Kolistine Dirençli *E. coli* Suşuyla Gelişen ÜSİ Olgusu ve Sonuçlar

Dr. Okan Derin

Kocaeli VM Medical Park Hastanesi

KLİMİK Derneği Çalışma Grupları Olgu Tartışmaları: Antibiyotik Direnci: Şimdi Nasıl Tedavi Edelim, Yönetelim?

Sunum Planı

- Gerekçe
- Hastane kökenli Gram negatif enterik patojenlerde direncin epidemiyolojisi
- Tedavi seçenekleri
- Çin'den gelen bilgi: Horizontal gen transferi ile kolistin direnci
- İlk olgu Amerika'dan: plazmid aracılı
- Tepkiler
- Türkiye'de durum
- Sonuç

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LETTER TO THE EDITOR

Escherichia coli Harboring *mcr-1* and bla_{CTX-M} on a Novel IncF Plasmid: First Report of *mcr-1* in the United States

Patrick McGann,[a] Erik Snesrud,[a] Rosslyn Maybank,[a] Brendan Corey,[a] Ana C. Ong,[a] Robert Clifford,[a] Mary Hinkle,[a] Timothy Whitman,[b] Emil Lesho,[a] Kurt E. Schaecher[c]

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The recent discovery of a plasmid-borne colistin resistance gene, *mcr-1*, in China heralds the emergence of truly pan-drug-resistant bacteria (1). The gene has been found primarily in *Escherichia coli* but has also been identified in other members of the *Enterobacteriaceae* in human, animal, food, and environmental samples on every continent (2–5). In response to this threat, starting in May 2016, all extended-spectrum-β-lactamase (ESBL)-producing *E. coli* clinical isolates submitted to the clinical microbiology laboratory at the Walter Reed National Military Medical Center (WRNMMC) have been tested for resistance to colistin by Etest. Here we report the presence of *mcr-1* in an *E. coli* strain cultured from a patient with a urinary tract infection (UTI) in the United States. The strain was resistant to colistin, but it remained susceptible to several other agents, including amikacin, piperacillin-tazobactam, all carbapenems, and nitrofurantoin (Table 1).

E. coli MRSN 388634 was cultured from the urine of a 49-year-old female who presented to a clinic in Pennsylvania on 26 April 2016 with symptoms indicative of a UTI. The isolate was forwarded to WRNMMC, where susceptibility testing indicated an ESBL phenotype, and *mcr-1* was detected by real-time PCR (6). Whole-genome sequencing (WGS) of MRSN 388634 was performed using a PacBio RS II system and a MiSeq benchtop sequencer.

TABLE 2 Characteristics of plasmids in *E. coli* MRSN 388634

Plasmid name	Size (kb)	Inc[a]	Copy no.[b]	Antibiotic resistance genes[c]
pMR0516mcr	225.7	F18:A-:B1	2	*strA*, *strB*, $bla_{CTX-M-55}$, bla_{TEM-1B}, ***mcr-1***, *sul2*, *tet*(A), *dfrA14*
pMR0416ctx	47	N	1	*aac(3)-IVa*, *aph(4)-Ia*, $bla_{CTX-M-14}$, *fosA3*, *mph*(A), *floR*, *sul2*

[a] Data represent plasmid incompatibility (Inc) group designations, as determined by Plasmid Finder version 1.2 (10).
[b] Data represent average numbers of copies per cell, normalized to the chromosomal read coverage.
[c] The gene of interest is indicated in bold.

KLİMİK Derneği Çalışma Grupları Olgu Tartışmaları: Antibiyotik Direnci: Şimdi Nasıl Tedavi Edelim, Yönetelim?

Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

Yi-Yun Liu, Yang Wang*, Timothy R Walsh, Ling-Xian Yi, Rong Zhang, James Spencer, Yohei Doi, Guobao Tian, Baolei Dong, Xianhui Huang, Lin-Feng Yu, Danxia Gu, Hongwei Ren, Xiaojie Chen, Luchao Lv, Dandan He, Hongwei Zhou, Zisen Liang, Jian-Hua Liu, Jianzhong Shen*

Summary

Background Until now, polymyxin resistance has involved chromosomal mutations but has never been reported via horizontal gene transfer. During a routine surveillance project on antimicrobial resistance in commensal *Escherichia coli* from food animals in China, a major increase of colistin resistance was observed. When an *E coli* strain, SHP45, possessing colistin resistance that could be transferred to another strain, was isolated from a pig, we conducted further analysis of possible plasmid-mediated polymyxin resistance. Herein, we report the emergence of the first plasmid-mediated polymyxin resistance mechanism, MCR-1, in Enterobacteriaceae.

Methods The *mcr-1* gene in *E coli* strain SHP45 was identified by whole plasmid sequencing and subcloning. MCR-1 mechanistic studies were done with sequence comparisons, homology modelling, and electrospray ionisation mass spectrometry. The prevalence of *mcr-1* was investigated in *E coli* and *Klebsiella pneumoniae* strains collected from five provinces between April, 2011, and November, 2014. The ability of MCR-1 to confer polymyxin resistance in vivo was examined in a murine thigh model.

Findings Polymyxin resistance was shown to be singularly due to the plasmid-mediated *mcr-1* gene. The plasmid carrying *mcr-1* was mobilised to an *E coli* recipient at a frequency of 10^{-1} to 10^{-3} cells per recipient cell by conjugation, and maintained in *K pneumoniae* and *Pseudomonas aeruginosa*. In an in-vivo model, production of MCR-1 negated the efficacy of colistin. MCR-1 is a member of the phosphoethanolamine transferase enzyme family, with expression in *E coli* resulting in the addition of phosphoethanolamine to lipid A. We observed *mcr-1* carriage in *E coli* isolates collected from 78 (15%) of 523 samples of raw meat and 166 (21%) of 804 animals during 2011–14, and 16 (1%) of 1322 samples from inpatients with infection.

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See Comment page 132

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Clonal transmission of a colistin-resistant *Escherichia coli* from a domesticated pig to a human in Laos

Abiola Olumuyiwa Olaitan[1], Boupha Thongmalayvong[2], Kongsap Akkhavong[2], Silaphet Somphavong[3], Phimpha Paboriboune[3], Syseng Khounsy[4], Serge Morand[5] and Jean-Marc Rolain[1,*]

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Sir,

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However, the extensive use of antibiotics in food-animal production has been shown to increase the risk of transferring resistant bacteria to humans.[3] In this study, we investigated the possible link between colistin-resistant *Escherichia coli* isolated from domesticated pigs and humans in a rural area in Laos.

