

Vankomisine İntrensek Dirençli
Enterococcus gallinarum* ve *Enterococcus casseliflavus
Vakalarının Deęerlendirilmesi

Dr.Ali Gökhan AKÇAY
Gülhane Eğitim ve Araştırma Hastanesi

KLİMİK 2024



- alıřma Ekibimiz -



Dr.Ali Gökhan AKAY



Dr.Melih Ayberk KAPICI



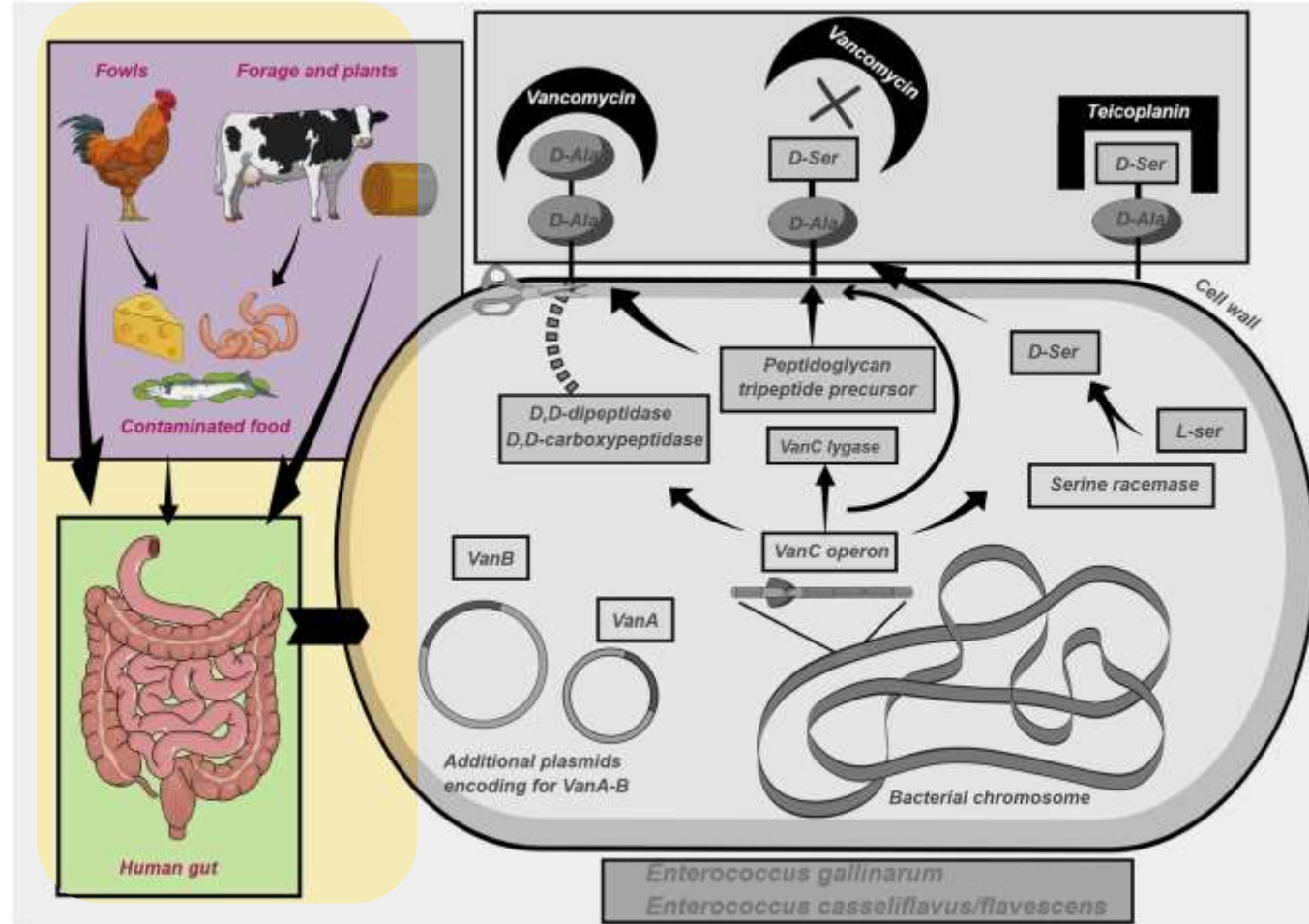
Dr.Elif DOĐAN



Do.Dr.Aysun YALI



Prof.Dr.Cemal BULUT



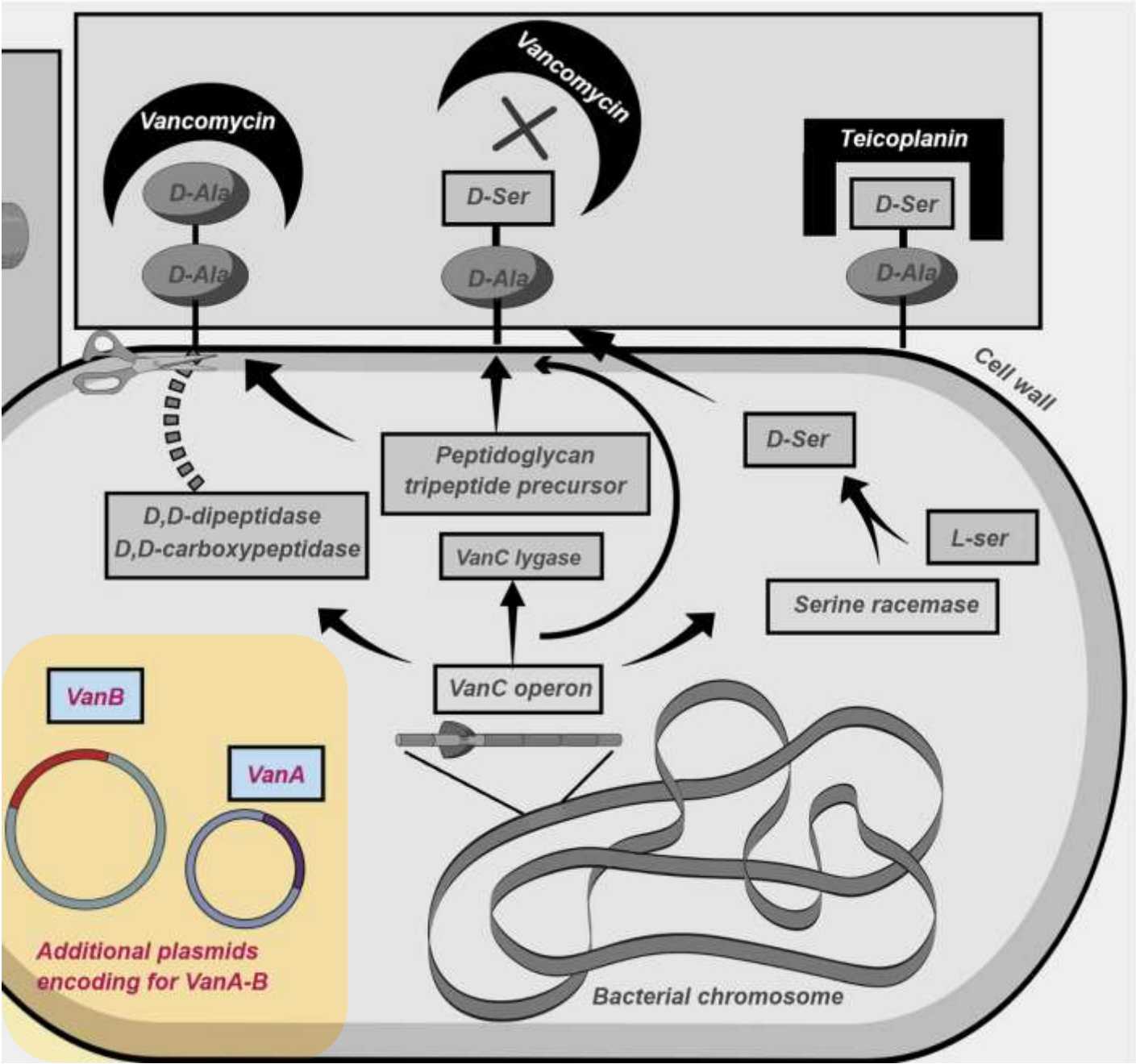
Enterococcus gallinarum

Sağlıklı bireylerde %9 fekal taşıyıcılık

