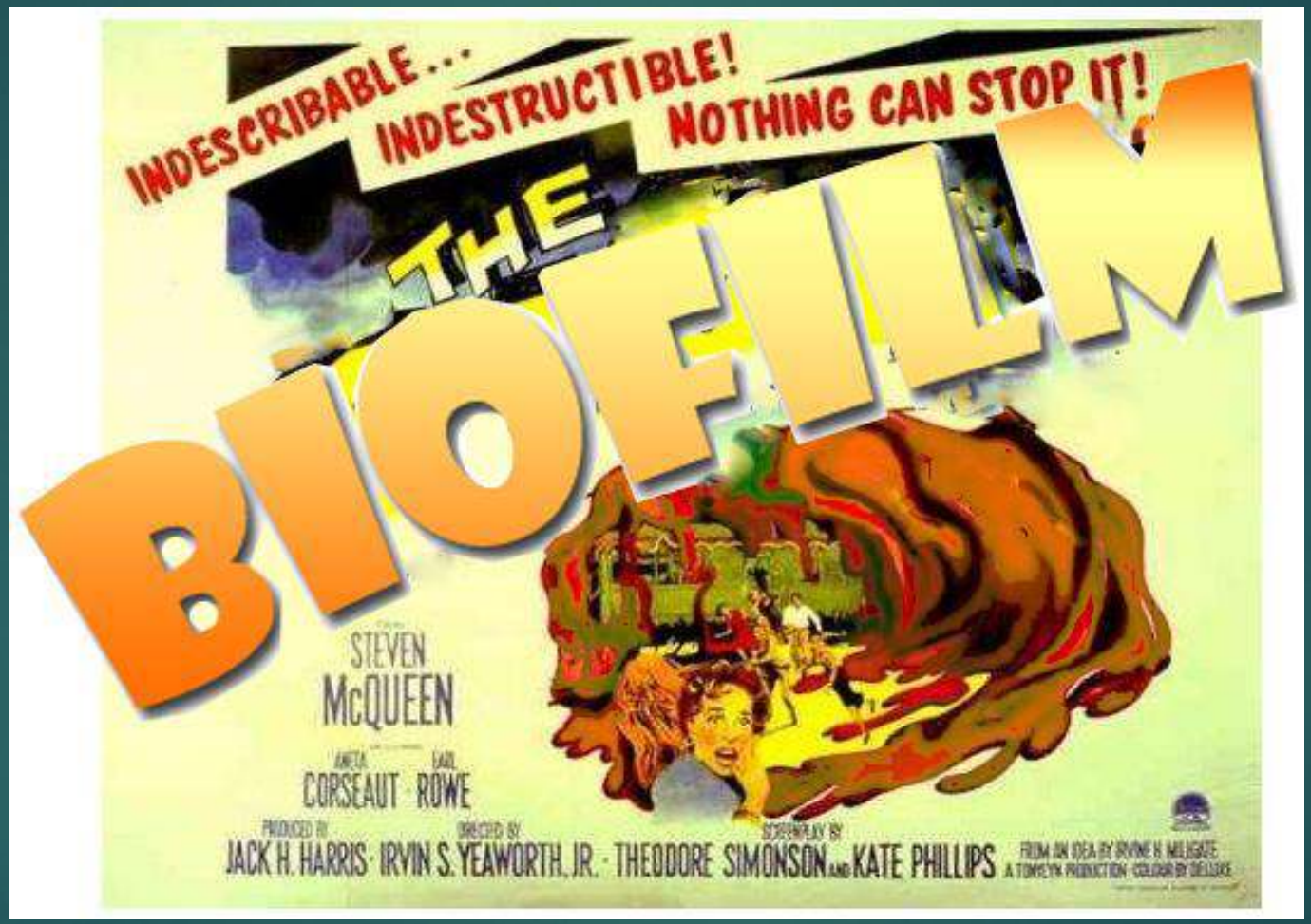
Abstract

We present a protein structure-based phylogeny of Classes A, C and D of the serine β-lactamases, and a new, detailed, sequence-based phylogeny of the Class A β-lactamases. In addition, we discuss the historical evolution of Classes C and D. The evolutionary histories of all three classes indicate that the serine β-lactamases are ancient enzymes, originating over two billion years ago, and that some have been on plasmids for millions of years. We also discuss the recent, antibiotic-era, evolution of the serine β-lactamases in response to the clinical use of β-lactam antibiotics. We also discuss a method that is being used to predict the future evolution of β-lactamases in response to selection with new drugs

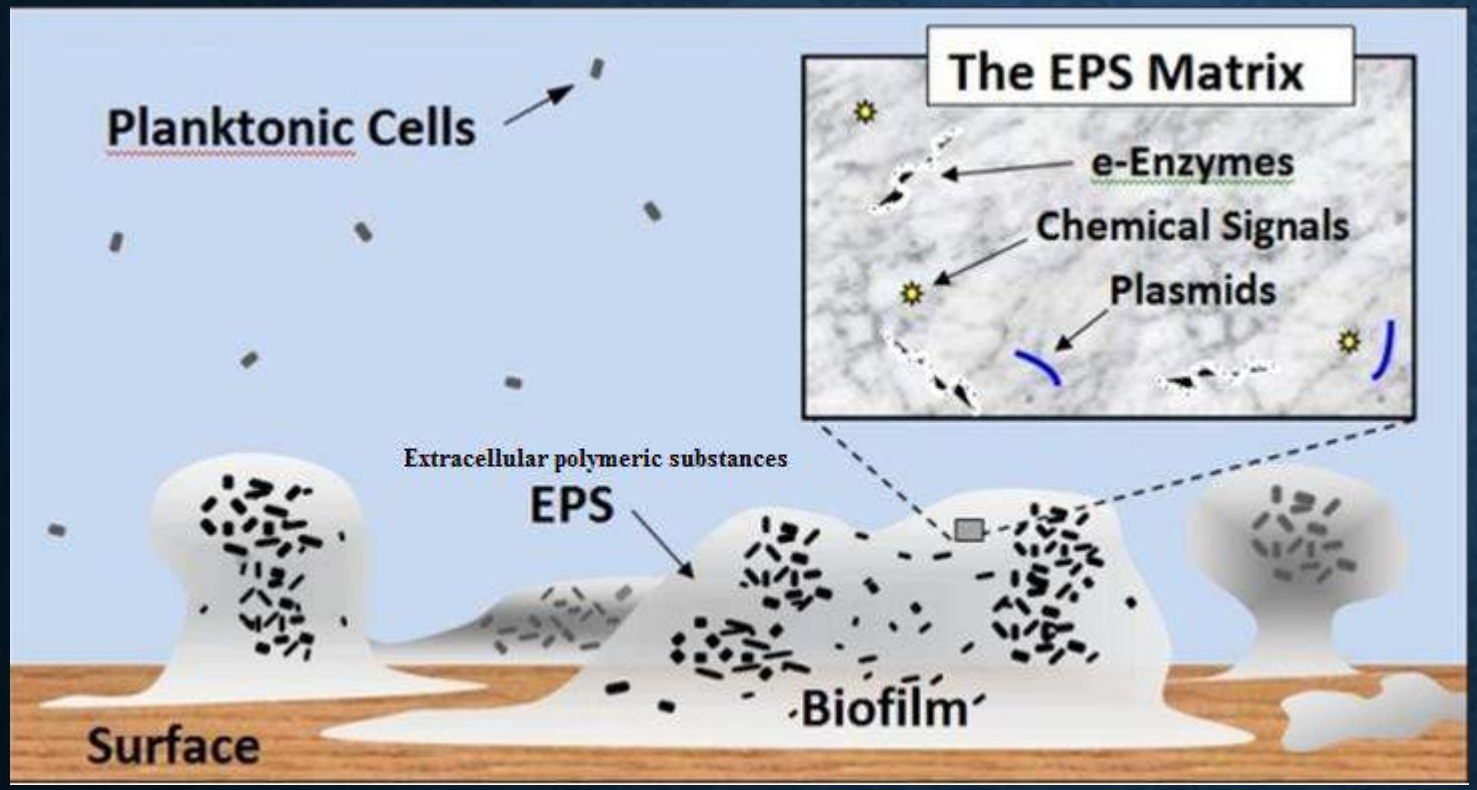
Hangi direnç mekanizmaları önem arz ediyor?

Table 8.1 Specimens distributed in the CAESAR EQA survey in 2016 and their important antimicrobial susceptibility features

Specimen number	Organism	Correct identification among participating laboratories (n = 254) (%)	Important antimicrobial susceptibility features of the strain
3682	E. coli	99	Acquired AmpC beta-lactamase enzyme (BIL-1) Reduced susceptibility to ertapenem
3683	K. pneumoniae	91	Both OXA-1 and SHV-1 enzymes Resistant to beta-lactam agents including inhibitor combinations, colistin (by EUCAST methodology) and quinolones Intermediately resistant to amikacin (by EUCAST methodology)
3684	P. aeruginosa	100	Resistant to carbapenems, likely to be mediated by porin loss/efflux as no known carbapenemase enzyme is present Resistant and intermediate to piperacillin-tazobactam by EUCAST and CLSI breakpoints, respectively
3685	S. aureus	98	mecC gene Resistant to beta-lactam agents and susceptible to all other antibiotics
3686	A. baumannii complex	91	Resistant to gentamicin and ciprofloxacin Susceptible to amikacin, colistin, imipenem, meropenem and tobramycin
3687	S. pneumoniae	98	Wild-type for penicillin (minimum inhibitory concentration ≤ 0.015 mg/L)


INDESCRIBABLE...
INDESTRUCTIBLE!
NOTHING CAN STOP IT!
THE
BIOFILM
STEVEN
McQUEEN
ANETA
CORSEAUT
EARL
ROWE
PRODUCED BY
JACK H. HARRIS
DIRECTED BY
IRVIN S. YEAWORTH, JR.
SCREENPLAY BY
THEODORE SIMONSON AND KATE PHILLIPS
FROM AN IDEA BY IRVINE H. MILLIGATE
A TONEYN PRODUCTION
COLOUR BY DE LUXE

BİYOFİLM


Planktonic Cells
The EPS Matrix
e-Enzymes
Chemical Signals
Plasmids
Extracellular polymeric substances
EPS
Biofilm
Surface

Neden Biyofilm önem arz ediyor?

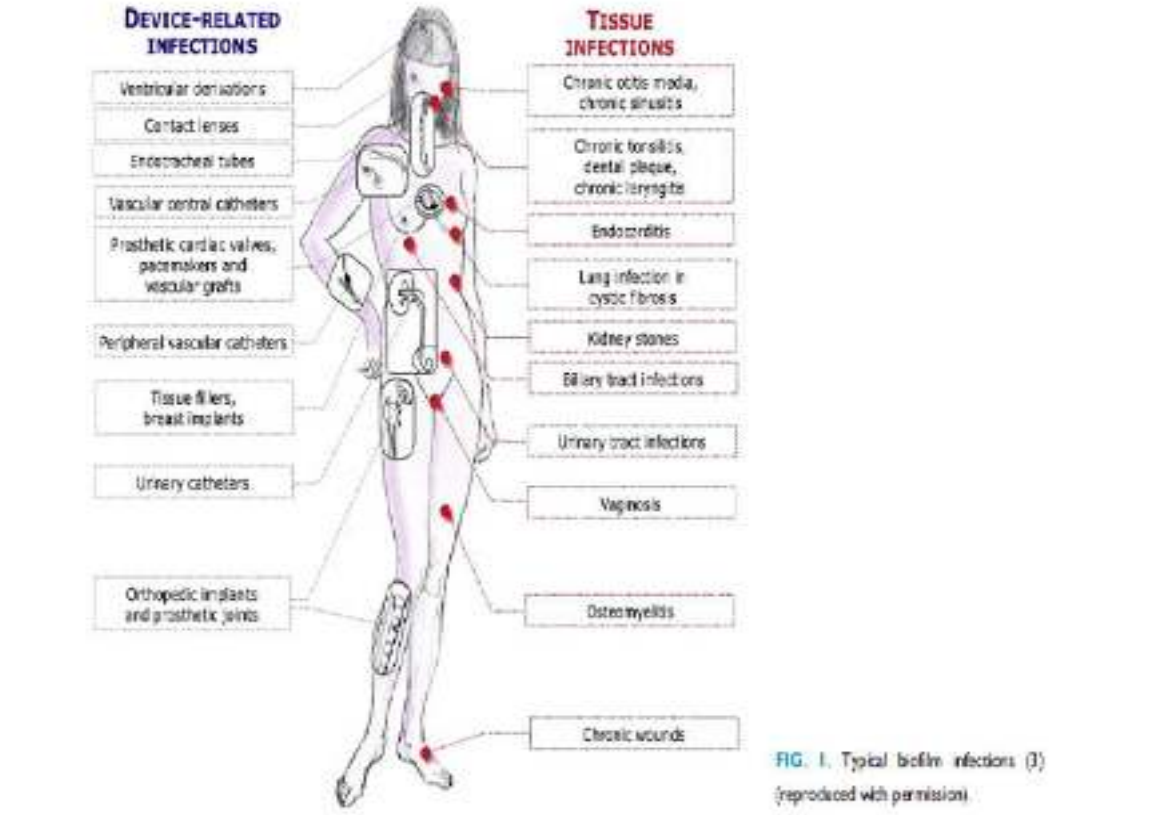


FIG. 1. Typical biofilm infections (3)
(reproduced with permission)

Bakteriyel enfeksiyonların %65-80'i artık bu grupta!
Costerton JW, Science, 1999

BİYOFİLM OLUŞTURAN PATOJENLER

Table 1 List of medical implants prone to biofilm formation with the causative agent.