In 2012, faecal samples were collected from 190 healthy individuals and

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EUROPEAN MEDICINES AGENCY
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19 July 2013
EMA/755938/2012

Use of colistin products in animals within the European Union: development of resistance and possible impact on human and animal health

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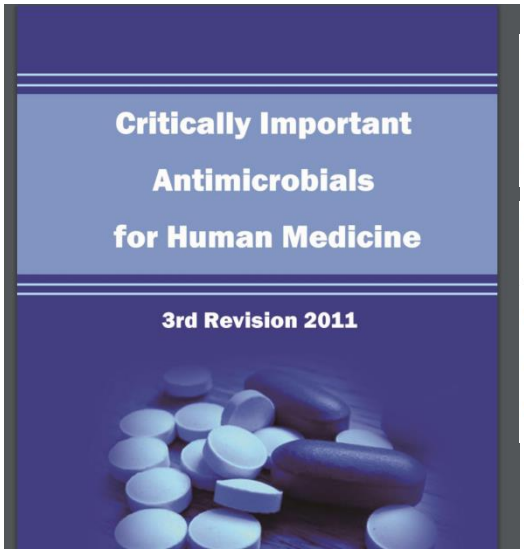

Criterion 1:
An antimicrobial agent which is the sole, or one of limited available therapy, to treat serious human disease.

Criterion 2:
Antimicrobial agent is used to treat diseases caused by either: (1) organisms that may be transmitted to humans from non-human sources or, (2) human diseases causes by organisms that may acquire resistance genes from non-human sources.

CRITICALLY IMPORTANT ANTIMICROBIALS			
Drug name*	**C1**	**C2**	**Comments**
Polymyxins	Yes	Yes	(Criterion 1) Limited therapy for infections with MDR *Enterobacteriaceae* (e.g. *Klebsiella* spp., *E. coli*, *Acinetobacter*, *Pseudomonas* spp.). (Criterion 2) May result from transmission of *Enterobacteriaceae* from non-human sources.
colistin polymyxin B			

E.coli

E. coli insanların normal mikrobiyotasının önemli bir elemanı, suda ve toprakta değişik çevrelerde yaşayabilir ve çoğalabilir

- Toplum ve hastane kökenli üriner sistem infeksiyonlarının en sık etkeni
- Tüm yaşlarda kan dolaşımı infeksiyonlarının en sık etkeni
- Karın içi infeksiyonlarla ilişkili
- Yenidoğanlarda menenjit ile ilişkili
- Gıda kaynaklı infeksiyonların en sık etkenlerinden biri

Enterik Gram Negatiflerde Direnç

- Beta laktamaz üretimi
  - AmpC Beta laktamazlar
  - GSBL üretimi
- Karbapenemaz üretimi
  - Serin karbapenemazlar (KPC, OXA-48)
  - Metallo beta laktamazlar (VIM, IPM, NDM-1)
- Aminoglikozid, Florokinolon vd..

E.coli AMD

	Percentage of Enterobacteriaceae healthcare-associated infections resistant to carbapenems	Estimated number of infections	Estimated number of deaths attributed
Carbapenem-Resistant *Klebsiella* spp.	11%	7,900	520
Carbapenem-resistant *E. coli*	2%	1,400	90

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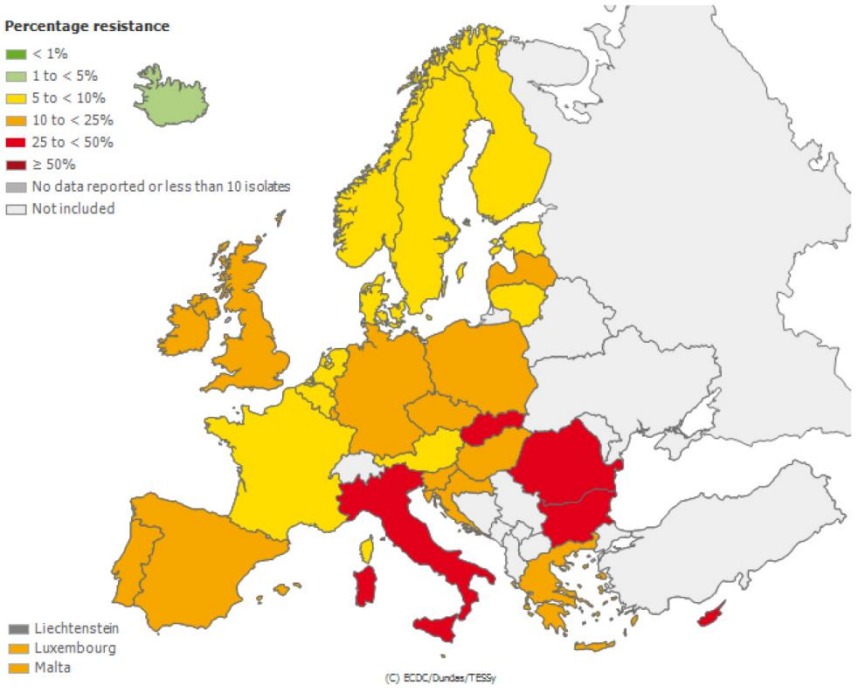
Proportion of 3rd gen. cephalosporins Resistant (R) *Escherichia coli* Isolates in Participating Countries in 2014



Proportion of Carbapenems Resistant (R) *Escherichia coli* Isolates in Participating Countries in 2014