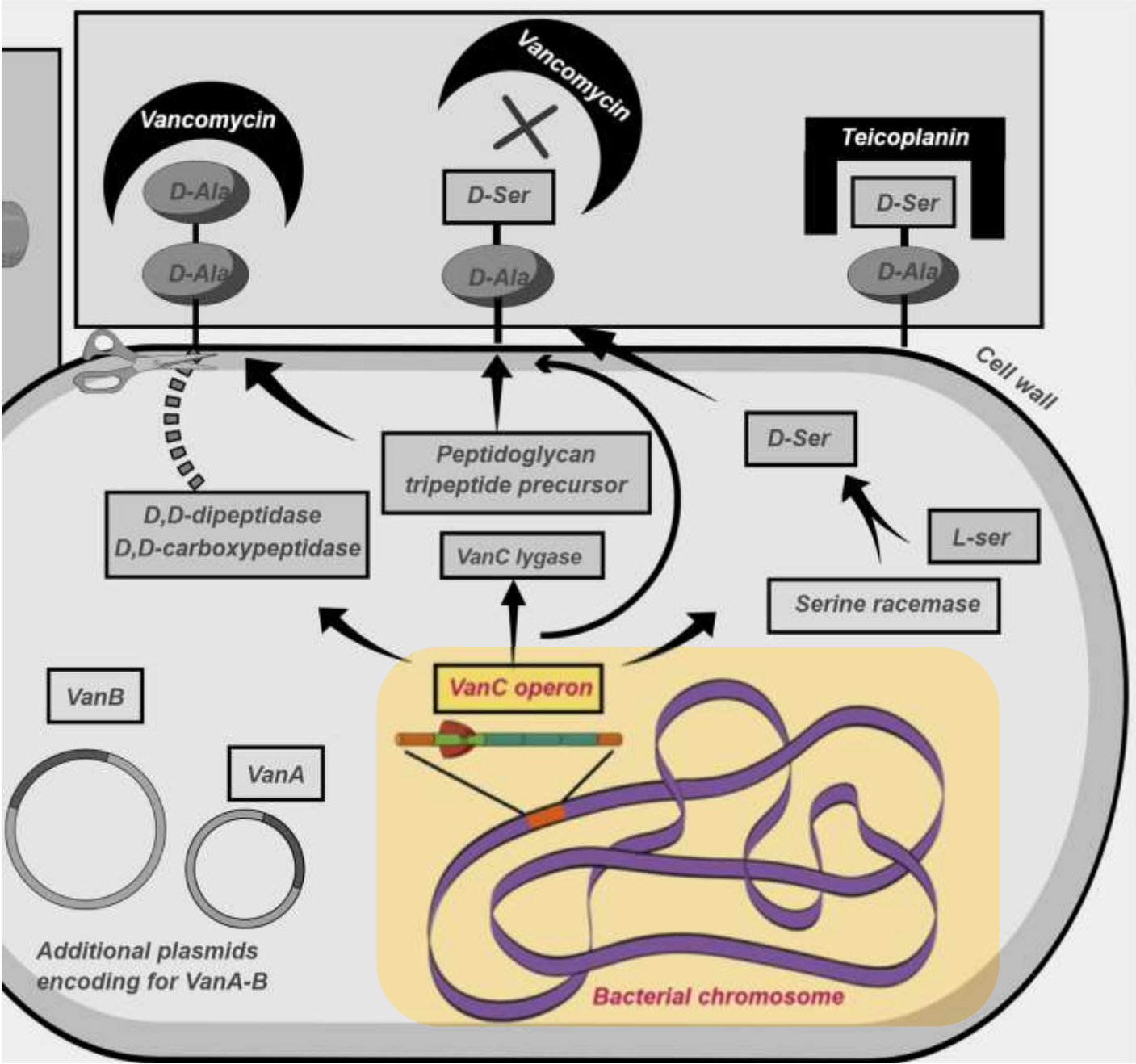
Enterococcus casseliflavus

Mera ve yem bitkileri kaynaklı

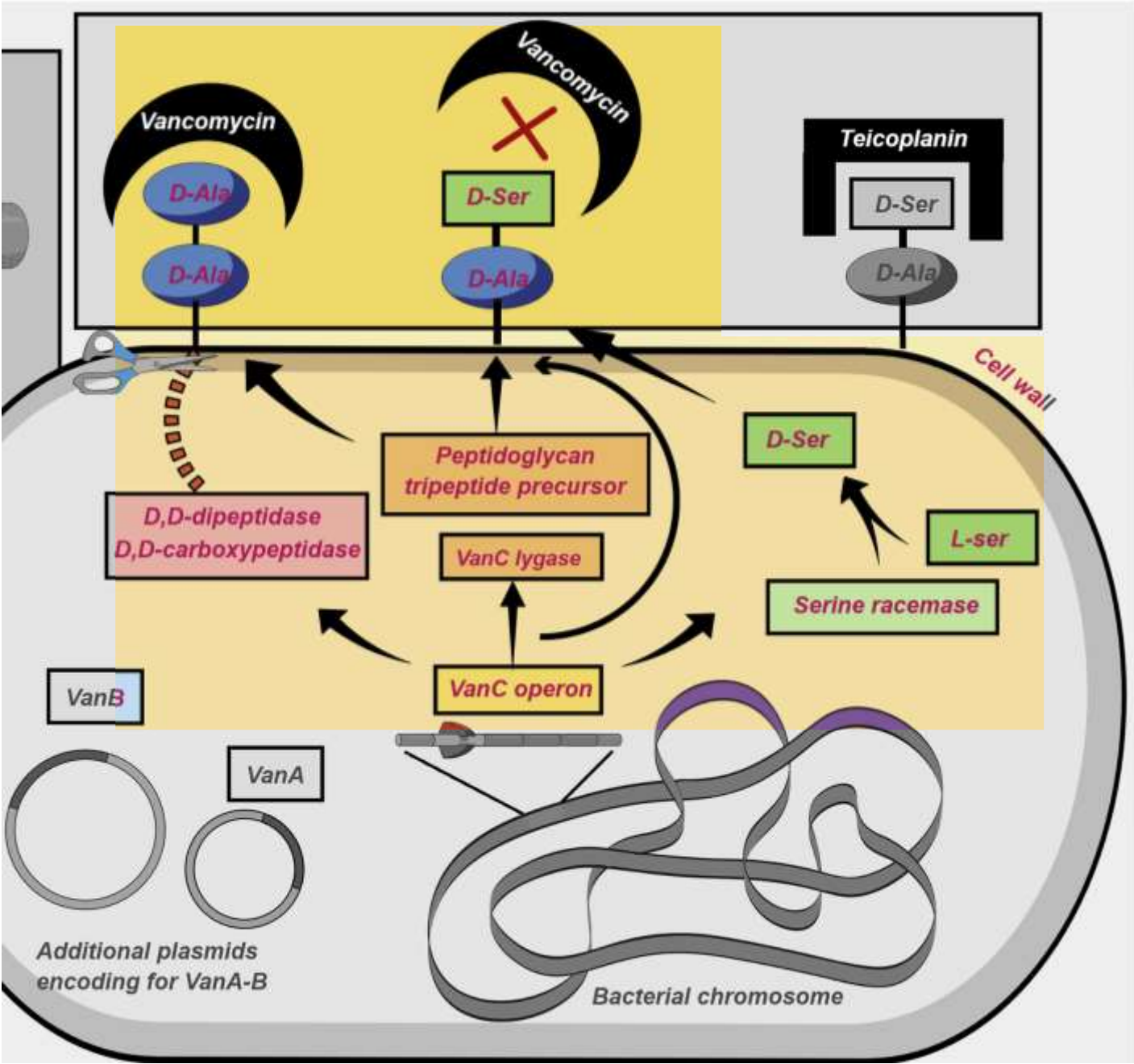
Giriş



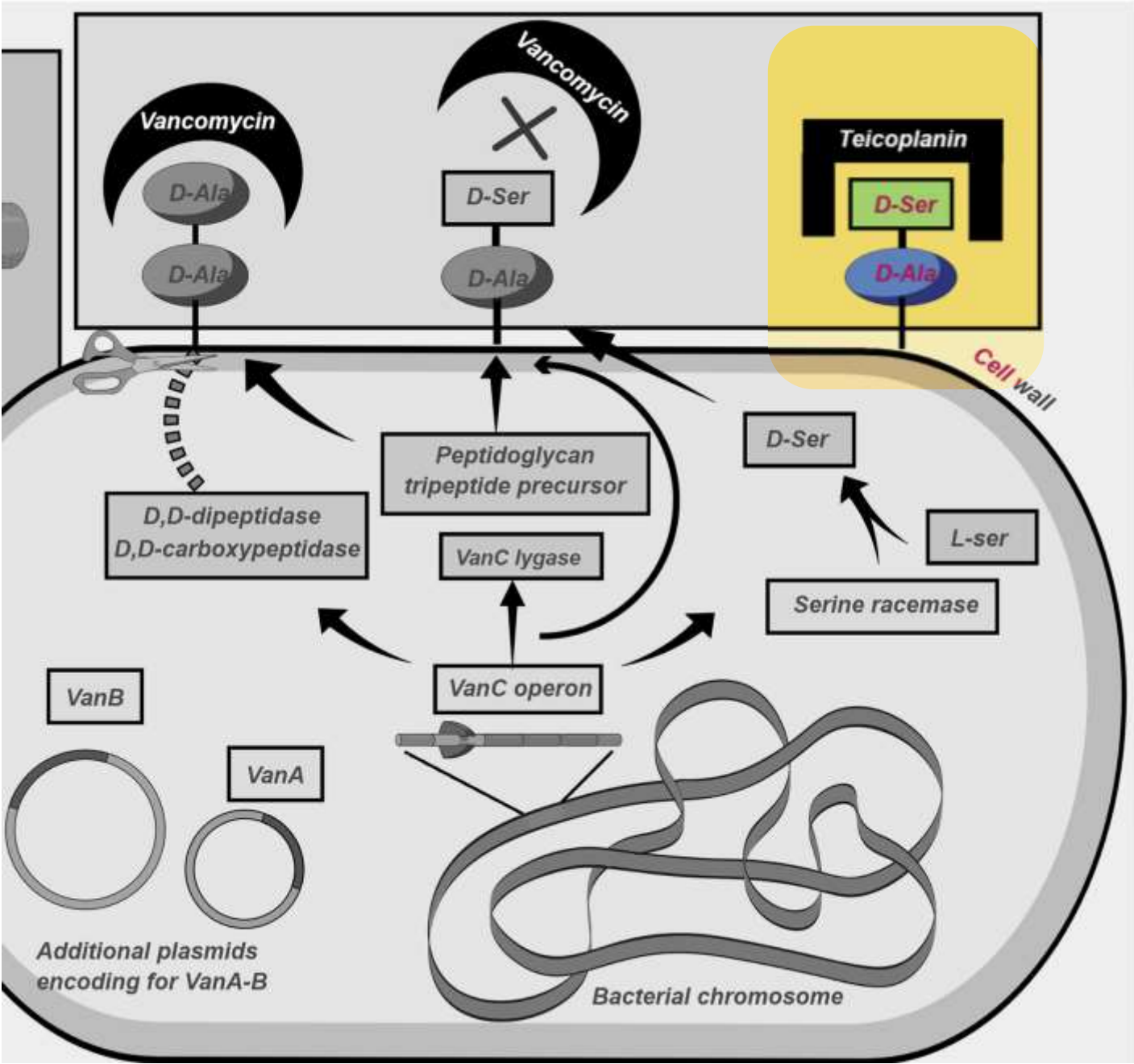
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Giriş