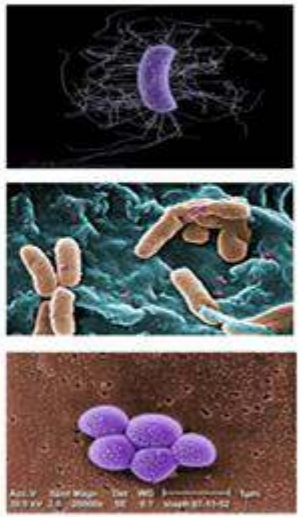
Medical device	**Bacteria**
Dental implants	*Staphylococcus aureus*, *Candida albicans*, *Streptococcus*
Urinary catheters	*S. epidermidis*, *K. pneumoniae*, *Enterococcus*, *Proteus mirabilis*, *P. aeruginosa*, *E. coli* and other gram-negative bacteria
Intra-urine devices	S. aureus, *S. epidermidis*, *P. aeruginosa*, *E. coli*, *Neisseria gonorrhoeae*, *Candida albicans* and *Candida dubliniesis*
Artificial hip prosthesis	*Staphylococcus* spp., *P. acnes*, *Salmonella enterica*, *Shigella*
Prosthetic heart valves	*Enterococcus*, *S. epidermidis*, *S. aureus*, *Streptococci*, *Diphtheria*, *Candida albicans* and gram-negative bacilli,
Synthetic vascular grafts	*S. aureus*, *Candida*, *Enterococcus*, *Streptococcus*
Ventilator tubing	*Acinetobacter baumannii* and *Pseudomonas aeruginosa*
Artificial voice prosthesis	*Candida albicans*, *S. aureus*, *P. aeruginosa*,
central venous catheters	*S. epidermidis*, *Enterococcus faecalis*, *K. pneumoniae*, *Candida albicans*, *P. aeruginosa*, *S. aureus*
Orthopedic implants	*S. epidermidis*, *P. aeruginosa*, *Enterococcus*, *S. aureus*

Hangi mikroorganizmaların direnci önem arz etmektedir?

Urgent
C. difficile
CRE
N. gonorrhoeae

Serious
Multidrug-resistant *Acinetobacter*; drug-resistant *Campylobacter*; fluconazole-resistant *Candida*; extended-spectrum Enterobacteriaceae, vancomycin-resistant enterococcus; multidrug-resistant *P. aeruginosa*

Concerning
Vancomycin-resistant *Staphylococcus aureus*
Erythromycin-resistant group A *Streptococcus*
Clindamycin-resistant group B *Streptococcus*



Reproduced from CDC.

CDC website. Antibiotic resistance threats in the United States, 2013.

Antimikrobiyal Direnç hangi hastalarda daha sık?

Table 1
Bivariable analysis of patient characteristics in the case-control study

Variable	Cases (n = 73)	Controls (n = 73)	Unadjusted Odds Ratio	p-value
Age (mean ± SD), *in years*	61.7	60.4	N/A	0.798
Male	49 (67.1)	52 (71.2)	0.82	0.591
Diabetes	42 (57.5)	10 (13.7)	8.53	< 0.001
Chronic pulmonary disease	35 (47.9)	12 (16.4)	4.68	< 0.001
Renal insufficiency	32 (43.8)	12 (16.4)	3.97	< 0.001
Malignancy	21 (28.8)	7 (9.6)	3.81	0.005
Corticosteroid intake	5 (6.8)	7 (9.6)	0.69	0.55
Urinary catheter in the past 30 days	62 (84.9)	58 (79.4)	1.46	0.39
Central venous catheter in the past 30 days	7 (9.6)	4 (5.5)	1.83	0.35
Mechanical ventilation in the past 30 days	43 (58.9)	39 (53.4)	1.25	0.50
Surgery in the past 30 days	19 (26.0)	5 (6.8)	4.78	0.003
Antibiotic use in the past 30 days	47 (64.3)	12 (16.4)	9.19	< 0.001
All-cause mortality	34 (46.6)	27 (37.0)	1.48	0.24

All numbers represent no. (%) unless otherwise specified

SD = standard deviation; N/A = not applicable

Table 2
Complications and outcome in patients with susceptible *Acinetobacter* infection vs. MDR Ab infection in the case-control study

Variable	Susceptible *Acinetobacter* infection (n = 33) n (%)	MDR-Ab infection (n = 40) n (%)
Sepsis	15 (45.4)	17 (42.5)
ARDS	2 (6.1)	0
Respiratory failure	4 (12.1)	8 (20.0)
ICU admission	5 (15.1)	8 (20.0)
AKI	8 (24.2)	10 (25.0)
Prolonged hospital stay	27 (81.2)	31 (77.5)
Persistence/progression of infection	5 (15.1)	13 (32.5)
Recurrence of infection	6 (18.2	8 (20.0)
All-cause mortality	12 (36.4)	22 (55.0)

MDR-Ab = multidrug-resistant Acinetobacter; ARDS = adult respiratory distress syndrome; ICU = intensive care unit; AKI = acute kidney injury

Zeina A. Kanafani, Nada Zahreddine, Ralph Tayyar, Jad Sfeir, George F. Araj, Ghassan M. Matar, Souha S. Kanj. Multi-drug resistant Acinetobacter species: a seven-year experience from a tertiary care center in Lebanon.
Antimicrobial Resistance & Infection Control 2018;**7**:9

Antimikrobiyal Direnç hangi hastalarda daha sık?

	Carbapenem-nonsusceptible *A. baumannii-calcoaceticus* complex positive on admission	Carbapenem-nonsusceptible *A. baumannii-calcoaceticus* complex acquired during ICU stay	Carbapenem-nonsusceptible *A. baumannii-calcoaceticus* complex negative	*P* value
	n = 69	(*n* = 89)	*n* = 254	
SIRS Score ≥ 2	64 (92.8)	81 (91.0)	232 (91.3)	
Score < 2	5 (7.2)	8 (9.0)	22 (8.7)	
qSOFA Score (%)				0.089
Score ≥ 2	51 (73.9)	78 (87.6)	205 (80.7)	
Score < 2	18 (26.1)	11 (12.4)	49 (19.3)	
Procedures (during ICU admission)				
Mechanical ventilation (%)	63 (91.3)	88 (98.9)	220 (86.6)	0.004
Mechanical ventilation (days) median(IQR)	5 (2–8)	8 (4–16)	3 (1–6)	
≥ 5 days (%)	36 (52.2)	63 (70.8)	83 (32.7)	<0.01
< 5 days (%)	33 (47.8)	26 (29.2)	171 (67.3)	

Yulia Rosa Saharman, Anis Karuniawati, Rudyanto Sedono, Dita Aditianingsih, Pratiwi Sudarmono, Wil H. F. Goessens, Corné H. W. Klaassen, Henri A. Verbrugh Juliëtte A. Severin. Endemic carbapenem-nonsusceptible *Acinetobacter baumannii-calcoaceticus* complex in intensive care units of the national referral hospital in Jakarta, Indonesia. *Antimicrobial Resistance & Infection Control* 2018;7:5

Antimikrobiyal Direnç hangi hastalarda daha sık?

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	n = 69	(*n* = 89)	*n* = 254	
Central venous catheter (%)	66 (95.7)	85 (95.5)	212 (83.5)	<0.01
Central venous catheter (days) median(IQR)	6 (3–9)	10 (5–17)	4 (2–7)	
≥ 5 days (%)	41 (59.4)	71 (79.8)	111 (43.7)	<0.01
< 5 days (%)	28 (40.6)	18 (20.2)	143 (56.3)	
Urine catheter	69 (100)	89 (100)	254 (100)	N/A
Urine catheter (days) median (IQR)	6 (3–10)	10 (6–18)	5 (3–7)	
< 5 days (%)	26 (37.7)	13 (14.6)	122 (48.0)	<0.01
≥ 5 days (%)	43 (62.3)	76 (85.4)	132 (52.0)	

Yulia Rosa Saharman, Anis Karuniawati, Rudyanto Sedono, Dita Aditianingsih, Pratiwi Sudarmono, Wil H. F. Goessens, Corné H. W. Klaassen, Henri A. Verbrugh Juliëtte A. Severin. Endemic carbapenem-nonsusceptible *Acinetobacter baumannii-calcoaceticus* complex in intensive care units of the national referral hospital in Jakarta, Indonesia. *Antimicrobial Resistance & Infection Control* 2018;7:5

Antimikrobiyal Direnç hangi hastalarda daha sık?

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	n = 69	(*n* = 89)	*n* = 254	
Any antibiotic (%)	68 (98.6)	89 (100)	249 (98.0)	0.411
Carbapenem (%)	42 (60.9)	62 (69.7)	95 (37.4)	<0.01
Outcomes				
Length of stay (days), median (IQR)	5 (3–9)	11 (5–18)	4 (3–7)	<0.01
Death	22 (31.9)	38 (42.7)	59 (23.2)	0.002

Yulia Rosa Saharman, Anis Karuniawati, Rudyanto Sedono, Dita Aditianingsih, Pratiwi Sudarmono, Wil H. F. Goessens, Corné H. W. Klaassen, Henri A. Verbrugh Juliëtte A. Severin. Endemic carbapenem-nonsusceptible *Acinetobacter baumannii-calcoaceticus* complex in intensive care units of the national referral hospital in Jakarta, Indonesia. *Antimicrobial Resistance & Infection Control* 2018;7:5

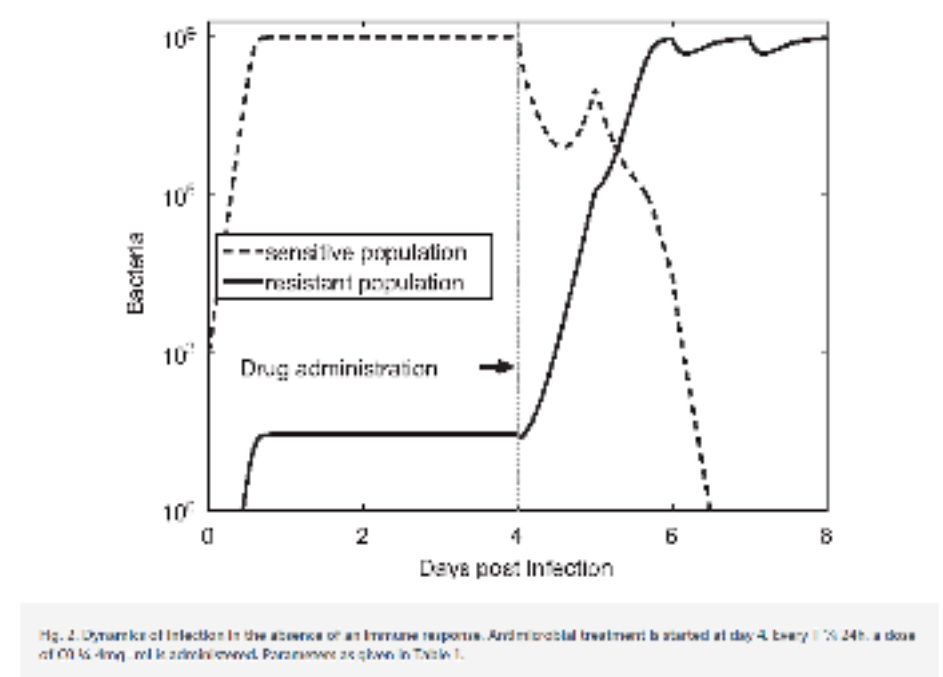
Antimikrobiyal direnç neden önemlidir?

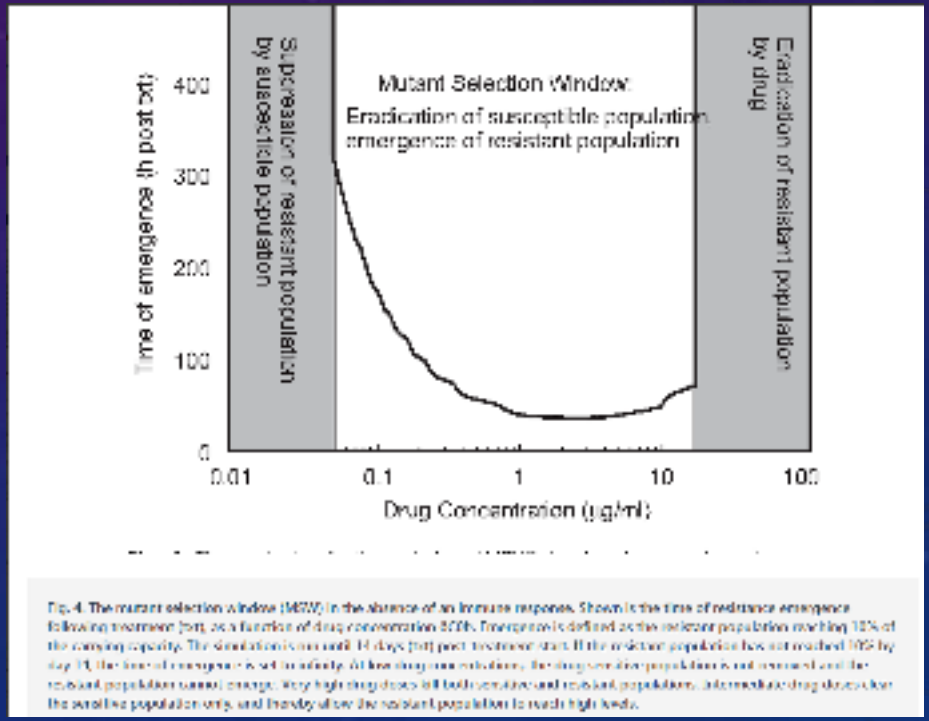
Multidrug-Resistant *Pseudomonas aeruginosa*: Clinical Impact

Outcomes*	Patients With MDR Infection (n=82)	Controls (n=82)	*P* Value
Mortality, No. (%)	18 (21)	10 (12)	.004
Hospital LOS, d (median)	20	10	.001
Need for surgery (including amputation), No. (%)	22 (27)	13 (16)	.05
Other performed procedures, No. (%)	31 (38)	9 (11)	.001
Discharged to chronic care facility, No. (%)	45 (55)	20 (24)	.012
Full activity at discharge, No .(%)	28 (34)	48 (59)	.015

*Multivariate analysis.
Aloush V, et al. *Antimicrob Agents Chemother*. 2006;50:43-48.