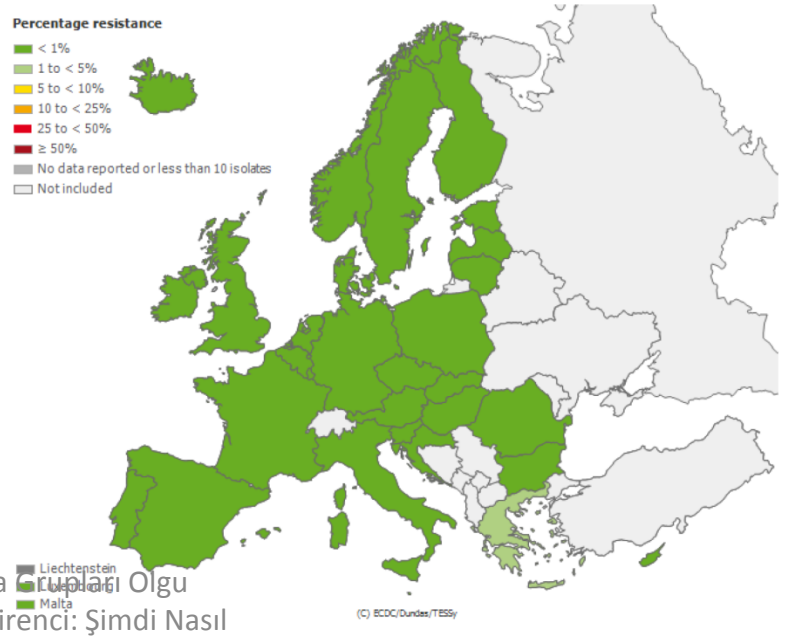
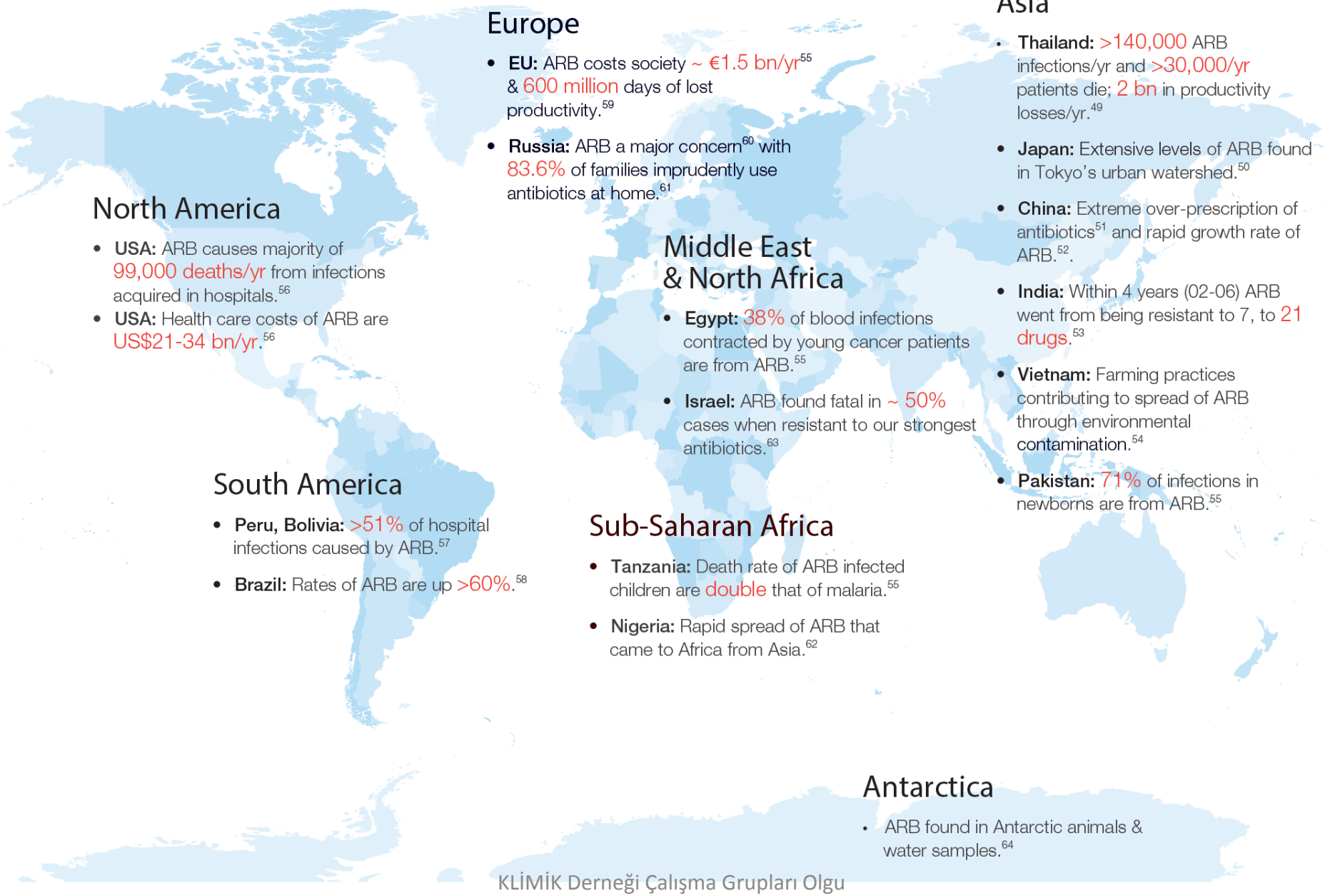


Table 29. Resistance levels for *E. coli* and *K. pneumoniae* among blood and CSF isolates in Turkey

Antibiotic class	*E. coli*		*K. pneumoniae*	
	N	Resistance (%)	N	Resistance (%)
Aminopenicillins (R)[a]	1 424	67	NA	NA
3rd-generation cephalosporins (R)[b]	2 223	44	1 168	56
3rd-generation cephalosporins (I+R)[b]	2 223	45	1 168	59
Aminoglycosides (R)[c]	2 401	22	1 280	30
Fluoroquinolones (R)[d]	2 020	41	1 171	34
Fluoroquinolones (I+R)[d]	2 020	42	1 171	39
Carbapenems (R)[e]	2 046	4	1 083	11
Carbapenems (I+R)[e]	2 046	5	1 083	15

NA: not applicable.
[a] The aminopenicillins group consists of amoxicillin and ampicillin.
[b] The third-generation cephalosporin group consists of cefotaxime, ceftriaxone and ceftazidime.
[c] The aminoglycoside group consists of amikacin, gentamicin and tobramycin.
[d] The fluoroquinolone group consists of ciprofloxacin, ofloxacin and levofloxacin.
[e] The carbapenem group consists of imipenem and meropenem.