Giriş



Recovery of Resistant Enterococci during Vancomycin Prophylaxis

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We report a case of a patient undergoing hemodialysis who developed a wound infection and subsequently bacteremia with a strain of vancomycin-resistant enterococcus identified as *Enterococcus gallinarum*. He had been receiving vancomycin prophylaxis before developing these infections. Both isolates were susceptible to ampicillin, rifampin, teicoplanin, and daptomycin (LY146032).

There are approximately 80,000 people receiving hemodialysis in the United States. Over the past several years, it has become common practice to prophylactically administer vancomycin to these patients. In many respects, vancomycin is ideally suited to this purpose, since skin flora, composed primarily of gram-positive bacteria, commonly infect these patients and vancomycin resistance in these organisms has only rarely been reported (9, 15). In addition, the drug may be given weekly during hemodialysis. Emerging resistance, however, is always a potential problem with the administration of prophylactic antibiotics. We report the first case of bacteremia with a vancomycin-resistant enterococcus recovered in the United States in a hemodialysis patient receiving prophylactic vancomycin. Susceptibilities to several newly developed antibiotics are also reported.

Case report. A 67-year-old man was admitted to the North Carolina Memorial Hospital on 6 September 1986 for evaluation of fever and swelling over his left femoral hemodialysis graft. Seventeen months before admission, the patient began hemodialysis. At that time, vancomycin (1 g intravenously [i.v.] each week) was administered. Vancomycin levels in serum between 14 and 21 µg/ml were reported on several occasions.

During the next year, his course was marked by repeated episodes of graft failure due to thrombus formation. On 12 June 1986, a left femoral graft was placed. One month later, swelling was noted around the graft site and an ultrasound of the area revealed several cystic collections.

Cultures of spontaneous drainage from one of these collections grew *Escherichia coli*, *Klebsiella pneumoniae*, and an *Enterococcus* sp. Broth microdilution testing of the enterococcal isolate revealed that the vancomycin MIC was 16 µg/ml. The patient was maintained on his weekly vancomycin, and on 6 September he returned to the North Carolina Memorial Hospital after 48 h of fever and chills. His oral temperature was 100.2°F (ca. 37.9°C), and his physical exam was remarkable for a foul-smelling exudate from a wound over his graft site.

Enterococci were recovered from three of four blood cultures taken upon admission. Microdilution MIC testing (8) revealed that for this isolate, penicillin and ampicillin MICs were 1.0 µg/ml and the vancomycin MIC was 16.0 µg/ml. The vancomycin MIC was confirmed by broth microdilution MIC testing (8). Kill-curve studies (11) with measured levels in serum of vancomycin (20 µg/ml) and gentamicin (5 µg/ml) demonstrated synergy for the blood isolate

(data not shown). Broth microdilution MICs of other agents with antistreptococcal activity are reported in Tables 1 and 2.

The bacteremia of the patient was treated with 2 g of piperacillin i.v. every 8 h and 150 mg of gentamicin i.v. after each dialysis. His temperature rapidly returned to normal, and he was sent home to complete a 4-week course of vancomycin and gentamicin. The blood and wound-drainage isolates were sent to the Centers for Disease Control in Atlanta, Ga., for identification and confirmation of the vancomycin MIC findings. The blood and wound isolates were identified as *Enterococcus gallinarum*. The MIC of vancomycin for both isolates was 16 µg/ml.

The patient did well until 15 December 1986, when he again experienced rigors and fever. A golf-ball-sized mass was palpable in his left groin, and when it was aspirated, an *E. gallinarum* isolate for which the vancomycin MIC was 16 µg/ml was recovered. Four of four blood cultures, however, grew *Pseudomonas aeruginosa*, and his graft was removed. He did well after a 4-week course of ceftazidime and tobramycin.

Discussion. Vancomycin resistance in gram-positive organisms is highly unusual. It had been reported in only two genera of gram-positive organisms, *Leuconostoc* (12) and *Lactobacillus* (2, 17). The enterococci, which include the species *E. faecalis*, *E. durans*, *E. faecium*, and *E. avium*, have been reported to be susceptible to vancomycin, with MICs in the range of 0.5 to 8.0 µg/ml (1, 3, 5, 7, 10, 14). Recently Uttley et al. (16) have isolated eight vancomycin-resistant *Enterococcus* strains from the blood of patients with end-stage renal disease. There have been no previous reports of *E. gallinarum* of human origin. For the blood and wound isolates of enterococci reported here, the vancomycin MICs were 16 µg/ml.