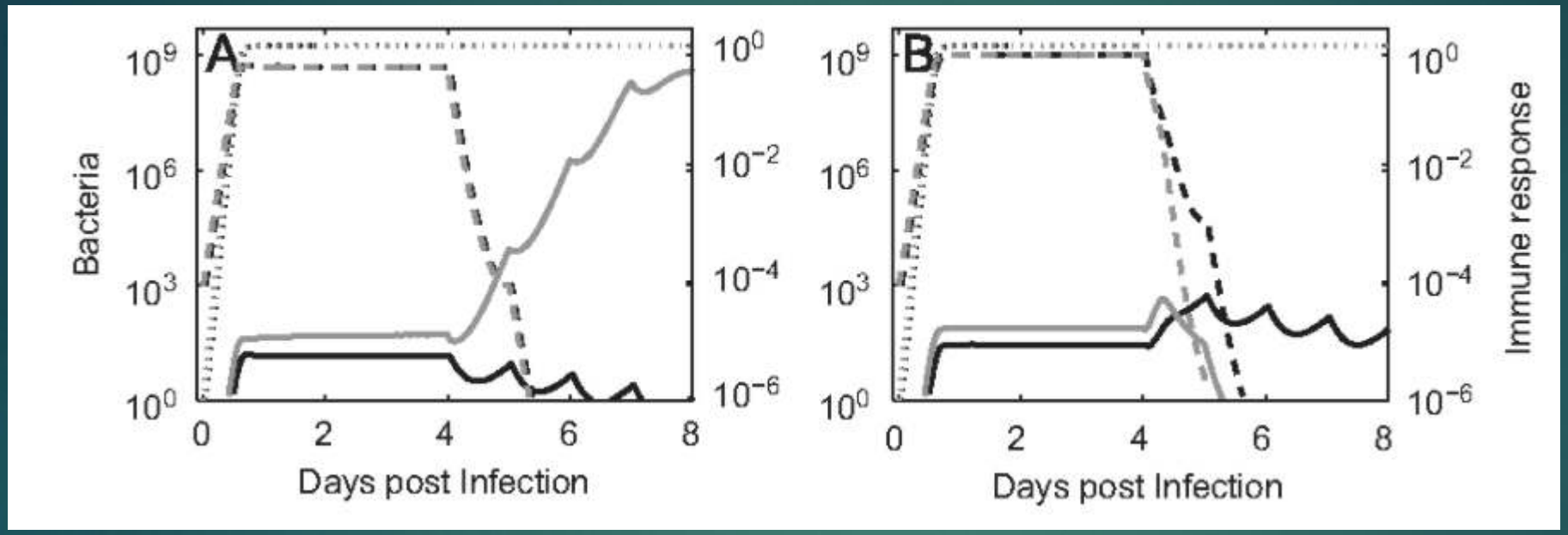
ANTİMİKROBİYAL DİRENÇ- İMMÜN SİSTEM İLİŞKİSİ NEDİR?





Handel A, Margolis E, Levin R B. Exploring the role of the immune response in preventing antibiotic resistance. J Theor Biol 2008;256 (4):655-62

Antimikrobiyal Direnç- İmmün sistem ilişkisi nedir?



ANTİMİKROBİYAL DİRENÇ- İMMÜN SİSTEM İLİŞKİSİ NEDİR?

- **İmmün cevap mutant seleksiyon penceresine baskı yapar ve daraltır**
- **Bu baskı dirençli mikroorganizma seleksiyonunu azaltır**

- **Optimum doz stratejisine katkıda bulunur**

- **Antibiyotiğe bağlı olarak ortaya çıkan dirençli bakteri kolonizasyonunu azaltarak flora bakterilerinin korunmasına katkıda bulunur**

Antimikrobiyal Direnç- İmmün sistem ilişkisi nedir?

- **Tedaviye uyumsuzluğun negatif etkilerini azaltır.**
- **Yüksek bakteri yükünde düşük immün cevap, düşük bakteri yükünde yüksek immün cevap gelişmektedir.**
- **Bu nedenle antibiyotik tedavisiyle bakteri yükü azaldığında immün cevabın seviyesi de artmaktadır.**

Sepsis- Genetik ilişkisi

critical care review

Genetic Polymorphisms in Sepsis and Septic Shock*

Role in Prognosis and Potential for Therapy

Cheryl L. Holmes, MD; James A. Russell, MD; and Keith R. Walley, MD

Genetic epidemiologic studies suggest a strong genetic influence on the outcome from sepsis, and genetics may explain the wide variation in the individual response to infection that has long puzzled clinicians. Several candidate genes have been identified as important in the inflammatory response and investigated in case-controlled studies, including the tumor necrosis factor (TNF)-α and TNF-β genes, positioned next to each other within the cluster of human leukocyte antigen class III genes on chromosome 6. Other candidate genes for sepsis and septic shock include the interleukin (IL)-1 receptor antagonist gene, the heat shock protein gene, the IL-6 gene, the IL-10 gene, the CD-14 gene, the Toll-like receptor (TLR)-4 gene, and the TLR-2 gene, to name a few. In this review, we summarize the evidence for a genetic susceptibility to development of sepsis and death from sepsis, discuss design of clinical genetics studies relevant to the study of complex disorders, consider the candidate genes likely to be involved in the pathogenesis of sepsis, and discuss the potential for targeted therapy of sepsis and septic shock based on genetic variability.
(CHEST 2003; 124:1103–1115)

Key words: heat-shock protein; interleukin; polymorphism; septicemia; sepsis syndrome; tumor necrosis factor

Abbreviations: APC = activated protein C; CI = confidence interval; HLA = human leukocyte antigen; HSP = heat shock protein; IL = interleukin; IL-1ra = interleukin 1 receptor antagonist; LPS = lipopolysaccharide; MHC = major histocompatibility complex; MODY = maturity-onset diabetes of youth; mRNA = messenger RNA; NF = nuclear factor; NO = nitric oxide; NOD = nucleotide-binding oligomerization domain; PAMP = pathogen-associated microbial pattern; PRR = pattern recognition receptor; sCD-14 = soluble CD-14; SNP = single-nucleotide polymorphism; TF = tissue factor; TLR = Toll-like receptor; TNF = tumor necrosis factor

ANTİMİKROBİYAL DİRENCİN SAĞKALIMA ETKİSİ

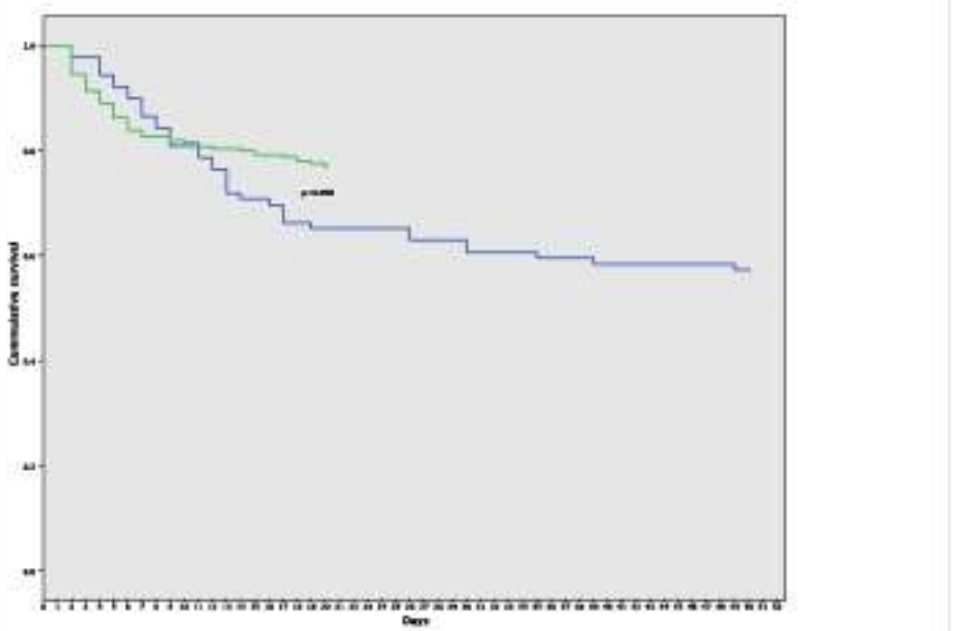
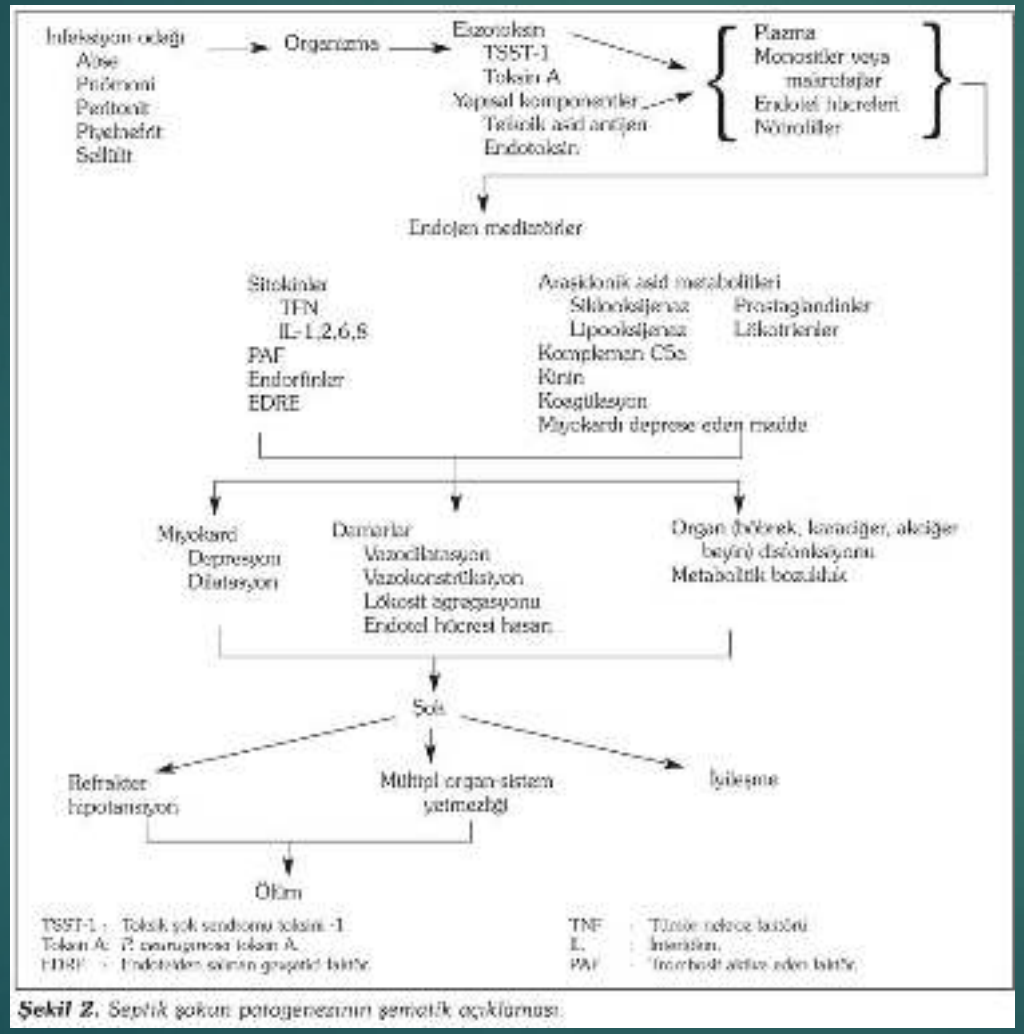


Fig. 3
Survival analysis of ICU patients according to their carbapenem-nonsusceptible *Acinetobacter baumannii-calcoaceticus* complex status. Note: Survival of patients with carbapenem-nonsusceptible *A. baumannii-calcoaceticus* complex acquired during their ICU stay (blue line) compared with the survival of patients that remained negative for carbapenem-nonsusceptible *A. baumannii-calcoaceticus* complex in their screening and clinical cultures (green line)

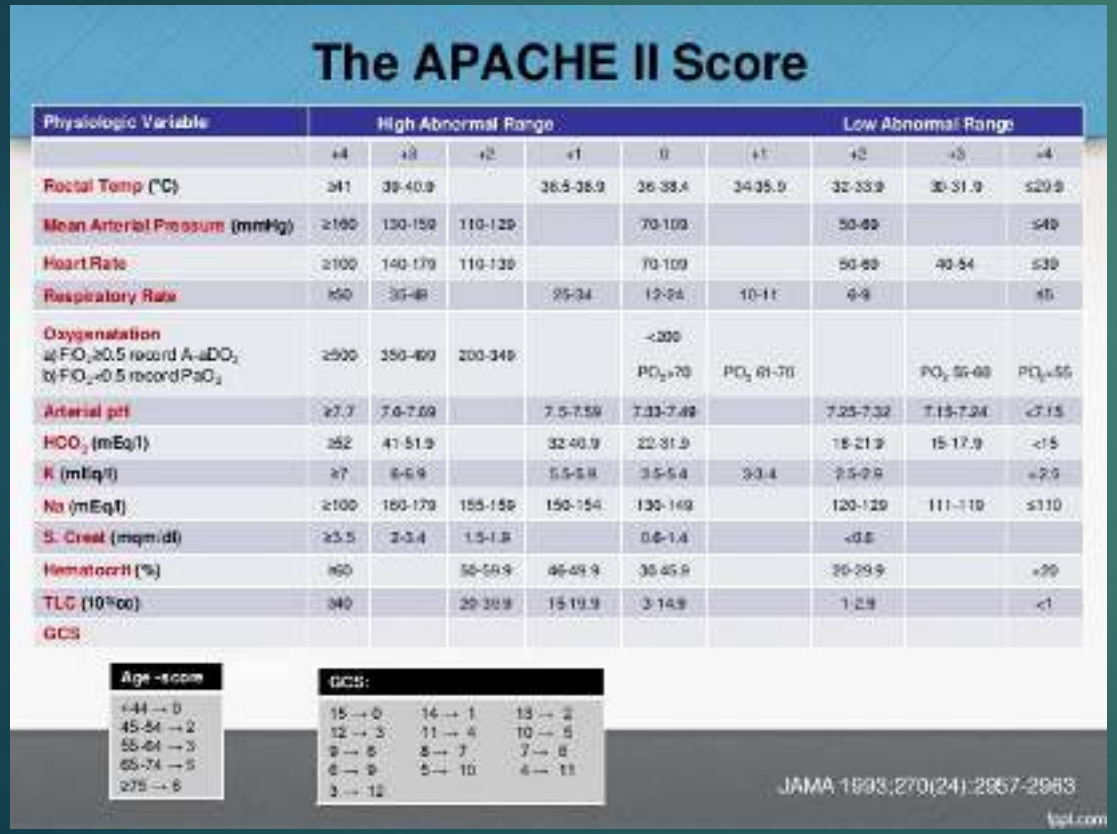
Yulia Rosa Saharman, Anis Karuniawati, Rudyanto Sedono, Dita Aditianingsih, Pratiwi Sudarmono, Wil H. F. Goessens, Corné H. W. Klaassen, Henri A. Verbrugh Juliëtte A. Severin. Endemic carbapenem-nonsusceptible *Acinetobacter baumannii-calcoaceticus* complex in intensive care units of the national referral hospital in Jakarta, Indonesia. *Antimicrobial Resistance & Infection Control* 2018;7:5