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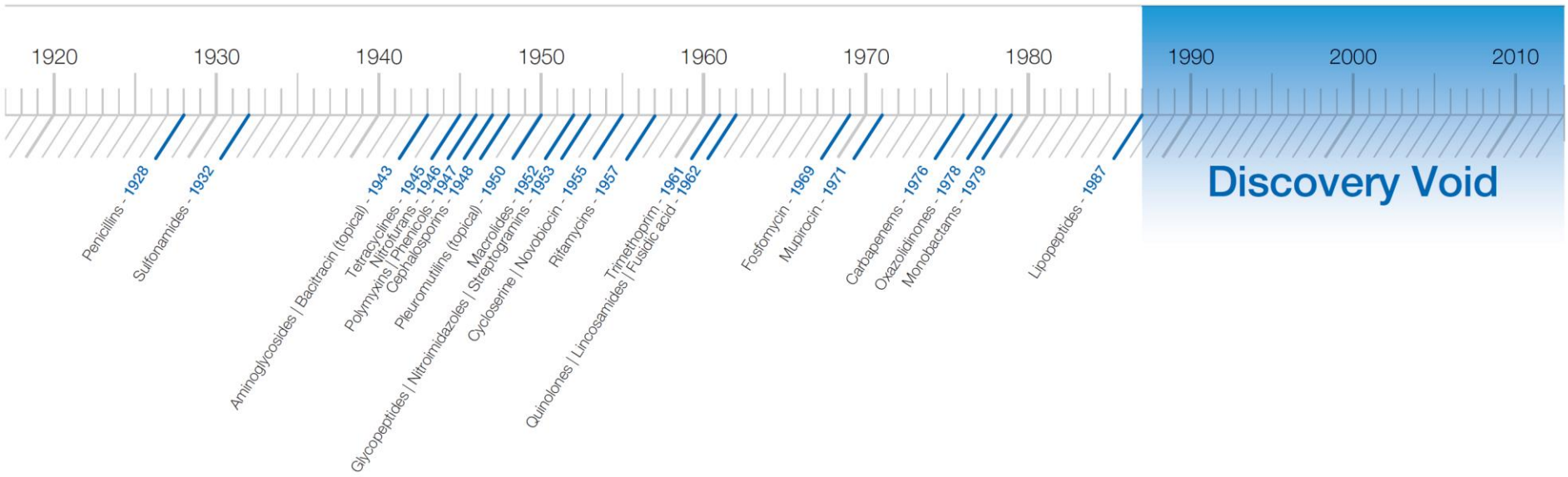
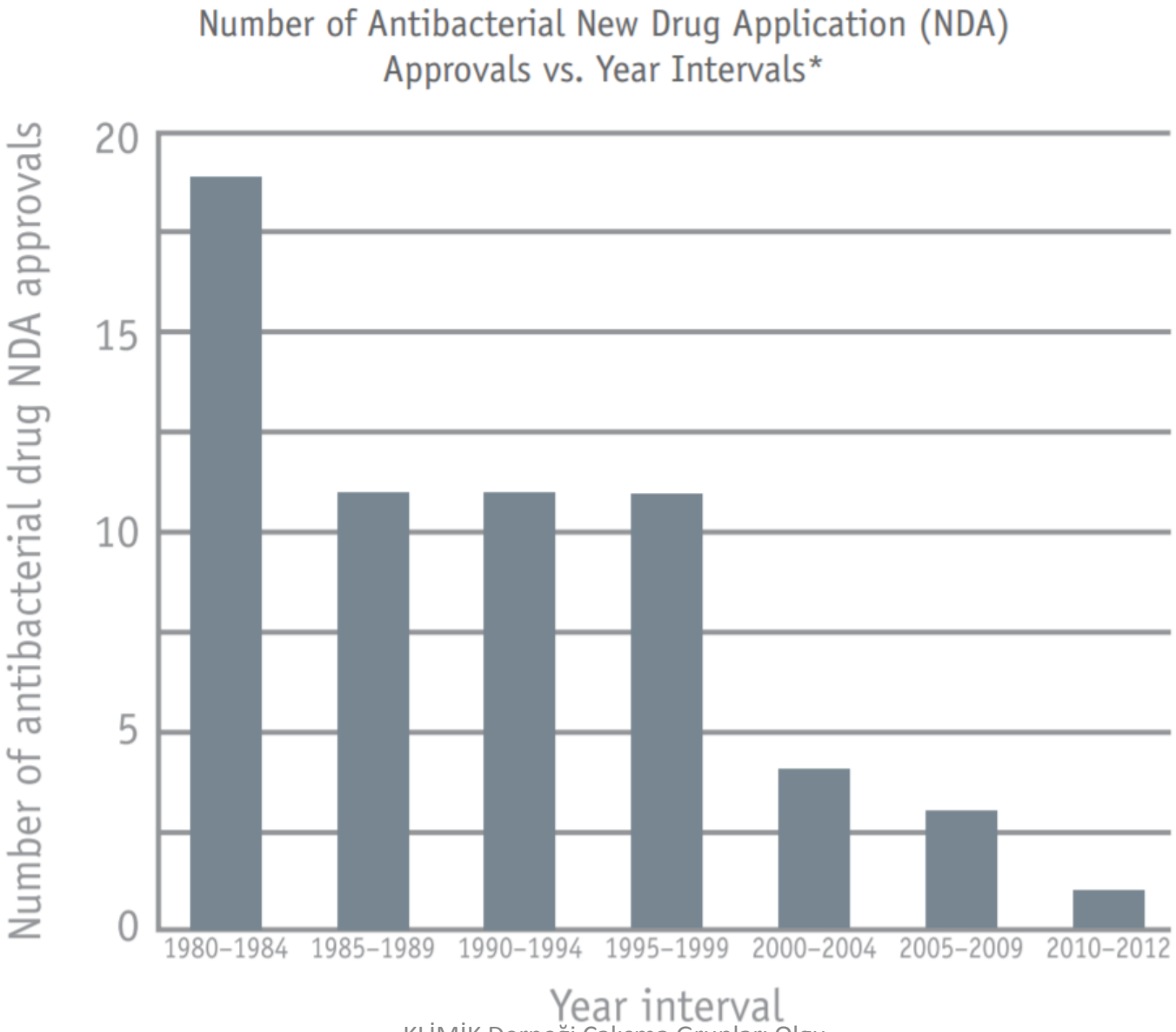
The discovery dates of distinct classes of antibiotics. No new classes have been discovered since 1987.





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Direncin Moleküler Temeli

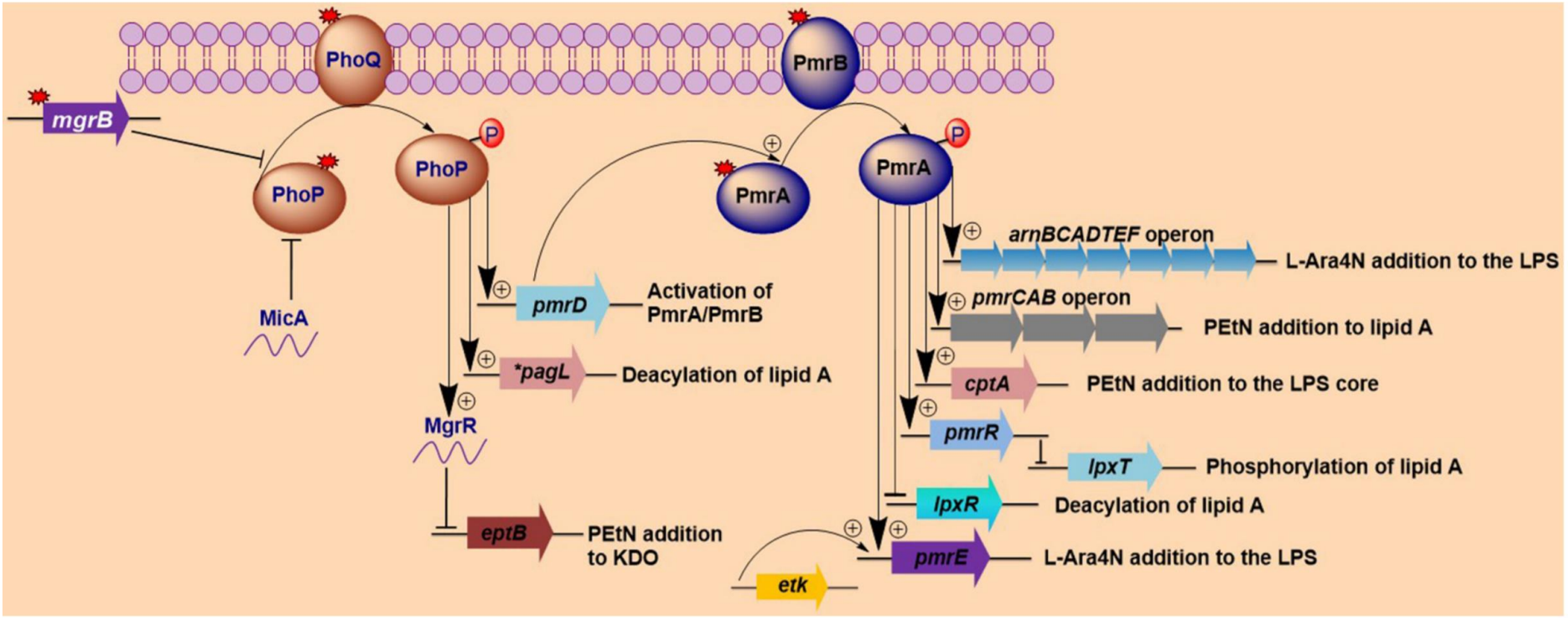
- Vertikal evrim
  - Mevcut genlerde mutasyon
- Horizontal evrim
  - Mobil genetik elementler (Fajlar, plazmidler, transpozonlar)