The *E. gallinarum* isolates could be clearly differentiated from both *Leuconostoc* sp. and *Lactobacillus* sp. The MICs of vancomycin for both isolates were relatively low compared with those reported for *Leuconostoc* sp. (MIC range, 500 to >2,000 µg/ml). In addition, both *Enterococcus* isolates were able to split arginine and acidify litmus milk, characteristics which are not found in *Leuconostoc* sp. (6). Also, the *E. gallinarum* isolates failed to produce gas in *Lactobacillus* MRS broth, and *Leuconostoc* sp. produces gas in this broth (6). For certain lactobacilli, vancomycin MICs may be similar to those for the isolates described here. However, the Gram stain, colonial morphology, and definitive physiologic characteristics unique to *E. gallinarum* clearly indicate that these isolates were not lactobacilli.

It was clear that the blood and wound isolates were the

* Corresponding author.

CRIME, PASSION AND LUST FOR POWER—
 SERGIO LEONE'S EXPLOSIVE SAGA OF GANGLAND AMERICA.



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Ocak 2022, v12

This genus includes several species. The most frequent enterococci recovered in clinical samples are *E. faecalis*, *E. faecium*, *E. avium*, *E. casseliflavus*, *E. durans*, *E. gallinarum*, *E. hirae*, *E. mundtii* and *E. raffinosus*. Unless otherwise indicated, breakpoints apply to all members of the *Enterococcus* genus.

Haziran 2023, v13.1

The *Enterococcus* genus includes several species. The most frequent enterococci recovered in clinical samples are *E. faecalis* and *E. faecium* but also *E. avium*, *E. casseliflavus*, *E. durans*, *E. gallinarum*, *E. hirae*, *E. mundtii* and *E. raffinosus* are occasionally encountered. Listed breakpoints have been largely developed using pre-clinical and clinical data on *E. faecalis* and *E. faecium*. The applicability of these breakpoints to other *Enterococcus* species is less certain as both clinical and pre-clinical data for these are mostly lacking. During 2023, in collaboration between EUCAST and experts in enterococci, data and breakpoints for other enterococci will be developed. Until then, use breakpoints below or the [EUCAST Guidance Document on how to test and interpret results when there are no breakpoints](#).

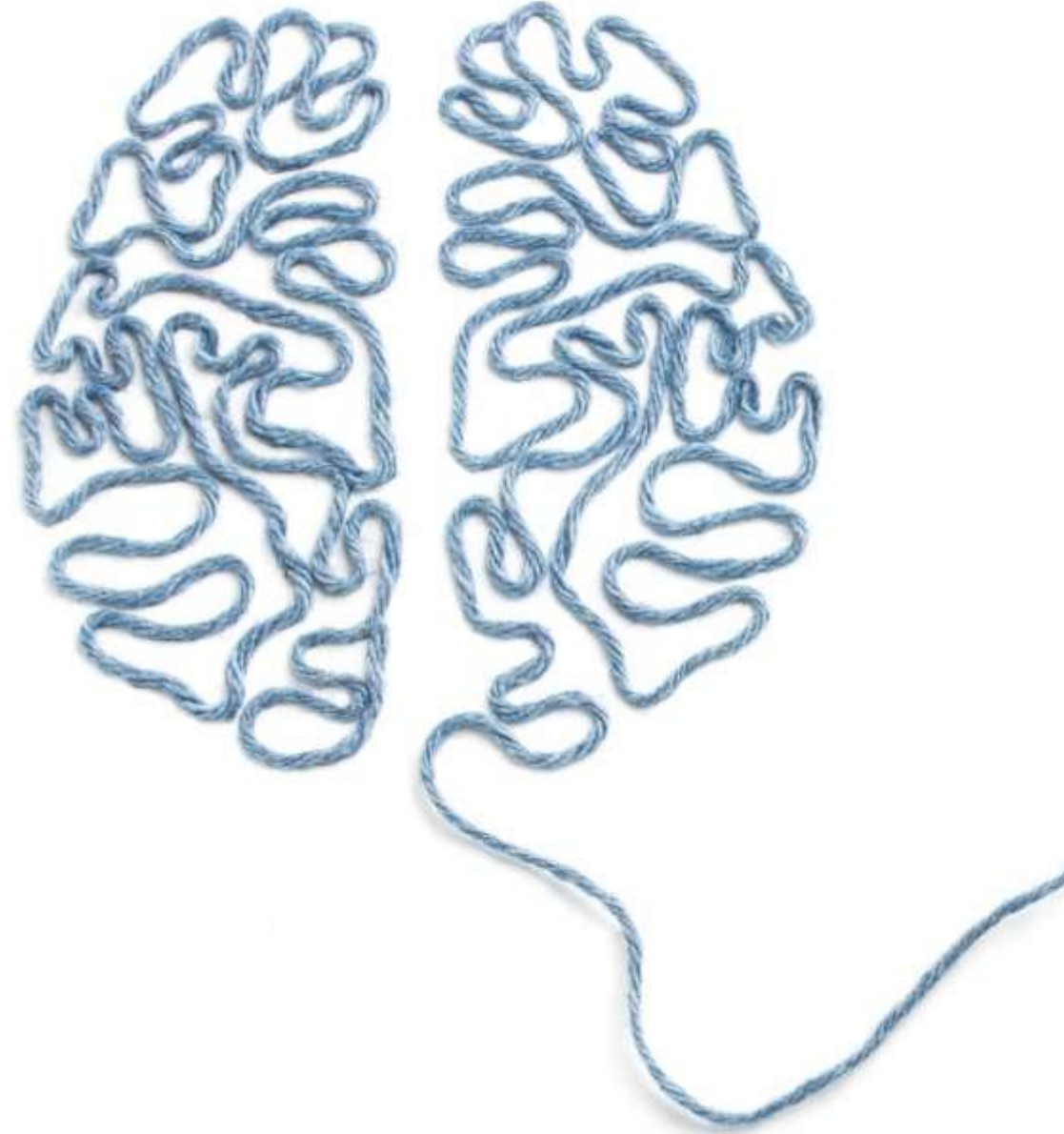
1 Ocak 2024, v14

1/A. Vancomycin resistance is the expected phenotype for *E. casseliflavus* and *E. gallinarum* and therefore susceptibility testing should not be performed.