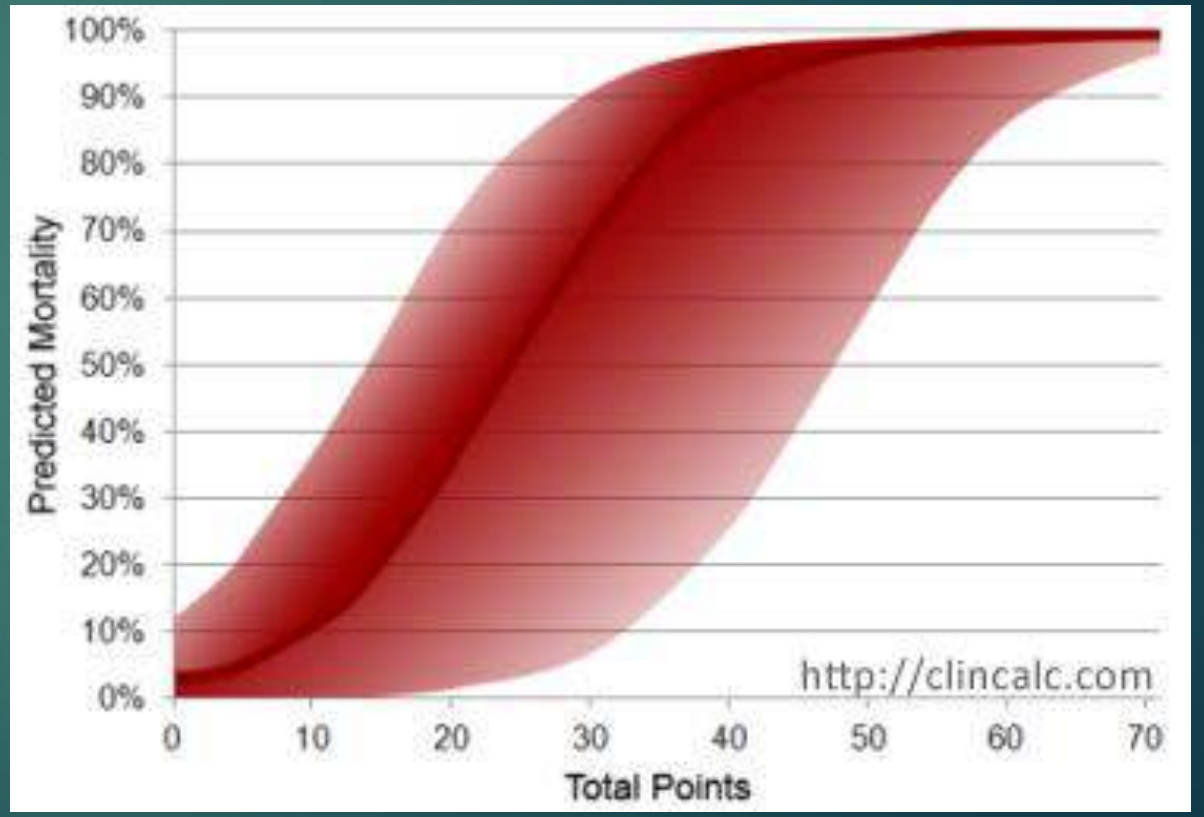
Antimirobiyal direncin sağkalıma etkisi



Şekil 2. Septik şokun patogenezinin şematik açıklanması

Antimikrobiyal direncin sağkalıma etkisi

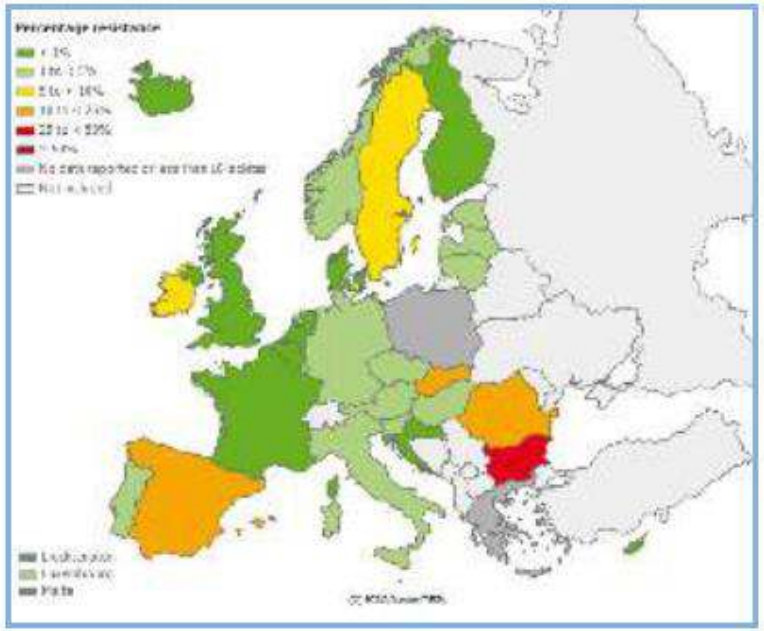




Türkiye’ de antibakteriyel direncin son durumu nedir?

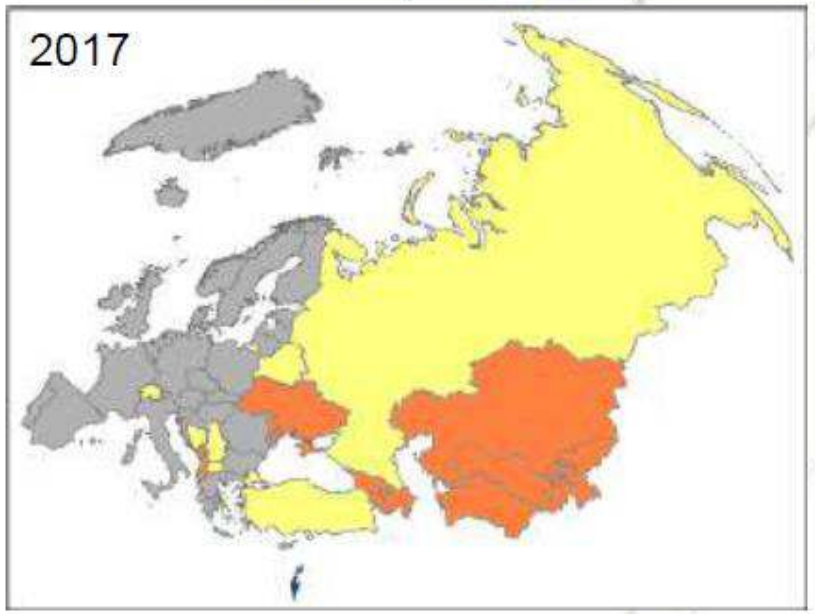
AMD Sürveyansının Avrupa'da yaygınlaştırılması

European Antimicrobial Resistance Surveillance Network (EARS-Net)



European Centre for Disease Prevention and Control

Central Asian and Eastern European Surveillance of Antimicrobial Resistance (CAESAR)



World Health Organization Regional Office for Europe

Türkiye’ de antibakteriyel direncin son durumu nedir?

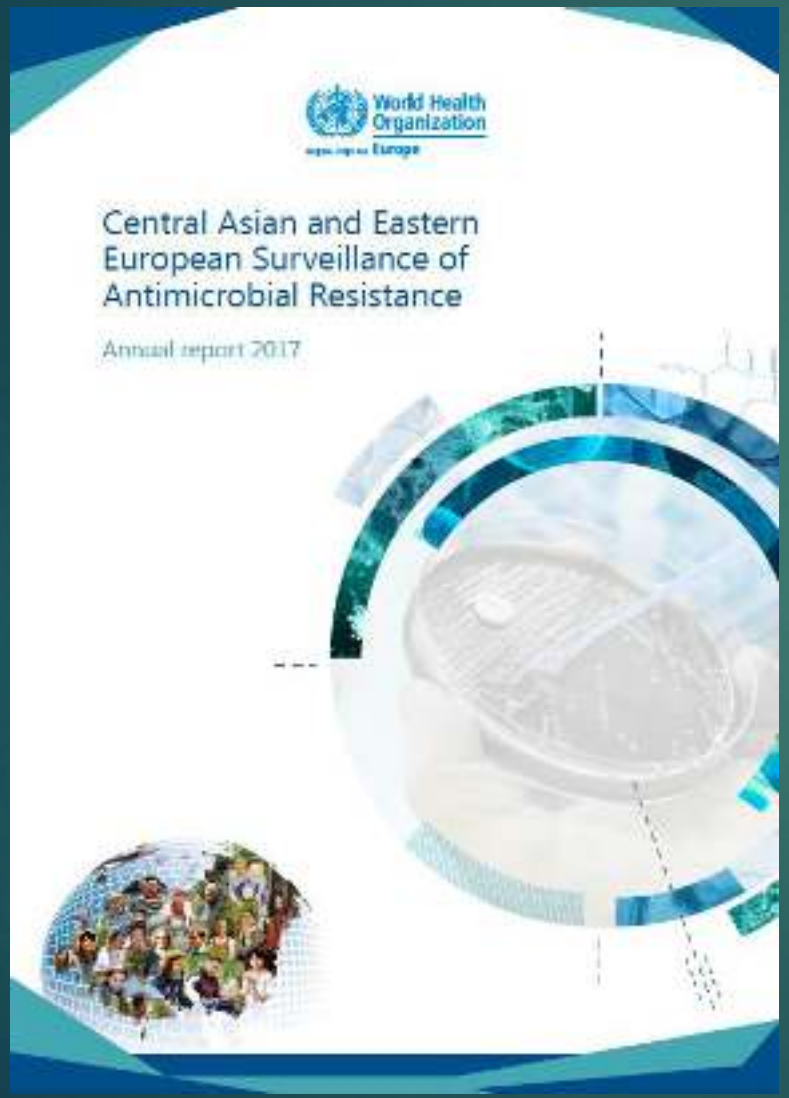


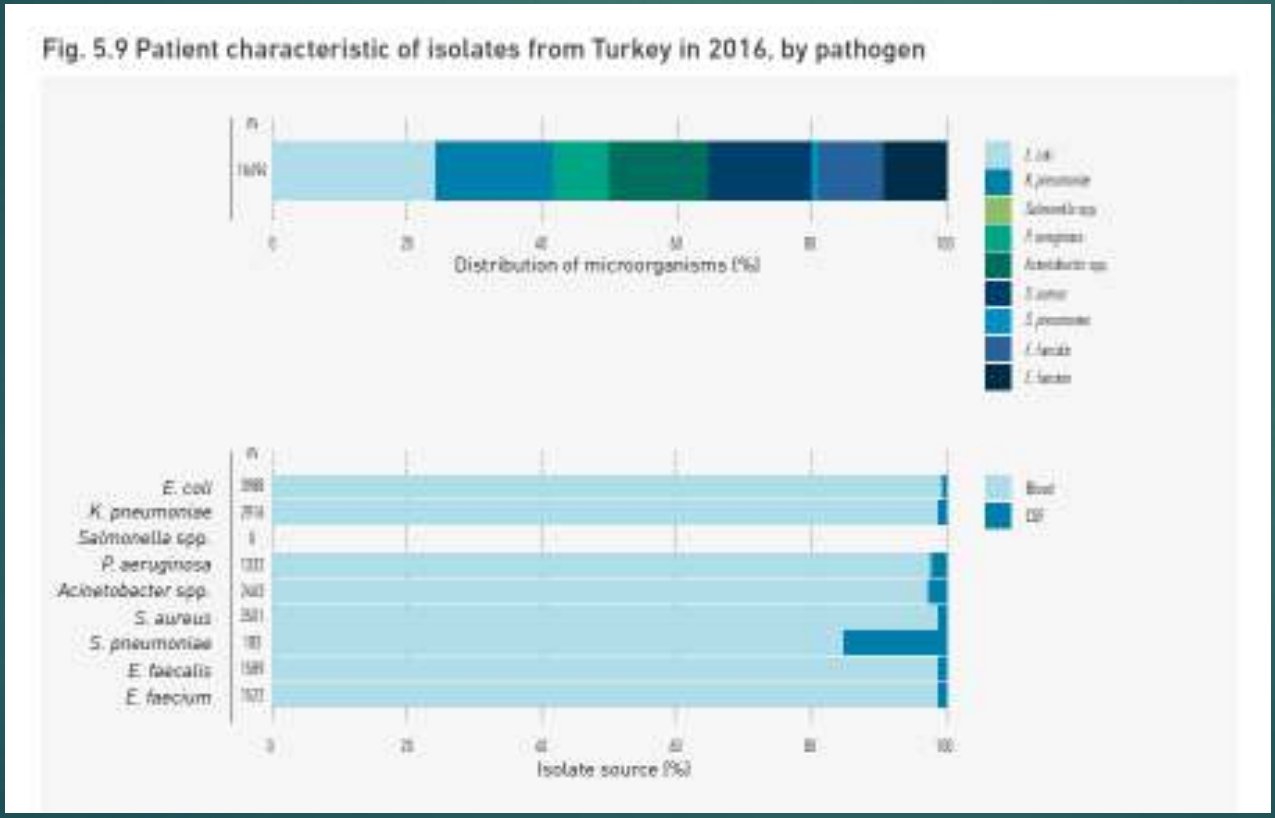
Table 2.5 Quality control

Country or area	Laboratory quality assurance system in place	Participation in CAESAR EQA exercise
Albania	✗	✓
Armenia	⚙	✓
Azerbaijan	✓	✓
Belarus	✓	✓
Bosnia and Herzegovina	✓	✓
Georgia	✓	✓
Kazakhstan	N/A	✗
Kyrgyzstan	⚙	✓
Montenegro	✓	✓
Republic of Moldova	✓	✓
Russian Federation	✓	✓
Serbia	✓	✓
Switzerland	✓	✗
Tajikistan	✗	✓
The former Yugoslav Republic of Macedonia	⚙	✓
Turkey	✓	✓
Turkmenistan	⚙	✓
Ukraine	✓	✓
Uzbekistan	⚙	✓
Kosovo*	⚙	✓
No	3	2
In progress	4	0
Yes	11	18