Çok İlaca Direnç

- Enterobacteriaceae'de ÇİD gelişimi için integron taşıyan elementlerin transferi önemli rol oynar
- *Salmonella* ve *Escherichia coli* için en çok bildirilen **kolistin** direnci PhoP–PhoQ ve/veya PmrA–PmrB mutasyonuna bağlı lipid A negatif yükünde azalma (kromozomal)

Rhouma, M., F. Beaudry, and A. Letellier, International Journal of Antimicrobial Agents, 2016. **48**(2): p. 119-126.

Kolistin Direnci –Kromozomal-



Front Microbiol. 2014; 5: 643.

Direncin Yayılımı

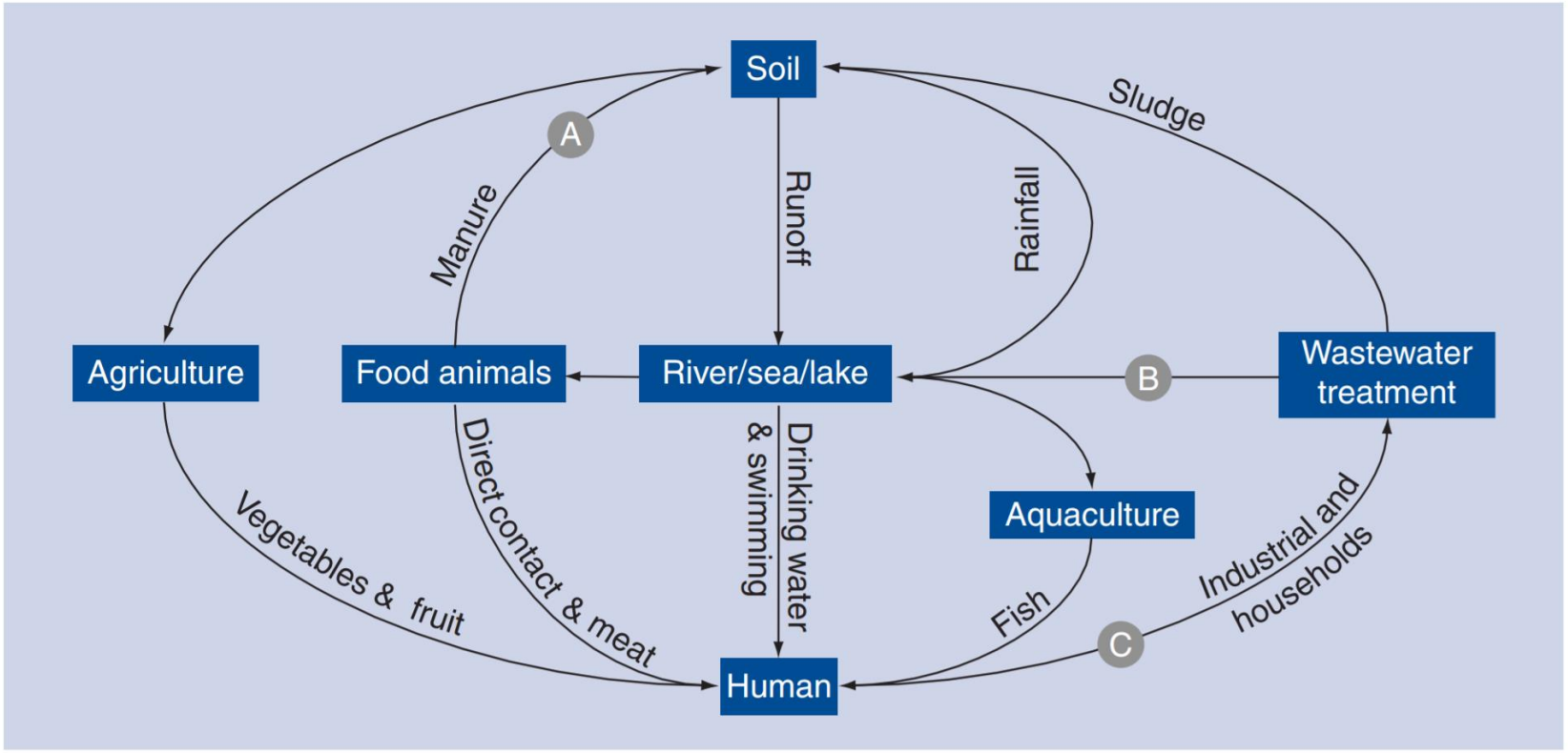


Figure 6. Potential antibiotic resistance gene dissemination. The arrows indicate possible points of dissemination among different environments. Supporting metagenomic studies are marked as follows: **(A)** [82], **(B)** [71] and **(C)** [48,52].

Schmieder R, Edwards R. Insights into antibiotic resistance through metagenomic approaches. Future microbiology. 2012;7(1):73-89.