Vancomycin, enterococci other than *E. casseliflavus* and *E. gallinarum*

Mortalite?
Enfeksiyöz Sendromlar?
Direnç durumu?

...



Yöntem



1 Ocak 2017 – 20 Ocak 2024



HBYS



Klinik
Laboratuvar
Antimikrobiyal duyarlılık verileri
Mortalite



CDC ve EUCAST



< 11 gün, mükerrer üreme

Bulgular



Bulgular



Enterococcus casseliflavus

n:13

13 üreme

Erkek: 11 (%84,6)



Enterococcus gallinarum

n:54

63 üreme (4 mükerrer)

Erkek: 30 (%55,5)

Bulgular

Enterococcus casseliflavus

Enterococcus gallinarum

> 18



Bulgular

Enterococcus casseliflavus

52,5 (SD ± 20,11)

Enterococcus gallinarum

61,1 (SD ± 20,2)



Bulgular

		<i>Enterococcus gallinarum</i>	<i>Enterococcus casseliflavus</i>	
		n=54 (%)	n=13 (%)	
Başvuru/Yatış Durumu	Poliklinik	7 , %11,7	3, %23	
	Yatış	Klinik	26, %43,3	7, %53,8
		Yoğun Bakım Ünitesi	24, %45	3, %23
		Toplam	51, %85	10, %76,9
Komorbidite	Anemi	-	1	
	Demans	1	-	
	Diyabetes Mellitus	25	2	
	Hipertansiyon	26	4	
	Kalp Yetmezliği	6	-	
	KOAH	4	1	
	Koroner Arter Hastalığı	4	3	
	Kronik Böbrek Yetmezliği	6	-	
	Malignite	Akciğer Ca	1	-
		Endometriyum Ca	2	-
		Glioblastoma Multiforme	1	-
		Kolon Ca	7	-
		Lenfoma	1	-
		Liposarkom	-	1
		Meme Ca	1	-
		Mide Ca	2	-
		Pankreas Ca	1	-
		Serviks Ca	1	-
	Toplam	17	1	
	Serebrovasküler Hastalık	1	1	
Periferik Arter Hastalığı	-	1		
Psikoz	1	-		
Yok	10	3		

Bulgular

		<i>Enterococcus gallinarum</i>	<i>Enterococcus casseliflavus</i>	
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	Koroner Arter Hastalığı	4	3	
	Kronik Böbrek Yetmezliği	6	-	
	Malignite	Akciğer Ca	1	-
		Endometriyum Ca	2	-
		Glioblastoma Multiforme	1	-
		Kolon Ca	7	-
		Lenfoma	1	-
		Liposarkom	-	1
		Meme Ca	1	-
		Mide Ca	2	-
		Pankreas Ca	1	-
		Serviks Ca	1	-
	Toplam	17	1	
	Serebrovasküler Hastalık	1	1	
Periferik Arter Hastalığı	-	1		
Psikoz	1	-		
Yok	10	3		

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	KOAH	4	1	
	Koroner Arter Hastalığı	4	3	
	Kronik Böbrek Yetmezliği	6	-	
	Malignite	Akciğer Ca	1	-
		Endometriyum Ca	2	-
		Glioblastoma Multiforme	1	-
		Kolon Ca	7	-
		Lenfoma	1	-
		Liposarkom	-	1
		Meme Ca	1	-
		Mide Ca	2	-
		Pankreas Ca	1	-
		Serviks Ca	1	-
	Toplam	17	1	
	Serebrovasküler Hastalık	1	1	
	Periferik Arter Hastalığı	-	1	
Psikoz	1	-		
Yok	10	3		

Bulgular

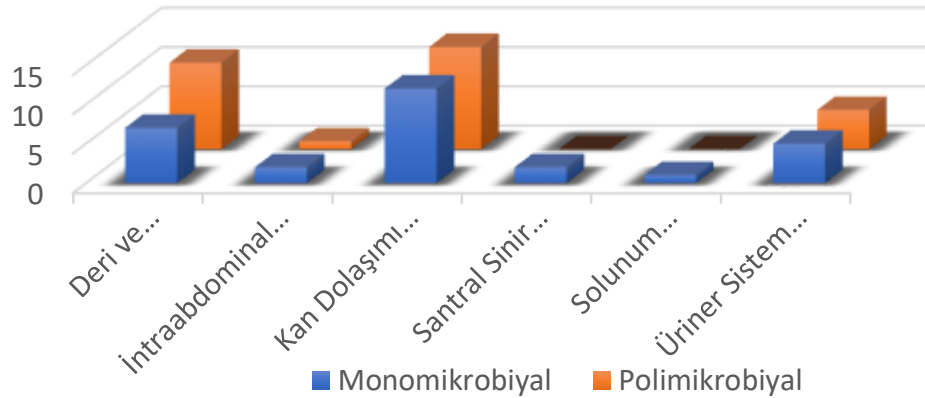
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		Endometriyum Ca	2	-
		Glioblastoma Multiforme	1	-
		Kolon Ca	7	-
		Lenfoma	1	-
		Liposarkom	-	1
		Meme Ca	1	-
		Mide Ca	2	-
		Pankreas Ca	1	-
Serviks Ca		1	-	
Toplam	17	1		
Serebrovasküler Hastalık	1	1		
Periferik Arter Hastalığı	-	1		
Psikoz	1	-		
Yok	10	3		

Bulgular

Sendromik Enfeksiyon Tanıları	<i>Enterococcus gallinarum</i>			<i>Enterococcus casseliflavus</i>		
	Toplam n, (%)	Monomikrobiyal n	Polimikrobiyal n	Toplam n, (%)	Monomikrobiyal n	Polimikrobiyal n
Deri ve Yumuşak Doku Enfeksiyonu	18, (30,5)	7	11	6, (46,1)	5	1
İntraabdominal Enfeksiyon	3, (5,08)	2	1	1, (7,69)	-	1
Kan Dolaşımı Enfeksiyonu	25, (42,3)	12	13	5, (38,4)	2	3
Santral Sinir Sistem Enfeksiyonu	2, (3,3)	2	-	-	-	-
Solunum Sistemi Enfeksiyonu	1, (1,6)	1	-	-	-	-
Üriner Sistem Enfeksiyonu	10, (16,9)	5	5	1, (7,69)	-	1
Genel Toplam	59, (100)	30	30	13, (100)	6	7