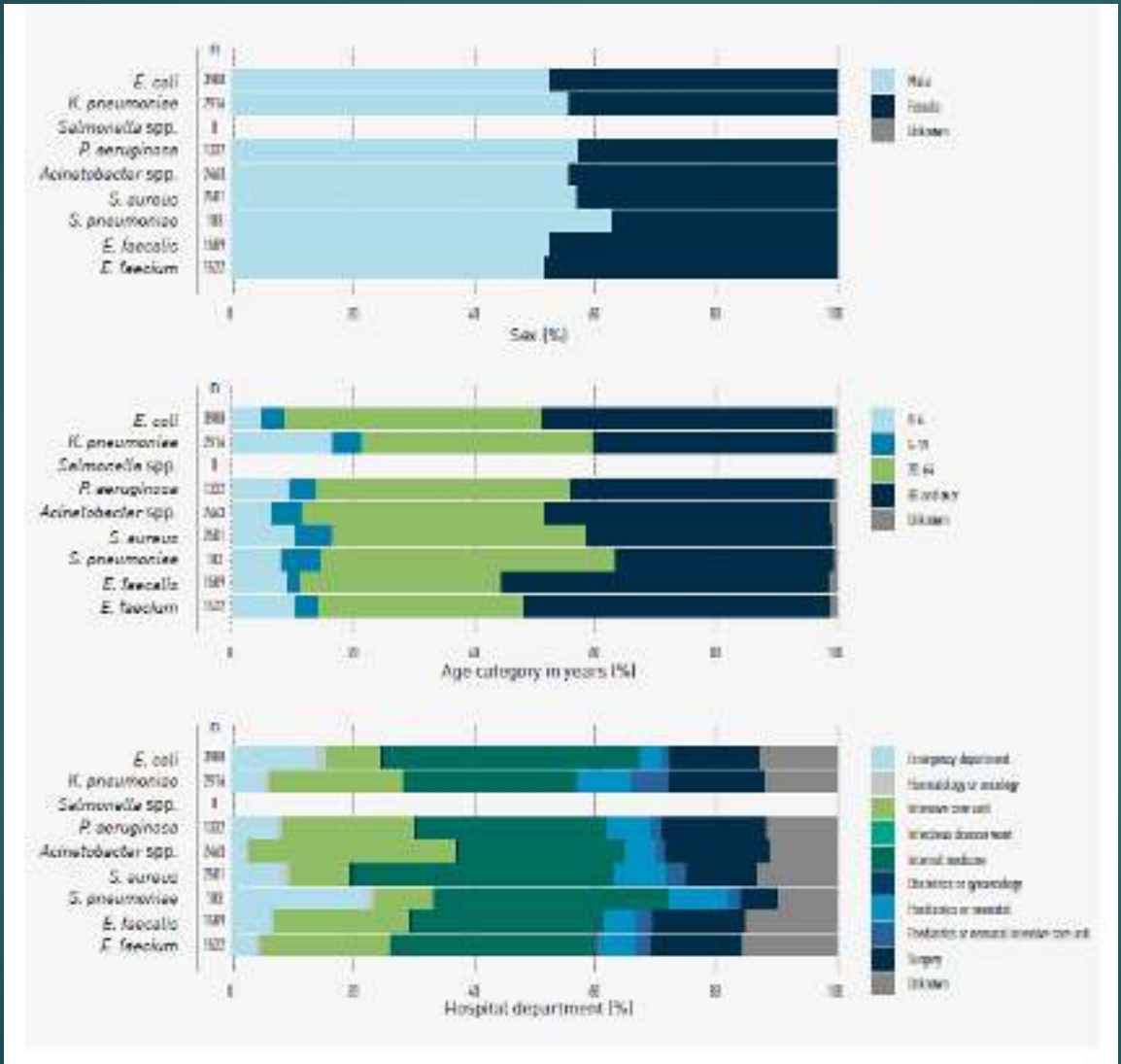
CAESAR sürveyansına Türkiye' den kaç merkez katılmaktadır?

The 105 laboratories participating in the network were selected from different geographical regions of the country to reflect the distribution of the population. In 2016, data from 67 laboratories were included: 35 clinical microbiology laboratories of university hospitals, 30 clinical microbiology laboratories of state hospitals and two clinical microbiology laboratories of private hospitals. These hospitals cover about 39% of the hospital beds in Turkey and about 22% of the population (of 80 417 526, data from 2017 *(1)*).

CAESAR sürveyansına Türkiye' den kaç suş kaydedilmiştir?



CAESAR sürveyansına Türkiye' den değerlendirmeye alınan suşların dağılımı nedir?



E.coli ve K.pneumoniae infeksiyonlarında antibiyotik seçimi

Table 5.45 Percentage of resistance for *E. coli* and *K. pneumoniae* among blood and CSF isolates in Turkey in 2016

Antibiotic (group)	*E. coli*		*K. pneumoniae*	
	N	Resistance (%)	N	Resistance (%)
Aminopenicillins (R)	2887	79	NA	NA
Amoxicillin-clavulanic acid (R)	3571	43	1908	77
Piperacillin-tazobactam (R)	3333	23	2460	59
Third-generation cephalosporins (R)	3546	51	2589	68
Third-generation cephalosporins (I+R)	3546	52	2589	68
Ceftazidime (R)	3349	44	2568	71
Ertapenem (R)	3198	7	2463	46
Carbapenems (R)	3865	3	2837	30
Carbapenems (I+R)	3865	5	2837	41
Aminoglycosides (R)	3679	27	2712	48
Amikacin (R)	3781	1	2820	22
Fluoroquinolones (R)	3670	50	2770	55
Fluoroquinolones (I+R)	3670	55	2770	64
Multidrug resistance (R)	3111	18	2361	35

NA: not applicable
The aminopenicillins group comprises amoxicillin and ampicillin.
The third-generation cephalosporins group comprises cefotaxime and ceftriaxone.
The carbapenems group comprises imipenem and meropenem.

P.aeruginosa ve *Acinetobacter spp.* enfeksiyonlarında antibiyotik seçimi

Table 5.46 Percentage of resistance for *P. aeruginosa* and *Acinetobacter* spp. among blood and CSF isolates in Turkey in 2016

Antibiotic (group)	*P. aeruginosa*		*Acinetobacter* spp.	
	N	Resistance (%)	N	Resistance (%)
Piperacillin-tazobactam (R)	1203	31	NA	NA
Ceftazidime (R)	1286	24	NA	NA
Cefepime (R)	1168	30	NA	NA
Carbapenems (R)	1281	37	2373	92
Carbapenems (I+R)	1281	48	2373	93
Aminoglycosides (R)	1305	27	2408	78
Amikacin (R)	1285	13	2287	68
Fluoroquinolones (R)	1252	35	2324	92
Multidrug resistance (R)	1090	28	2266	76

NA: not applicable.

The carbapenems group comprises imipenem and meropenem.

The aminoglycosides group comprises gentamicin and tobramycin.

The fluoroquinolones group comprises ciprofloxacin and levofloxacin.

For *P. aeruginosa*, multidrug resistance is defined as resistance to three or more antimicrobial groups among piperacillin-tazobactam, ceftazidime, fluoroquinolones, aminoglycosides and carbapenems. Isolates with missing data on three or more of the groups are excluded.

For *Acinetobacter* spp., multidrug resistance is defined as resistance to fluoroquinolones, aminoglycosides and carbapenems. Isolates with missing data on one or more of the groups are excluded.

S.aureus enfeksiyonlarında tedavi

Table 5.47 Percentage of resistance for *S. aureus* among blood and CSF isolates in Turkey in 2016

Antibiotic (group)	*S. aureus*	
	N	Resistance (%)
MRSA (R)	1887	23
Fluoroquinolones (R)	2195	13
Norfloxacin (R)	0	–
Vancomycin (R)	2465	0
Rifampicin (R)	4	100*
Linezolid (R)	2360	0

–: no data available.
* Few isolates were tested (N < 30), and the percentage of resistance should be interpreted with caution.
MRSA is calculated as resistance to cefoxitin or, if not available, oxacillin.
The fluoroquinolones group comprises ciprofloxacin, ofloxacin and levofloxacin.

S.pneumoniae enfeksiyonlarında antibiyotik seçimi

Table 5.48 Percentage of resistance for *S. pneumoniae* among blood and CSF isolates in Turkey in 2016

Antibiotic (group)	*S. pneumoniae*	
	N	Resistance (%)
Penicillins (R)	174	16
Penicillins (I+R)	174	47
Third-generation cephalosporins (R)	113	7
Third-generation cephalosporins (I+R)	113	29
Fluoroquinolones (R)	130	5
Norfloxacin (R)	0	–
Macrolides (R)	163	39
Macrolides (I+R)	163	42
Multidrug resistance (I+R)	155	30

–: no data available.
Resistance to penicillins is based on penicillin or, if not available, on oxacillin.
The third-generation cephalosporins group comprises cefotaxime and ceftriaxone.
The fluoroquinolones group comprises levofloxacin and moxifloxacin.
The macrolides group comprises erythromycin, clarithromycin, and azithromycin.
Multidrug resistance is defined as resistance to penicillins and macrolides. Isolates with missing data on one or more of the groups are excluded.

Enterokok enfeksiyonlarında antibiyotik seçimi

Table 5.49 Percentage of resistance for *E. faecalis* and *E. faecium* among blood and CSF isolates in Turkey in 2016

Antibiotic (group)	*E. faecalis*		*E. faecium*	
	N	Resistance (%)	N	Resistance (%)
Aminopenicillins (I+R)	1437	6	1392	91
High-level gentamicin (R)	767	60	851	65
Vancomycin (R)	1518	1	1467	15
Linezolid (I+R)	1425	0	1368	1

The aminopenicillins group comprises amoxicillin and ampicillin.

Kombinasyon tedavisi nezaman?

- Hasta sepsis, septik şok, ağır yanık durumu, endokardit ise
- Febril nötropeni hastasında MDR ve/veya Karbapenem dirençli Gram negatif bakteri enfeksiyonu olması ya da şüphesi durumunda
- Karbapenem dirençli *P.aeruginosa* ve *Acinetobacter spp.* enfeksiyonlarında biyofilm oluşumuna zemin varsa
- Hastane enfeksiyonu düşünülüyor ve hastane direnç oranları birinci basamak antibakteriyel ilaçlara yüksek ise

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ACINETOBACTER ENFEKSİYONLARINDA KOMBİNASYON ANTİBİYOTERAPİSİ

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Journal of Antimicrobial Chemotherapy

Polymyxin monotherapy or in combination against carbapenem-resistant bacteria: systematic review and meta-analysis

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Kombinasyon tedavisi sonuçları

Table 2. Outcomes of other combinations

						Mortality		Clinical failure		Microbiological failure	
Author	Year	Bacteria	Polymyxin	Combination	Infection	monotherapy	combination therapy	monotherapy	combination therapy	monotherapy	combination therapy
Falagas	2010	AB PA	colistin	piperacillin/tazobactam	mix			6/35 **(%17)**	6/16 **(%37)**		
Batirel	2014	AB	colistin	sulbactam	BSI	26/36 **(%36)**	32/69 **(%46)**				
Kalin	2014	AB	colistin	sulbactam	VAP	27/47 **(%57)**	27/35 **(%77)**			13/47 **(%27)**	5/35 **(%14)**
Yilmaz	2015	AB	colistin	sulbactam	VAP	7/17 **(%41)**	14/20 **(%70)**	4/17 **(%23)**	9/20 **(%45)**	8/17 **(%47)**	8/20 **(%40)**
Garnacho-Montero	2013	AB	colistin	vancomycin	VAP BSI	14/28 **(%50)**	14/29 **(%48)**	7/28 **(%25)**	10/29 **(%34)**	8/23 **(%34)**	11/29 **(%37)**
Petrosillo	2014	mix	colistin	vancomycin	mix	17/61 **(%27)**	14/42 **(%33)**				

ACİNETOBACTER ENFEKSİYONLARINDA KOMBİNASYON ANTİBİYOTERAPİSİ

- Çalışmalar arasındaki hasta ve dizayn farklılıkları farklı sonuçlar elde edilmesine sebep olmuştur, bu nedenle de meta-analizde monoterapi ve kombine tedavi sonuçları benzer bulunmuştur

- Kolistin+Rifampisin kombinasyonu mikrobiyolojik eradikasyon açısından diğer kombinasyonlardan daha etkin bulunmuş, ancak klinik başarı oranları açısından anlamlı farklılık tespit edilmemiştir.

MONOTERAPİ? KOMBİNASYON TEDAVİSİ?

Indian Journal of Medical Microbiology, (2012) 30(4): 448-52

Original Article

Colistin against colistin-only-susceptible *Acinetobacter baumannii*-related infections: Monotherapy or combination therapy?

F Şimşek, *H Gedik, MT Yıldırmak, NE İris, A Türkmen, A Ersoy, M Ersöz, A Gücüyener

Abstract

Purpose: To evaluate the outcomes of the patients who were infected with colistin-only-susceptible (COS) *Acinetobacter baumannii* and treated with either colistin monotherapy or colistin combined therapy. **Materials and Methods:** This retrospective case-control study was conducted in the training and research hospital with an 800 beds between August 2008 and December 2011. The patients, who were infected with COS *A. baumannii* and received either colistin monotherapy or colistin combined therapy, were included into the study. **Results:** In total, 51 patients fulfilling study criteria were evaluated. Colistin monotherapy was found effective as much as colistin combined therapy in terms of clinical and microbiological responses in patients with ventilator associated pneumonia (VAP) and also in patients with blood stream infections. **Conclusion:** Although there is no randomised controlled study yet, colistin monotherapy and colistin combined therapy are likely to achieve similar treatment responses rates. Heteroresistant strains can emerge in patients who receive colistin monotherapy.