Kolistin Direnç Epidemiyolojisi

- Türkiye'de
  - Acinetobacter için %0-6
  - Pseudomonas için %0-1.7
  - Karbapenem dirençli Klebsiella için: %0-2.7
- Dünya'da
  - Karbapenem dirençli Klebsiella için %0-45

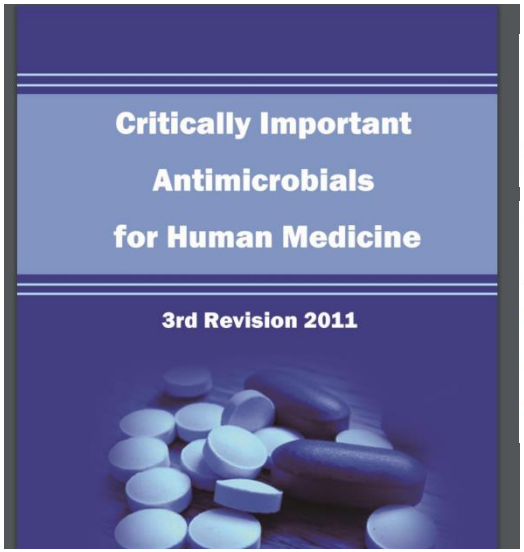
Kolistin Direnci İçin Risk Faktörleri

- Kolistin monoterapisi, uygunsuz doz
- Heteroresistans
- Selektif Gİ dekontaminasyon
- Klorhekzidin maruziyeti

ÇİD Enterobacteriaceae'de Tedavi Seçenekleri

- GSBL üreten kökenler:
  - Karbapenemler (Hayatı tehdit eden infeksiyonlar)
  - Fosfomisin, nitrofurantoin (Sistit)
- Karbapenemaz üreten kökenler
  - **Colistin** + Meropenem
  - Meropenem + Ertapenem*

*JAC. 69:1718, 2014



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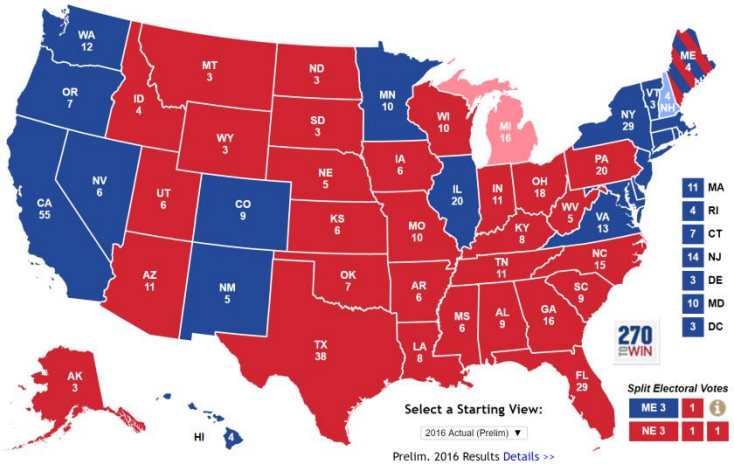

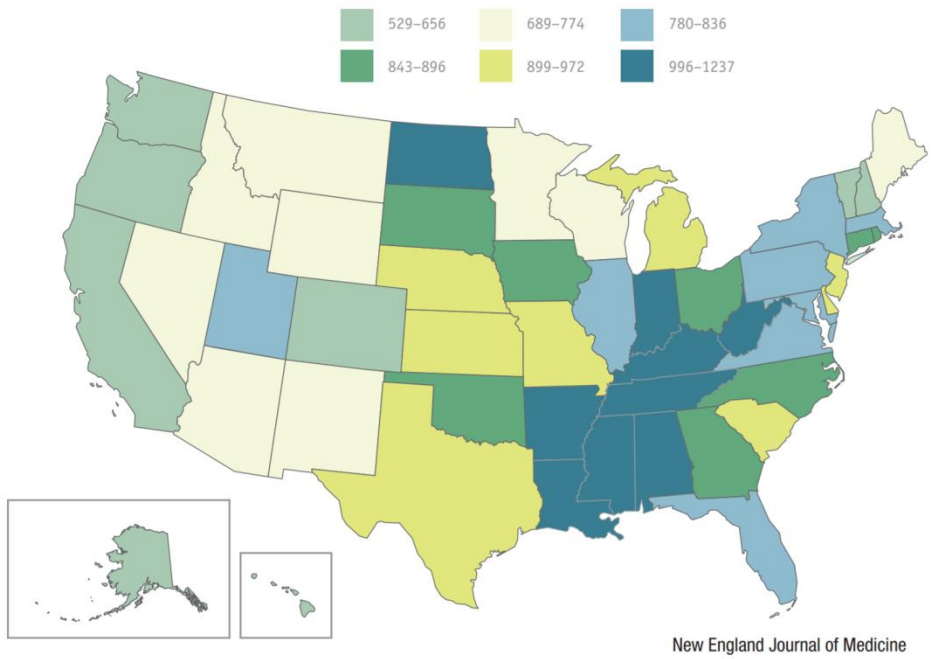

The frequency with which doctors prescribe antibiotics varies greatly from state to state. The reasons for this variation are being studied and might suggest areas where improvements in antibiotic prescribing (fewer unnecessary prescriptions) would be most helpful.

EUROPEAN MEDICINES AGENCY
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19 July 2013
EMA/755938/2012

Use of colistin products in animals within the European Union: development of resistance and possible impact on human and animal health

Colistin has been used regularly in veterinary medicine for decades, both as curative treatment and for prevention of disease. The antibiotic has been predominantly administered as group treatment for Gram-negative gastrointestinal infections in conditions of densely populated livestock by oral administration, the route by which the compound demonstrates poor systemic absorption. The use in veterinary medicine is being questioned given the ever growing need for antimicrobials for treatment of MDR infections in humans.

Clonal transmission of a colistin-resistant *Escherichia coli* from a domesticated pig to a human in Laos

Abiola Olumuyiwa Olaitan[1], Boupha Thongmalayvong[2], Kongsap Akkhavong[2], Silaphet Somphavong[3], Phimpha Paboriboune[3], Syseng Khounsy[4], Serge Morand[5] and Jean-Marc Rolain[1,*]

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In 2012, faecal samples were collected from 190 healthy individuals and

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Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study