K.pneumoniae

Enterococcus gallinarum

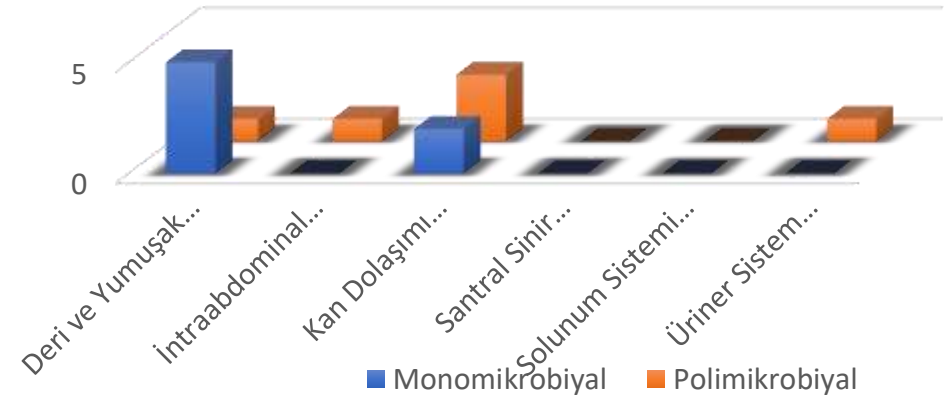


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Sendromik Enfeksiyon Tanıları	<i>Enterococcus gallinarum</i>			<i>Enterococcus casseliflavus</i>		
	Toplam n, (%)	Monomikrobiyal n	Polimikrobiyal n	Toplam n, (%)	Monomikrobiyal n	Polimikrobiyal n
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Genel Toplam	59, (100)	30	30	13, (100)	6	7

E.coli

Enterococcus casseliflavus



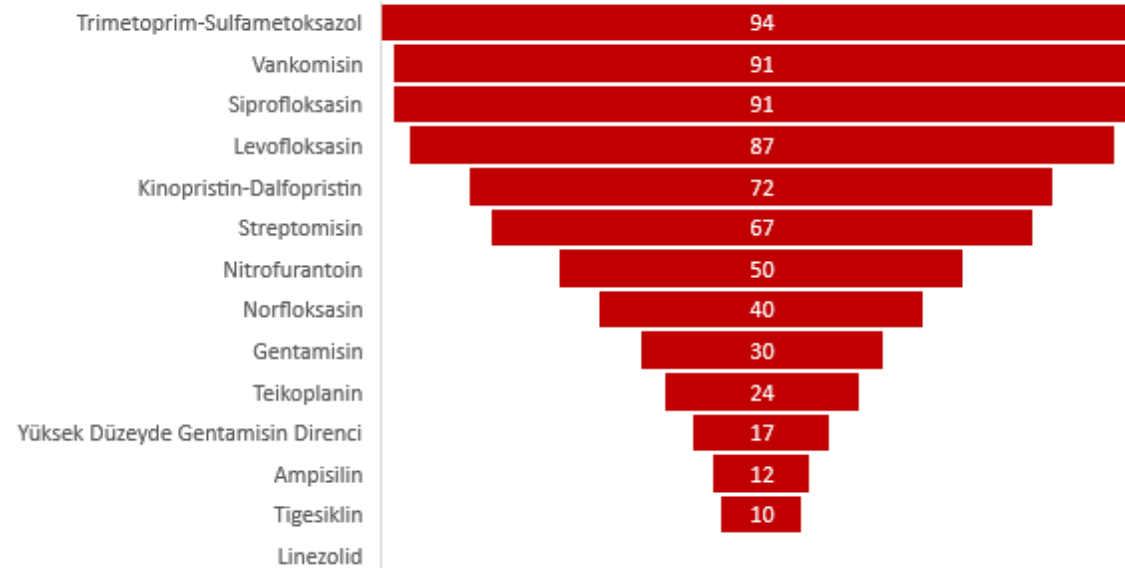
Bulgular

Antibiyotikler ve Grupları		<i>Enterococcus gallinarum</i>			<i>Enterococcus casseliflavus</i>		
		Sayı	Duyarlı	Dirençli	Sayı	Duyarlı	Dirençli
Penisilinler	Ampisilin	59	52	7	13	11	2
	Norfloksasin	5	3	2	3	3	3
Florokinolonlar	Siprofloksasin	33	3	30	9	6	3
	Levofloksasin	32	4	28	6	5	1
Aminoglikozidler	Gentamisin	10	7	3	2	2	-
	Streptomisin	6	2	4	3	2	1
Tetrasiklinler	Tigesiklin	50	40	10	10	9	1
Oksazolidinonlar	Linezolid	59	59	-	13	11	2
Diğer Gruplar	Nitrofurantoin	10	5	5	3	3	-
	Trimetoprim-Sulfametoksazol	49	3	46	10	-	10
Diğer Direnç Testleri	Yüksek Düzeyde Gentamisin Direnci	48	40	8	9	8	1
Glikopeptidler	Teikoplanin	58	44	14	13	11	2
	Vankomisin	55	5	50	13	2	11
Streptograminler	Kinoptistin-Dalropristin	7	2	5	2	-	2

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Antibiyotikler ve Grupları	Enterococcus gallinarum			Enterococcus casseliflavus			
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	Streptomisin	6	2	4	3	2	1
Tetrasiklinler	Tigesiklin	50	40	10	10	9	1
Oksazolidinonlar	Linezolid	59	59	-	13	11	2
Diğer Gruplar	Nitrofurantoin	10	5	5	3	3	-
	Trimetoprim-Sulfametoksazol	49	3	46	10	-	10
Diğer Direnç Testleri	Yüksek Düzeyde Gentamisin Direnci	48	40	8	9	8	1
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	Vankomisin	55	5	50	13	2	11
Streptograminler	Kinopristin-Dalfopristin	7	2	5	2	-	2