Key words: *Colistin, Acinetobacter baumannii, treatment, mortality, response*

Table 1: Demographic and clinical characteristics of the 51 patients infected with colistin-only sensitive *A. baumannii*

Demographic and clinical characteristics	No. of patients
Mean age	51.71 ± 18.82 years (14–87)
Male	31
Comorbidity	20
Malignancy	4
Heart dysfunction	12
Chronic obstructive pulmonary disease	7
Diabetes mellitus	6
Chronic and acute renal failure	2
Hypertension	9
Neurological diseases	3
Trauma	12
Haemathological disorders	3
Gastrointestinal disorders	8
Prior usage of combined antibiotics	50
Mechanic ventilation in ICU	46
Urinary catheter	42
Central venous catheter	45
Presence of concomitant other infection	28
Prosthetic material	1
Prior surgery	16
APACHE II score (n=39)	17.73 ± 6.24 (5–32)
Duration of mechanic ventilation (days)	79.54 ± 62.13 (2–205)
Length of stay at hospital prior to infection (days)	42.49 ± 27.54 (5–105)
Duration of hospitalisation subsequent to infection (days)	37.17 ± 33.43 (1–132)

Table 2: Clinical response rates of colistin monotherapy and combination therapies by sites of infections

Site of infection	Therapy	Clinical response	Microbiological response
Ventilator associated pneumonia (*n*=36)	Colistin monotherapy	7/15	10/15
	Colistin + Rifampicin	5/8	8/8
	Colistin + Carbapenem	1/4	¾
	Colistin + Tigecycline + Rifampicin	0/2	0/2
	Colistin + Tigecycline	1/4	2/4
	Colistin + Carbapenem + Rifampicin	1/2	1/2
	Colistin + Sulbactam-Ampicillin	1/1	1/1
Blood stream infection (*n*=6)	Colistin monotherapy	1/2	2/2
	Colistin + Cefoperazone-Sulbactam-	1/1	1/1
	Colistin + Rifampicin	1/3	2/3
Nosocomial pneumonia (*n*=1)	Colistin + Carbapenem	0/1	0/1
Urinary tract infection (*n*=1)	Colistin + Carbapenem+ Rifampicin	0/1	1/1
Surgical site infection (*n*=2)	Colistin monotherapy	2/2	2/2
Meningitis (*n*=2)	Colistin+ Carbapenem+ Rifampicin	0/2	2/2
Surgical site infection + Ventilator associated pneumonia (*n*=1)	Colistin monotherapy	0/1	0/1
Central line associated blood stream infection (*n*=1)	Colistin + Rifampicin	1/1	1/1
Intra abdominal infection (n=1)	Colistin + Sulbactam-Ampicillin	0/1	0/1
Total (*n*=51)		22/51	34/51

KOLİSTİN MONOTERAPİ ? KOMBİNE TERAPİ ?

in the fifth day of treatment. The 10-day crude mortality rates were 40% (8/20) in patients who received colistin monotherapy, and 22% (7/31) in patients who received combination therapy in all cases. There was no significant difference between both groups (*P*=0.182). The 10-day crude mortality rates in VAP cases were 40% (6/15) in patients who received colistin monotherapy, and 28% (6/21) in patients who received combination therapy. There was no significant difference between both groups (*P*=0.475).

The 28-day crude mortality rates were found insignificant as 50% (10/20) in patients who received colistin monotherapy, and 32% (10/31) in patients who received combination therapy statistically (*P*=0.244). The 28-day crude mortality rates were insignificant in VAP cases as 40% (6/15) in patients who received colistin monotherapy, and 47% (10/21) in patients who received combination therapy (*P* = 0.650). Mortality rates were found similar in patients

not be calculated. However, 10-day and 28-day mortality rates were found 0% and 14% in seven patients without concomitant infection and underlying conditions who were diagnosed with VAP (*n*=7), wound infection (*n*=1), surgical site infection (*n*=1), meningitis (*n*=1), respectively. Five of them received colistin monotherapy. Only one patient deceased due to meningitis.

(*P* = 0.650). Mortality rates were found similar in patients that received colistin within 72-h of identification and in patients that received colistin after 72-h of identification (57% versus 58%, *P* = 0.651). Mortality rates were

(57% versus 58%, *P* = 0.651). Mortality rates were significantly higher in patients who were supported with mechanical ventilation more than 10 days (*n*=22, 62%, OR=5.92; 95% CI 1.06–32.89; *P* = *0.027*). There were

THE LANCET
Infectious Diseases

Articles

Colistin alone versus colistin plus meropenem for treatment of severe infections caused by carbapenem-resistant Gram-negative bacteria: an open-label, randomised controlled trial

Mical Paul, MD, Prof George L Daikos, MD, Emanuele Durante-Mangoni, MD, Dafna Yahav, MD, Prof Yehuda Carmeli, MD, Yael Dishon Benattar, MA, Anna Skiada, MD, Roberto Andini, MD, Noa Eliakim-Raz, MD, Amir Nutman, MD, Oren Zusman, MD, Anastasia Antoniadou, MD, Pia Clara Pafundi, Amos Adler, MD, Yaakov Dickstein, MD, Ioannis Pavleas, MD, Rosa Zampino, MD, Vered Daitch, MA, Roni Bitterman, MD, Hiba Zayyad, MD, Fidi Koppel, BA, Inbar Levi, MA, Tanya Babich, MA, Prof Lena E Friberg, PhD, Prof Johan W Mouton, MD, Ursula Theuretzbacher, PhD, Prof Leonard Leibovici, MD

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Article Info

Summary

Background

Colistin–carbapenem combinations are synergistic in vitro against carbapenem-resistant Gram-negative bacteria. We aimed to test whether combination therapy improves clinical outcomes for adults with infections caused by carbapenem-resistant or carbapenemase-producing Gram-negative bacteria.

Methods

A randomised controlled superiority trial was done in six hospitals in Israel, Greece, and Italy. We included adults with bacteraemia, ventilator-associated pneumonia, hospital-acquired pneumonia, or urosepsis caused by carbapenem-non-susceptible Gram-negative bacteria. Patients were randomly assigned (1:1) centrally, by computer-generated permuted blocks stratified by centre, to intravenous colistin (9-million unit loading dose, followed by 4·5 million units twice per day) or colistin with meropenem (2-g prolonged infusion three times per day). The trial was open-label, with blinded outcome assessment. Treatment success was defined as survival, haemodynamic stability, improved or stable Sequential Organ Failure Assessment score, stable or improved ratio of partial pressure of arterial oxygen to fraction of expired oxygen for patients with pneumonia, and microbiological cure for patients with bacteraemia. The primary outcome was clinical failure, defined as not meeting all success criteria by intention-to-treat analysis, at 14 days after randomisation. This trial is registered at ClinicalTrials.gov, number NCT01732250, and is closed to accrual.

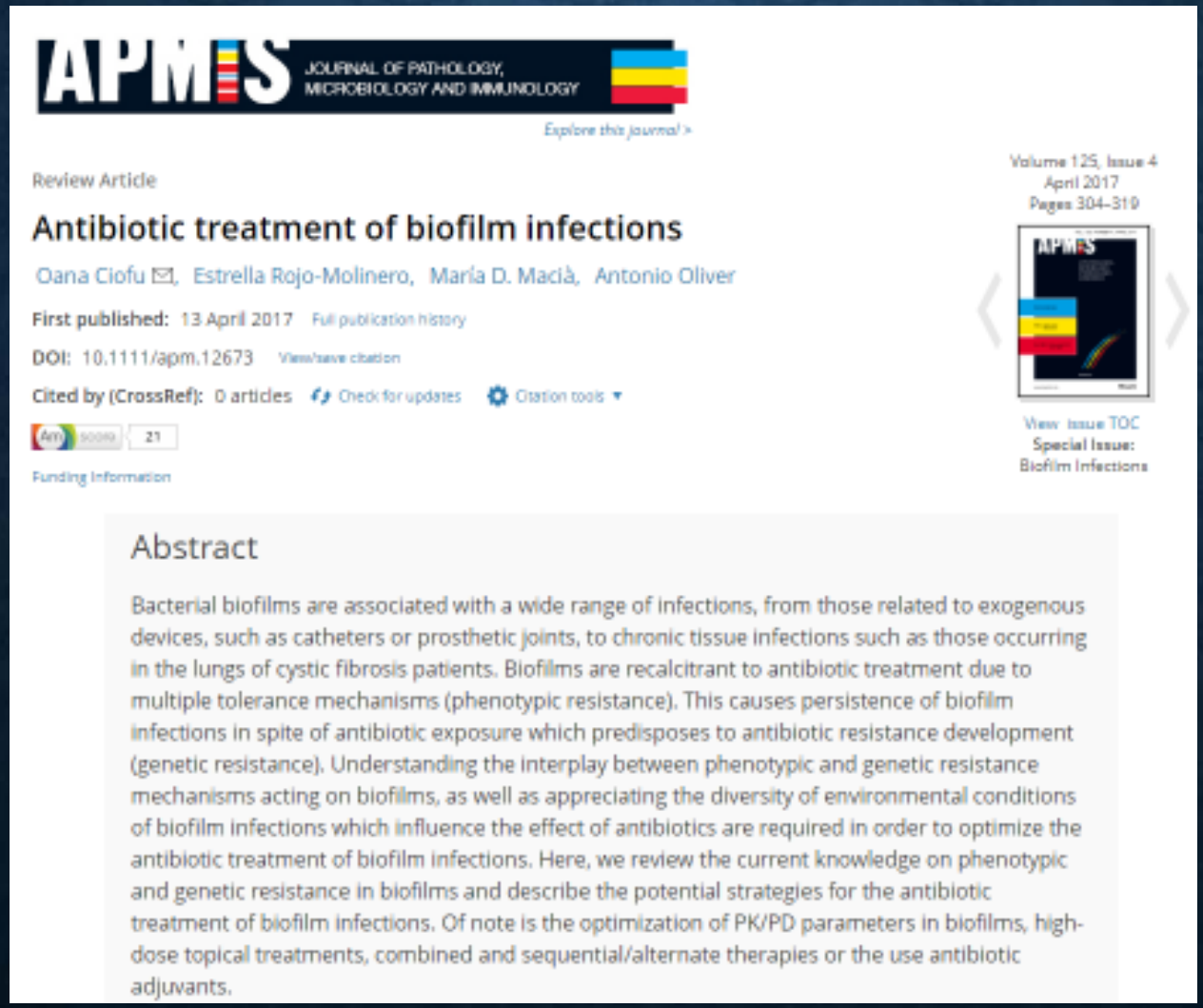
Findings

Between Oct 1, 2013, and Dec 31, 2016, we randomly assigned 406 patients to the two treatment groups. Most patients had pneumonia or bacteraemia (355/406, 87%), and most infections were caused by *Acinetobacter baumannii* (312/406, 77%). No significant difference between colistin monotherapy (156/198, 79%) and combination therapy (152/208, 73%) was observed for clinical failure at 14 days after randomisation (risk difference −5·7%, 95% CI −13·9 to 2·4; risk ratio [RR] 0·93, 95% CI 0·83–1·03). Results were similar among patients with *A baumannii* infections (RR 0·97, 95% CI 0·87–1·09). Combination therapy increased the incidence of diarrhoea (56 [27%] *vs* 32 [16%] patients) and decreased the incidence of mild renal failure (37 [30%] of 124 *vs* 25 [20%] of 125 patients at risk of or with kidney injury).

Interpretation

Combination therapy was not superior to monotherapy. The addition of meropenem to colistin did not improve clinical failure in severe *A baumannii* infections. The trial was unpowered to specifically address other bacteria.

BİYOFİLM İNFEKSİYONLARINDA ANTİMİKROBİYAL TEDAVİ



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Review Article

Antibiotic treatment of biofilm infections

Oana Ciofu ✉, Estrella Rojo-Molinero, María D. Macià, Antonio Oliver

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Special Issue:
Biofilm Infections

Abstract

Bacterial biofilms are associated with a wide range of infections, from those related to exogenous devices, such as catheters or prosthetic joints, to chronic tissue infections such as those occurring in the lungs of cystic fibrosis patients. Biofilms are recalcitrant to antibiotic treatment due to multiple tolerance mechanisms (phenotypic resistance). This causes persistence of biofilm infections in spite of antibiotic exposure which predisposes to antibiotic resistance development (genetic resistance). Understanding the interplay between phenotypic and genetic resistance mechanisms acting on biofilms, as well as appreciating the diversity of environmental conditions of biofilm infections which influence the effect of antibiotics are required in order to optimize the antibiotic treatment of biofilm infections. Here, we review the current knowledge on phenotypic and genetic resistance in biofilms and describe the potential strategies for the antibiotic treatment of biofilm infections. Of note is the optimization of PK/PD parameters in biofilms, high-dose topical treatments, combined and sequential/alternate therapies or the use antibiotic adjuvants.

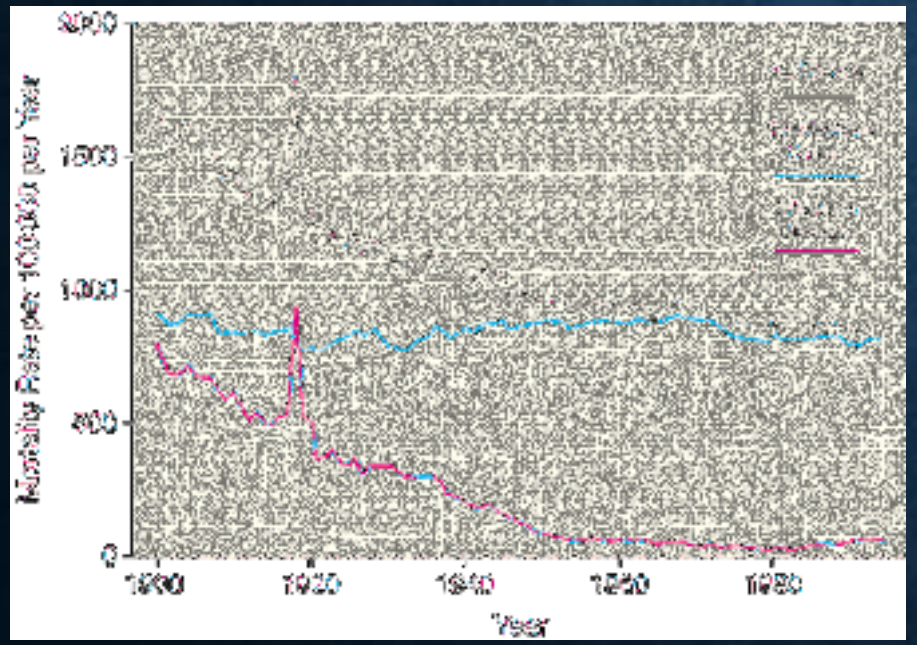
Table 2. Summary of current topical antibiotic treatment regimens according to the site of biofilm infection