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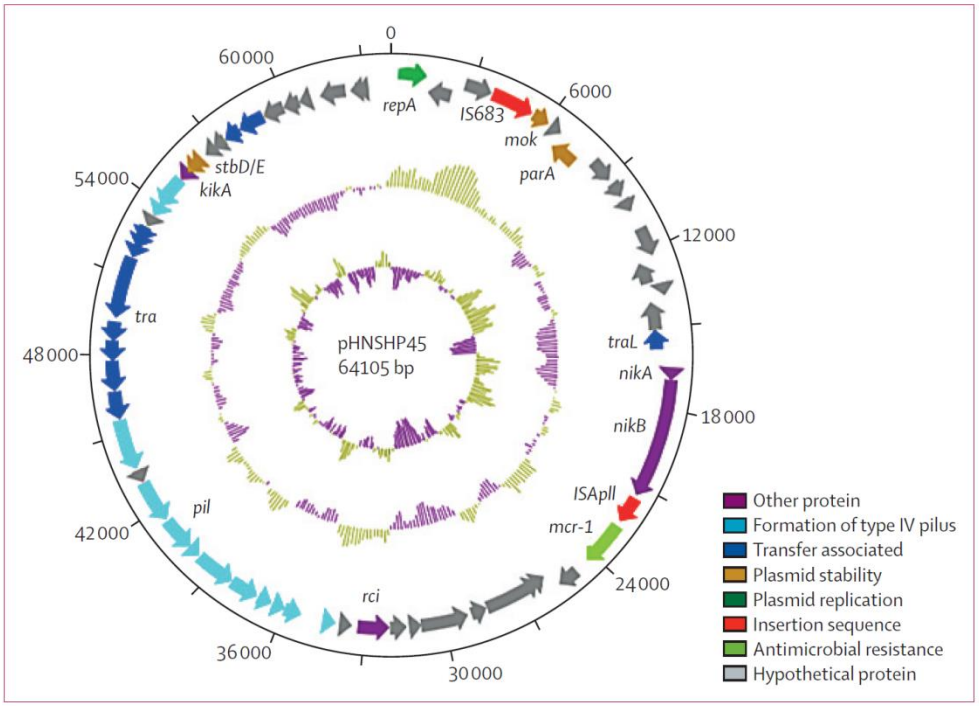
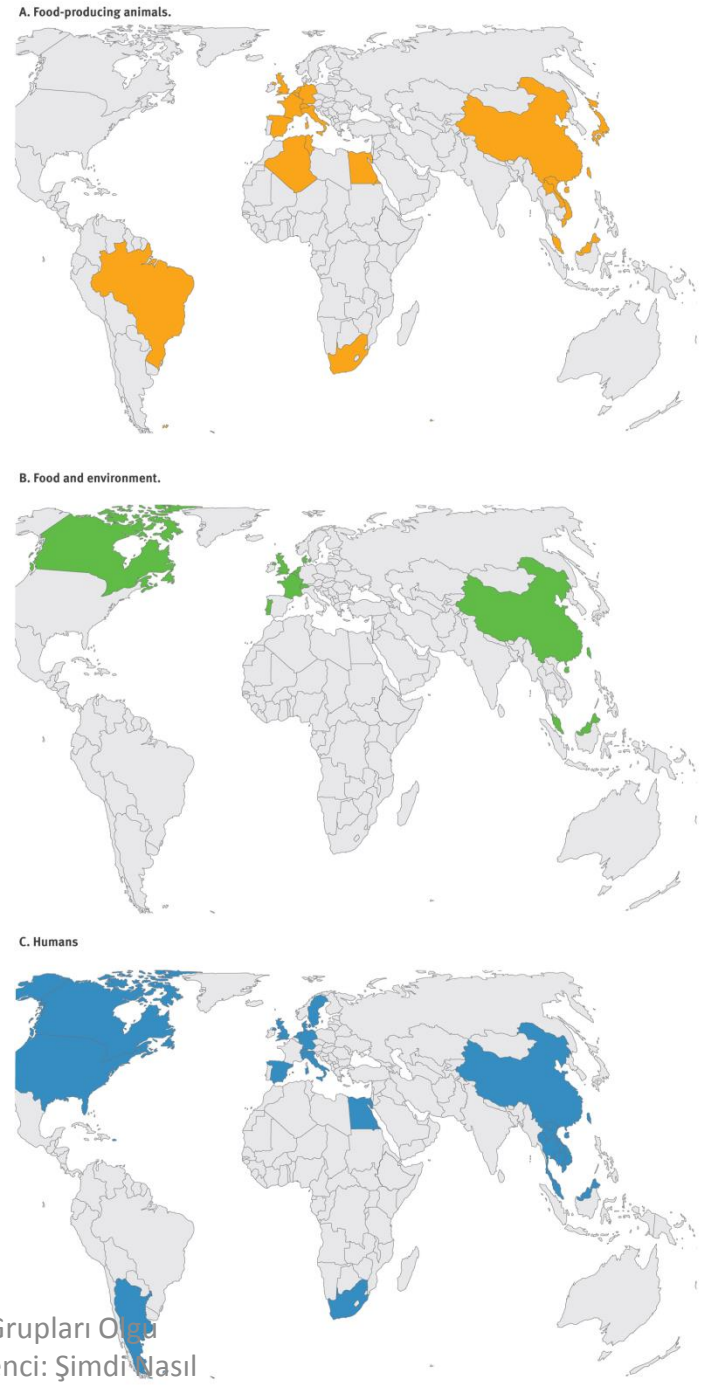


Figure 2: Structure of plasmid pHNSHP45 carrying *mcr-1* from *Escherichia coli* strain SHP45

	Year	Positive isolates (%)/number of isolates
Escherichia coli		
Pigs at slaughter	All	166 (20·6%)/804
Pigs at slaughter	2012	31 (14·4%)/216
Pigs at slaughter	2013	68 (25·4%)/268
Pigs at slaughter	2014	67 (20·9%)/320
Retail meat	All	78 (14·9%)/523
Chicken	2011	10 (4·9%)/206
Pork	2011	3 (6·3%)/48
Chicken	2013	4 (25·0%)/16
Pork	2013	11 (22·9%)/48
Chicken	2014	21 (28·0%)/75
Pork	2014	29 (22·3%)/130
Inpatient	2014	13 (1·4%)/902
Klebsiella pneumoniae		
Inpatient	2014	3 (0·7%)/420

Table 2: Prevalence of colistin resistance gene *mcr-1* by origin

mcr-1 yayılımı



http://ecdc.europa.eu/en/publications/Publications/enterobacteriaceae-risk-assessment-diseases-caused-by-antimicrobial-resistant-microorganisms-europe-june-2016.pdf

Table 1
Reports of the emergence of plasmid-mediated *mcr-1* colistin resistance gene globally.