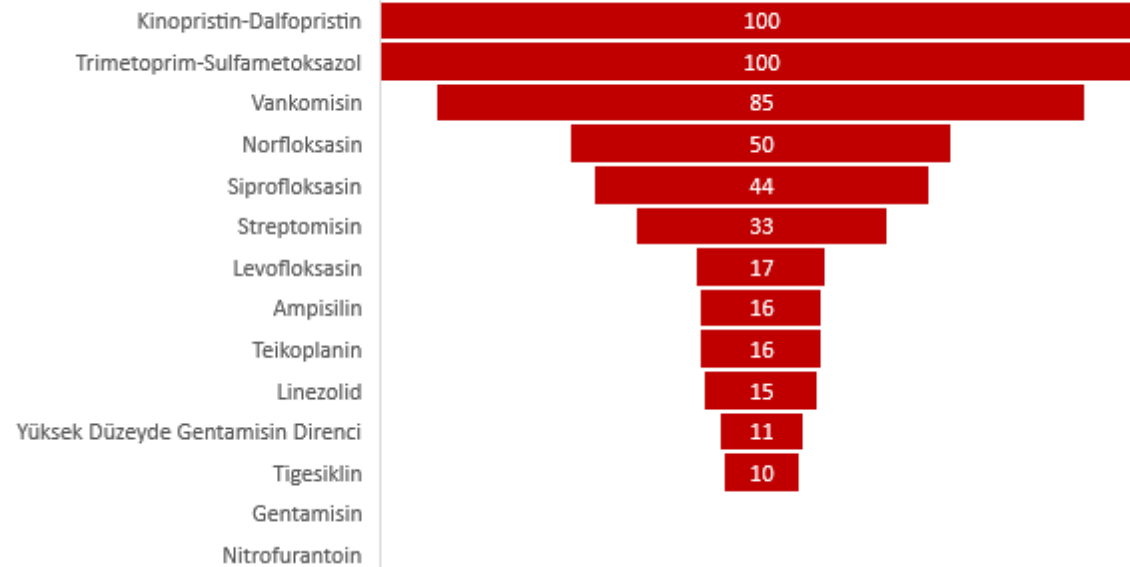
Enterococcus gallinarum %



Bulgular

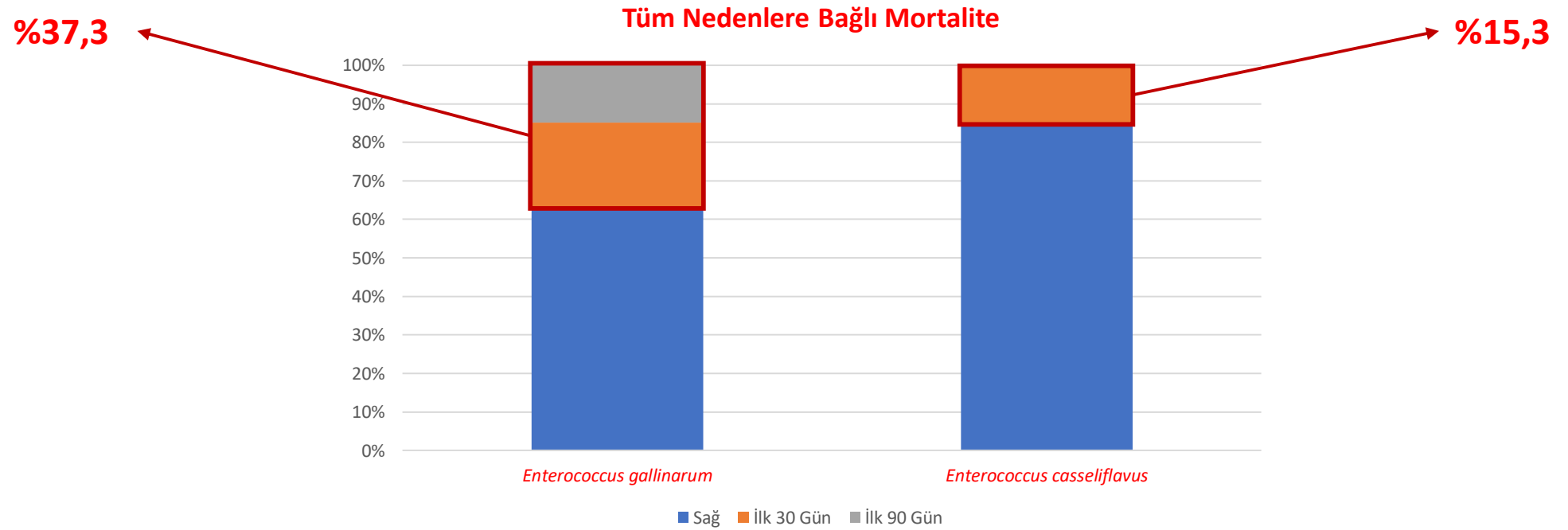
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Streptograminler	Kinopristin-Dalfopristin	7	2	5	2	-	2

Enterococcus casseliflavus %



Bulgular

	Sağ	30 Günlük Mortalite	90 Günlük Mortalite
<i>Enterococcus gallinarum</i>	34	12	8
<i>Enterococcus casseliflavus</i>	11	2	0



Tartışma

- ❑ Reid ve ark; EG+EC:20 bakteriyemi, 1992-1998, %20 mortalite
- ❑ Britt ve ark; EG+EC: 48 bakteriyemi, 2010-2013, 30 günlük mortalite %10,4
- ❑ Güncel EUCAST önerileri ve çalışmamız ışığında;
 - ✓ Rutin vankomisin direnci bakılmaması önerisi,
 - ✓ Non-faecium non-faecalis VRE etkenleri arasında, EG ve EC'nin nadir görülmesi,
 - ✓ %37,3 leri bulan mortalite oranları ile,

« ... Antibiyogram sonucu beklenirken, EG ve EC olgularının, vankomisine intrensek dirençli olduğu, ancak ampisilin, linezolid, tigesikline ve teikoplanine duyarlı olduğunun akılda tutulması gerektiğini önermekteyiz. »



Teşekkürler...