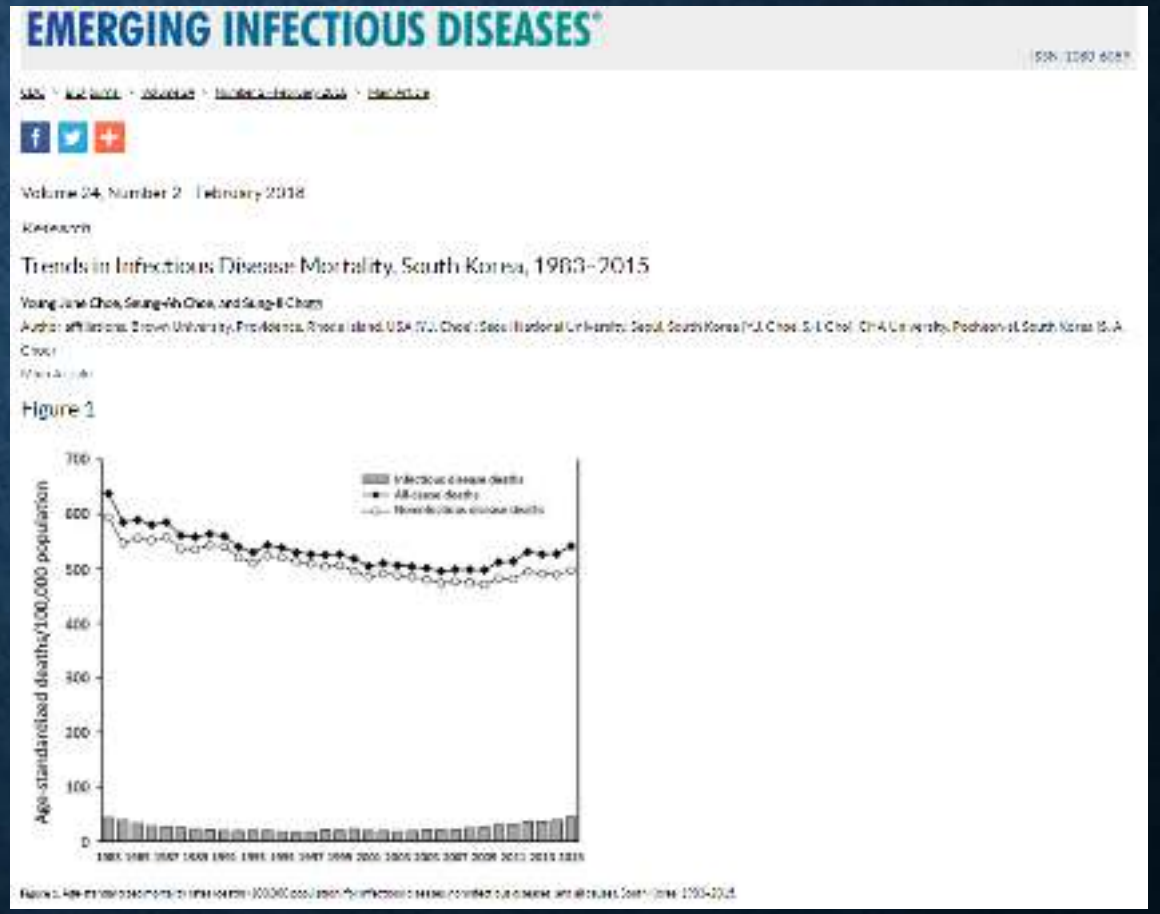
Biofilm site of infection	Antibiotic regimen	Duration	Route of administration	References
Lung infection in CF	0.5–2 MU colistin, twice daily	Continuous	Inhalation	[86-91]
	300 mg tobramycin, twice daily	28 days on/off cycles	Inhalation	
	112 mg tobramycin dry powder, twice daily	On/off cycles	Inhalation	
	75 mg aztreonam, three times daily	28 days on/off cycles	Inhalation	
	32.5 mg or 65 mg ciprofloxacin, once daily	28 days	Inhalation	
	240 mg levofloxacin, twice daily	28 days on/off cycles	Inhalation	
Lung infection in non-CF bronchiestasis	1 MU colistin, twice daily	Continuous	Inhalation	[92-96]
	300 mg tobramycin, twice daily	28 days	Inhalation	
	32.5 mg ciprofloxacin, twice daily	28 days	Inhalation	
	80 mg gentamicin, twice daily	Continuous	Inhalation	
Rhinosinusitis	3 drops ofloxacin 0.3%, three times daily	28 days	Nasal drops	[97]
	125 mg mupirocin + saline, twice daily	–	Rinonasal rinses	[98]
Wounds	Mupirocin 2% ointment	–	Cutaneous	[99]
	Metronidazole 0.8% gel	–	Cutaneous	[100]
	Silver sulfadiazine 1% cream	7 days	Cutaneous	[101]
Endotracheal tubes	120 mg vancomycin HCL + 2 mL saline, three times daily	14 days	Inhalation	[102]
	80 mg gentamicin + 2 mL saline, three times daily	14 days	Inhalation	

BİYOFİLM İLİŞKİLİ ENFEKSİYONLARDA TEDAVİ

Catheters	3 mg/mL minocycline + 30 mg/mL EDTA	12–24 h	Catheter lumen	[78, 103-109]
	2 mg/mL linezolid + 2000 U/mL heparin	12–24 h	Catheter lumen	
	2.5 mg/mL vancomycin + 2500 or 5000 U/mL heparin	12–24 h	Catheter lumen	
	5 mg/mL cefazoline + 2500 or 5000 U/mL heparin	12–24 h	Catheter lumen	
	10 mg/mL cotrimoxazole + 2500 U/mL heparin	12–24 h	Catheter lumen	
	50 mg/mL daptomycin	24 h	Catheter lumen	
	10 mg/mL tigecycline	24 h	Catheter lumen	
	10 mg/mL rifampicin	24 h	Catheter lumen	
	0.5 mg/mL ceftazidime	12–24 h	Catheter lumen	
	0.2 mg/mL ciprofloxacin + 5000 U/mL heparin	12–24 h	Catheter lumen	
	1 mg/mL gentamicin + 2500 U/mL heparin	12–24 h	Catheter lumen	
	2 mg/mL liposomal amphotericin B	8–12 h	Catheter lumen	
	Minocycline-rifampin	-	Coating	
Orthopedic procedures	1 g tobramycin + 12 or 24 MU colistin + 40 g polymethylmethacrylate	-	Intraoperative (beads)	[110-113]
	40 mg/mL tobramycin + 1 g vancomycin + 10 mL packet of calcium sulfate	-	Intraoperative (beads)	
	2 mg/mL gentamicin aqueous solution	-	Intraoperative (injection)	

İNFEKSİYON HASTALIKLARINA BAĞLI MORTALİTE




EMERGING INFECTIOUS DISEASES

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Research

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Figure 1

Armstrong GL, Conn LA, Pinner RW. Trends in Infectious Disease Mortality in the United States During the 20th Century. *JAMA.* 1999;281(1):61–66. doi:10.1001/jama.281.1.61

MORTALİTE-YAŞ- İNFEKSİYON HASTALIKLARI İLİŞKİSİ

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Research

Trends in Infectious Disease Mortality, South Korea, 1983–2015

Young June Choe, Seung-Ah Choe, and Sung-Il Cho

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Main Article

Figure 2

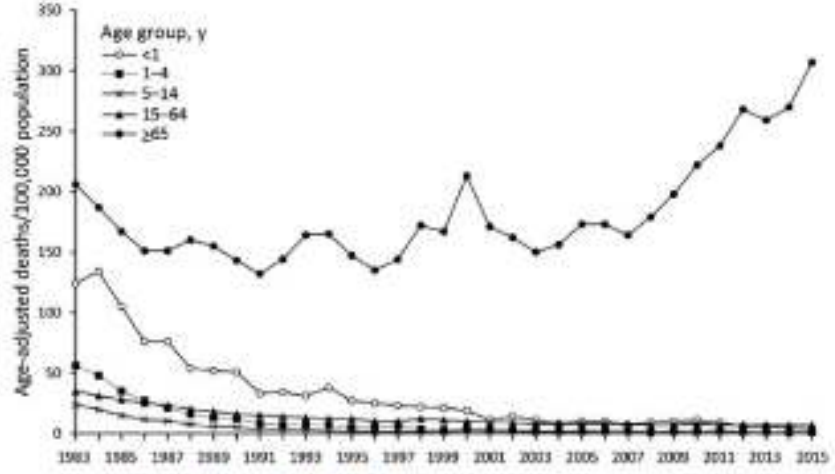
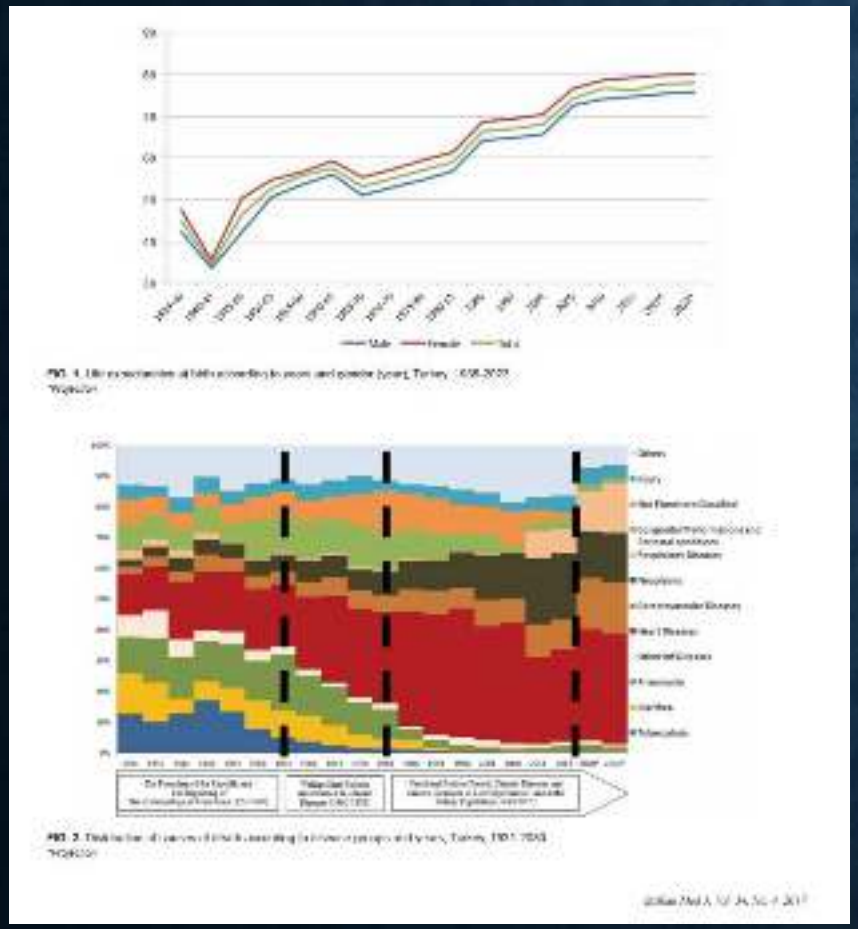


Figure 2. Age-specific infectious disease mortality rates, South Korea, 1983–2015.

ÜLKEMİZDE ENFEKSİYON HASTALIKLARININ DURUMU (1931-2013)



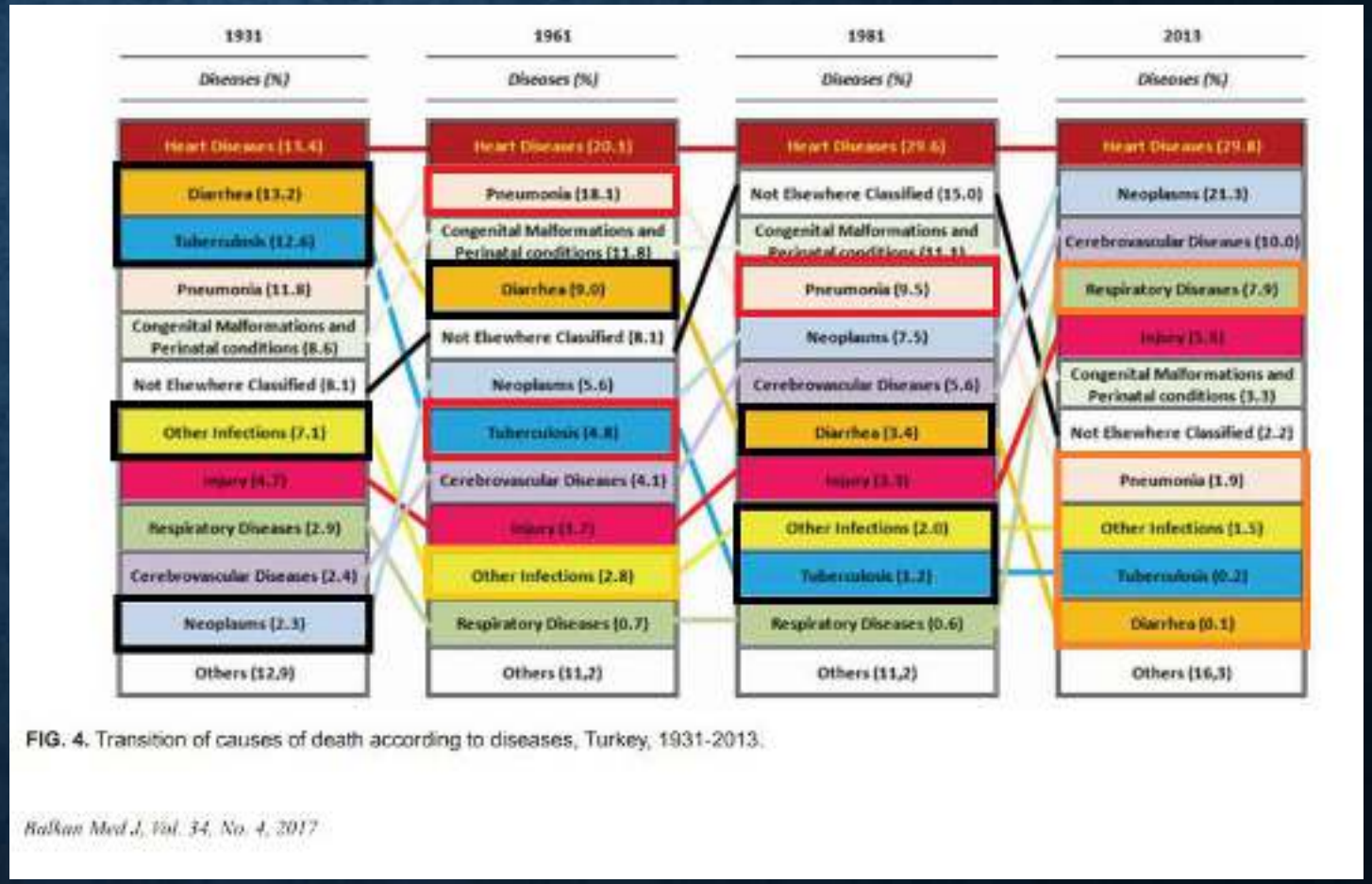


FIG. 4. Transition of causes of death according to diseases, Turkey, 1931-2013.

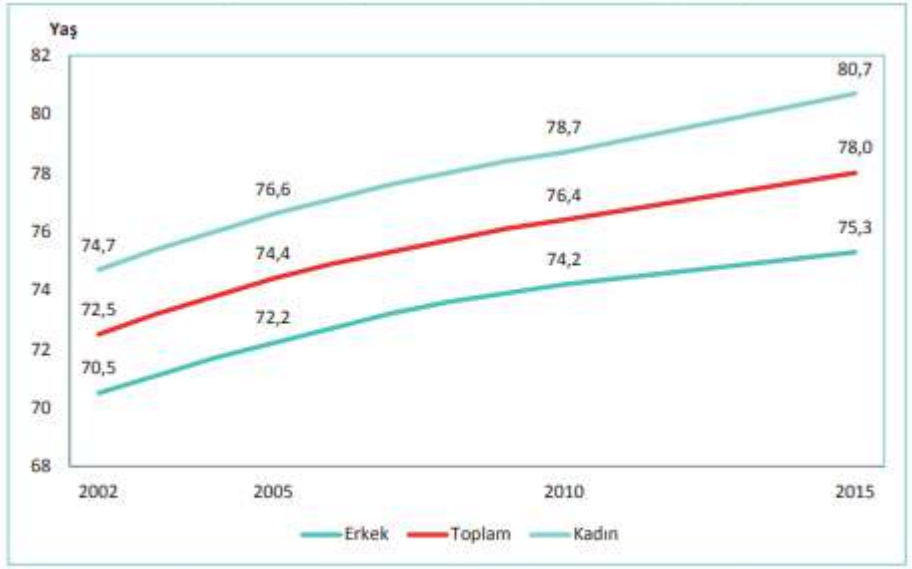
Balkan Med J, Vol. 34, No. 4, 2017

Bakar C, et al. Turkey's Epidemiological and Demographic Transitions: 1931-2013. Balkan Med J. 2017.

Tablo 2.1. ICD-10 Ana Tanı Gruplarına ve Cinsiyete Göre Ölüm Nedenlerinin Dağılımı, (%), Türkiye, 2013, 2014, 2015

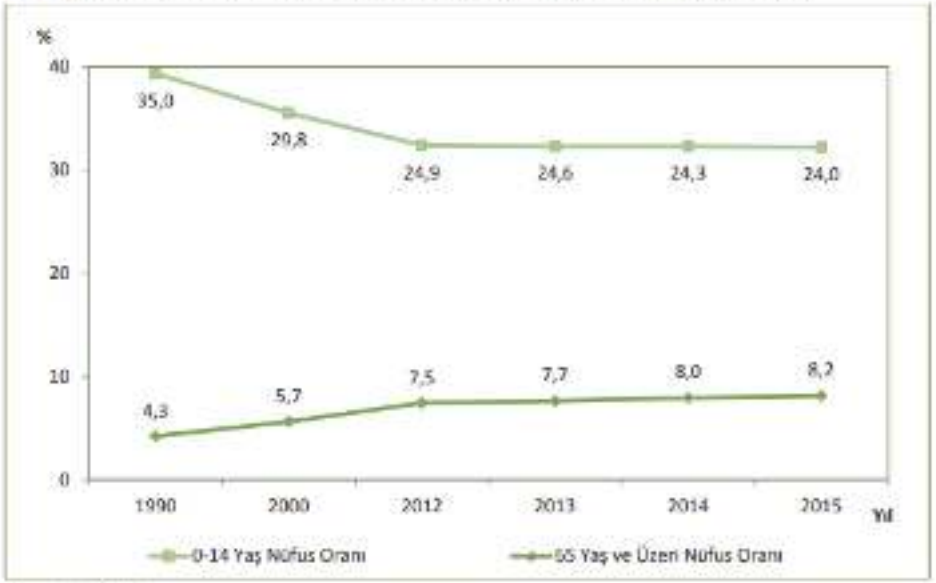
ICD-10 Ana Tanı Kodları	Kod	2013			2014			2015		
		Erkek	Kadın	Toplam	Erkek	Kadın	Toplam	Erkek	Kadın	Toplam
Bazı Enfeksiyöz ve Paraziter Hastalıklar	A00-B99	1,73	1,80	1,77	1,75	1,82	1,78	2,01	2,24	2,11

Şekil 2.1. Yıllara ve Cinsiyete Göre Doğumda Beklenen Yaşam Süresi, (Yaş), Türkiye



Kaynak: 2002, 2005 ve 2010 yılları TÜİK Nüfus Projeksiyonları, 2015 yılı TÜİK Hayat Tabloları 2013-2015 Haber Bülteni (06 Ekim 2016 tarih ve 21509 sayılı)

Şekil 1.5. Yıllara Göre 0-14 Yaş Nüfus ve 65 Yaş ve Üzeri Nüfus Oranları, (%), Türkiye



Kaynak: TÜİK

Tablo 3.3. ICD-10 Ana Tanı Gruplarına ve Cinsiyetlere Göre Hastane Yatışlarının Dağılımı, (%), Türkiye, 2013, 2014, 2015

ICD-10 Ana Tanı Kodları	Kod	2013			2014			2015		
		Erkek	Kadın	Toplam	Erkek	Kadın	Toplam	Erkek	Kadın	Toplam
Bazı Enfeksiyöz ve Paraziter Hastalıklar	A00-B99	3,7	2,6	3,1	3,4	2,4	2,9	3,1	2,2	2,6

Tablo 1.2. Yaş Gruplarına Göre Nüfus, 2000, 2015

Yaş Grubu	2000	2015
0-4	6.584.822	6.381.516
5-9	6.756.617	6.337.719
10-14	6.878.656	6.166.985
15-19	7.209.475	6.585.500
20-24	6.690.146	6.314.167
25-29	5.895.255	6.263.249
30-34	5.009.655	6.428.150
35-39	4.854.387	6.203.323
40-44	4.068.756	5.552.580
45-49	3.368.769	4.590.079
50-54	2.717.349	4.632.909
55-59	2.058.422	3.681.170
60-64	1.829.288	3.108.467
65-69	1.645.517	2.356.385
70-74	1.172.643	1.626.184
75 +	1.064.170	2.512.670
Türkiye	67.803.927	78.741.053

Kaynak: TÜİK

Tablo 1.1. Genel Demografik Göstergeler, Türkiye

	2000	2000	2012	2013	2014	2015
Toplam Nüfus	66.473.055	67.803.927	75.627.384	76.667.864	77.695.904	78.741.053
Kırsal Nüfus Oranı (%)	38,7	30,8	23,7	13,3	13,8	13,4
Kentsel Nüfus Oranı (%)	61,3	69,2	76,3	86,7	87,2	87,6
0-14 Yaş Nüfus Oranı (%)	35,0	29,8	24,9	24,6	24,3	24,0
65 Yaş ve Üzeri Nüfus Oranı (%)	4,3	5,7	7,5	7,7	8,0	8,2
Genç Bağımlılık Oranı (0-14 Yaş) (%)	57,6	46,3	36,9	36,3	35,8	35,0
Yaşlı Bağımlılık Oranı (65 + Yaş) (%)	7,0	8,8	11,1	11,3	11,8	12,2
Toplam Yaş Bağımlılık Oranı (%)	64,7	55,1	48,0	47,6	47,6	47,6
Yıllık Nüfus Artış Hızı (‰)	21,7	18,5	12,0	13,7	13,3	13,4
Kaba Doğum Hızı (‰)	20,1	21,0	17,2	17,0	17,4	16,9
Kaba Ölüm Hızı (‰)	7,1	7,3	5,0	4,9	5,1	5,2
Toplam Doğurganlık Hızı (Kadın Başına)	2,0	2,0	2,1	2,1	2,2	2,1

Kaynak: TÜİK

SONUÇ

- **Antimikrobiyal direnç doğal bir canlı cevabı olup, direnç tanımında hız ölçüt olmalı ve hızın artışı uyarıcı olmalıdır.**

- **Antibiyotik kullanımı direnç gelişiminin tek sorumlusu değildir, çok faktörlü bir etkinin sonucudur.**

SONUÇ

- **<u>İMMÜNİTE</u> antibiyotik direnci gelişimine ve MDR bakterilerle oluşabilecek enfeksiyonlara karşı en önemli koruma mekanizmasıdır.**

- **<u>EL YIKAMA</u> hala yeteri kadar dikkate alınmayan en önemli enfeksiyon kontrol önlemidir**

SONUÇ

- **Tedavi için antibiyotik seçiminde:**

- lokal ya da hastanın geçmiş antibiyotik direnç oranları,
- hastanın komorbiditesi,
- hastaneye/yoğun bakıma yatış hikayesi,
- invaziv girişim hikayesi,
- enfeksiyonun ciddiyeti ya da mortal olması,
- kullandığı diğer ilaçlarla etkileşimi,
- immün durumu dikkate alınarak seçilmelidir

SONUÇ

- **Çok ilaca dirençli *Acinetobacter spp*. ve *Pseudomonas aeruginosa* infeksiyonlarında kombinasyon tedavisi biyofilm oluşumu açısından dikkate alınmalıdır**

- **Pnömokoklarda direnç ve orta duyarlılık oranları %50' lere yaklaştığından akut bakteriyel menenjit tedavisine Vankomisin eklenmesi artık kaçınılmaz olmuştur.**

SONUÇ

- Mikrobiyolojik cevabın ya da eradikasyonun herzaman klinik cevap olarak sonuçlanmayacağı akılda tutulmalıdır.

- Altta yatan hastalıklar ya da sistem bozuklukları enfeksiyonlarla birlikte daha da kötüleşmekte, fizyolojik dengenin sağlanıp sağlanamaması hastanın sonucunu belirlemektedir.

SONUÇ

- **Üriner sistem enfeksiyonlarında kolonizasyon sorunu hastalara ve meslektaşlarımıza iyi anlatılmalı ve gereksiz antibiyotik kullanımının azaltılması sağlanmalıdır.**

- **Yüksek riskli bölümlerde kolonizasyon taraması erken ve uygun antibiyotik tedavisi açısından faydalı olduğu gösterilmiştir**

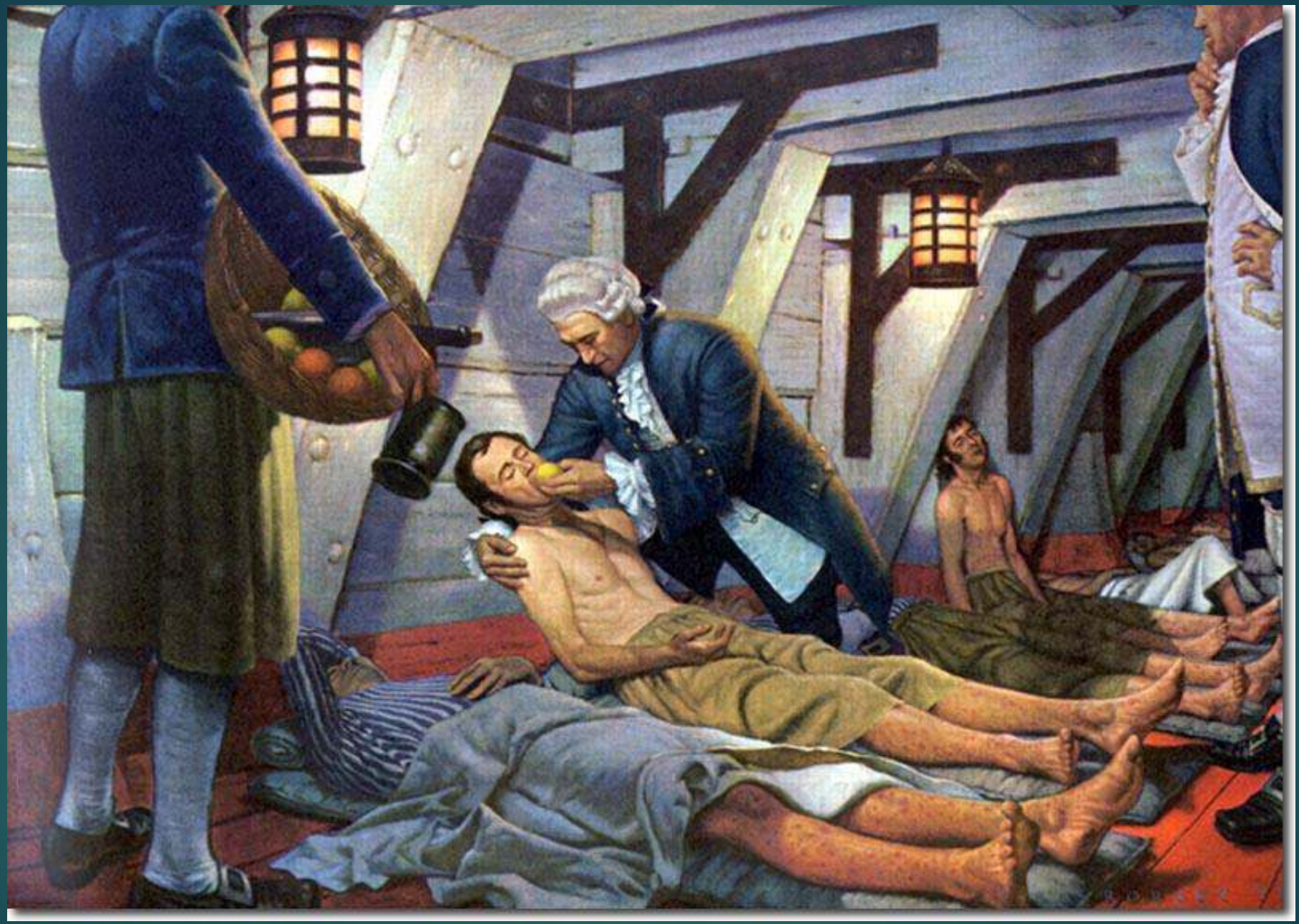
SONUÇ

- **Damar içi kateter uygulamalarında girişim öncesi asepsi-antisepsiye uyulması ve kateter bakımının uygun olarak yapılması katetere bağlı kan dolaşımı enfeksiyonlarını çok ciddi oranda azalttığı gösterilmiştir**

SONUÇ

- Dönüşümlü antibiyotik kullanımının antibiyotik direncini azaltmadığı yapılan çalışmalarda gösterildiğinden her hastane antibiyotik politikasını EKK ile belirlemelidir

- Yeni antibiyotikler için araştırmalara yatırımın arttırılması gereklidir.



In 1747, Dr. James Lind tested several scurvy treatments on crew members of the British naval ship Salisbury and discovered that lemons and oranges were most effective in treating the dreaded

"The microbe always has the last word."

LOUIS PASTEUR (1822-1895)

- Katkılar ve Sorular
- Sabrınız için teşekkür ederim