Country	Title	Author	Strain	Host (no. of *mcr-1* strains)	Journal	Year	Reference
China	Emergence of plasmid-mediated colistin resistance mechanism MCR-1 in animals and human beings in China: a microbiological and molecular biological study	Liu et al	*Escherichia coli*, *Klebsiella pneumoniae*	Animal (166), human (16), food (78)	Lancet Infectious Diseases	2016	[68]
Denmark	Detection of *mcr-1* encoding plasmid-mediated colistin-resistant *Escherichia coli* isolates from human bloodstream infection and imported chicken meat, Denmark, 2015	Hasman et al	*E. coli*	Food (5), human (1)	Eurosurveillance	2015	[69]
The Netherlands	Dissemination of the *mcr-1* colistin resistance gene	Arcilla et al	*E. coli*	Human (6)	Lancet Infectious Diseases	2016	[70]
France	Dissemination of the *mcr-1* colistin resistance gene	Webb et al	*Salmonella* spp.	Food (4)	Lancet Infectious Diseases	2016	[71]
Portugal	Dissemination of the *mcr-1* colistin resistance gene	Tse and Yuen	*Salmonella* spp.	Food (1)	Lancet Infectious Diseases	2016	[72]
Laos, Thailand and Algeria	Dissemination of the *mcr-1* colistin resistance gene	Olaitan et al	*E. coli*	Animal (4), human (8)	Lancet Infectious Diseases	2016	[73]
China	Dissemination of the *mcr-1* colistin resistance gene	Hu et al	*E. coli*	Human (27)	Lancet Infectious Diseases	2016	[74]
Germany	Colistin resistance gene *mcr-1* in extended-spectrum β-lactamase-producing and carbapenemase-producing Gram-negative bacteria in Germany	Falgenhauer et al	*E. coli*	Animal (3), human (1)	Lancet Infectious Diseases	2016	[75]
Belgium	Colistin resistance gene *mcr-1* harboured on a multidrug resistant plasmid	Malhotra-Kumar et al	*E. coli*	Animal (13)	Lancet Infectious Diseases	2016	[76]
Vietnam	Colistin-resistant *Escherichia coli* harbouring *mcr-1* isolated from food animals in Hanoi, Vietnam	Malhotra-Kumar et al	*E. coli*	Animal (9)	Lancet Infectious Diseases	2016	[77]
France	Co-occurrence of extended spectrum β lactamase and MCR-1 encoding genes on plasmids	Haenni et al	*E. coli*	Animal (106)	Lancet Infectious Diseases	2016	[78]
Cambodia	Colistin resistance gene *mcr-1* and pHNSHP45 plasmid in human isolates of *Escherichia coli* and *Klebsiella pneumoniae*	Stoesser et al	*E. coli*, *K. pneumoniae*	Human (1)	Lancet Infectious Diseases	2016	[79]
Malaysia and Portugal	Possible genetic events producing colistin resistance gene *mcr-1*	Petrillo et al	*E. coli*, *Salmonella* spp.	Database EMBL: animal (4), food (1), environment (1)	Lancet Infectious Diseases	2016	[80]
Japan	Investigation of a plasmid genome database for colistin-resistance gene *mcr-1*	Suzuki et al	*E. coli*, *Salmonella* spp.	Database GenEpid-J: animal (7)	Lancet Infectious Diseases	2016	[81]
Switzerland	Plasmid-mediated carbapenem and colistin resistance in a clinical isolate of *Escherichia coli*	Poirel et al	*E. coli*	Human (1)	Lancet Infectious Diseases	2016	[82]
China	Emergence of the *mcr-1* colistin resistance gene in carbapenem-resistant Enterobacteriaceae	Du et al	*E. coli*, *K. pneumoniae*	Human (4)	Lancet Infectious Diseases	2016	[83]
China	Carbapenem-resistant and colistin-resistant *Escherichia coli* co-producing NDM-9 and MCR-1	Yao et al	*E. coli*	Food (1)	Lancet Infectious Diseases	2016	[84]
France	Prevalence of *mcr-1* in commensal *Escherichia coli* from French livestock, 2007 to 2014	Perrin-Guyomard et al	*E. coli*	Animal (23)	Eurosurveillance	2016	[85]
Switzerland, Dominican Republic, India, Thailand and Vietnam	Occurrence of the plasmid-borne *mcr-1* colistin resistance gene in extended-spectrum-β-lactamase-producing Enterobacteriaceae in river water and imported vegetable samples in Switzerland	Zurfuh et al	Enterobacteriaceae	Environment (74), food (vegetables) (60)	Antimicrobial Agents and Chemotherapy	2016	[86]
Vietnam	Inducible colistin resistance via a disrupted plasmid-borne *mcr-1* gene in a 2008 Vietnamese *Shigella sonnei* isolate	Thanh et al	*Shigella sonnei*	Human (1)	Journal of Antimicrobial Chemotherapy	2016	[87]
Spain	Detection of plasmid mediated colistin resistance (MCR-1) in *Escherichia coli* and *Salmonella enterica* isolated from poultry and swine in Spain	Quesada et al	*E. coli*, *Salmonella* spp.	Animal (9)	Research in Veterinary Science	2016	[88]
Tunisia	Impact of food animal trade on the spread of *mcr-1*-mediated colistin resistance, Tunisia, July 2015	Grami et al	*E. coli*	Animal (37)	Eurosurveillance	2016	[89]
Canada	One case of *mcr-1* resistance confirmed in British Columbia	—	*E. coli*	Human (1)	BC Centre for Disease Control (BCCDC)	2016	[90]
Italy	Antibiotic resistance—Italy: colistin, MCR-1, *E. coli*, turkeys, 2014	Battisti	*E. coli*	Animal (1)	ProMED mail (International Society for Infectious Diseases)	2016	[91]
China	Early emergence of *mcr-1* in *Escherichia coli* from food-producing animals	Shen et al	*E. coli*	Animal (104)	Lancet Infectious Diseases	2016	[92]
China	Dissemination of the *mcr-1* colistin resistance gene	Zhi et al	*E. coli*	Animal	Lancet Infectious Diseases	2016	[93]

(*continued on next page*)

http://dx.doi.org/10.1016/j.ijantimicag.2016.06.023

KLİMİK Derneği Çalışma Grupları Olgu Tartışmaları: Antibiyotik Direnci: Şimdi Nasıl Tedavi Edelim, Yönetelim?

AMERICAN SOCIETY FOR MICROBIOLOGY | Antimicrobial Agents and Chemotherapy

LETTER TO THE EDITOR

Escherichia coli Harboring *mcr-1* and bla_{CTX-M} on a Novel IncF Plasmid: First Report of *mcr-1* in the United States

Patrick McGann,[a] Erik Snesrud,[a] Rosslyn Maybank,[a] Brendan Corey,[a] Ana C. Ong,[a] Robert Clifford,[a] Mary Hinkle,[a] Timothy Whitman,[b] Emil Lesho,[a] Kurt E. Schaecher[c]

Multidrug-resistant Organism Repository and Surveillance Network, Walter Reed Army Institute of Research, Silver Spring, Maryland, USA[a]; Department of Infectious Diseases, Walter Reed National Military Medical Center, Bethesda, Maryland, USA[b]; Department of Pathology, Walter Reed National Military Medical Center, Bethesda, Maryland, USA[c]

The recent discovery of a plasmid-borne colistin resistance gene, *mcr-1*, in China heralds the emergence of truly pan-drug-resistant bacteria (1). The gene has been found primarily in *Escherichia coli* but has also been identified in other members of the *Enterobacteriaceae* in human, animal, food, and environmental samples on every continent (2–5). In response to this threat, starting in May 2016, all extended-spectrum-β-lactamase (ESBL)-producing *E. coli* clinical isolates submitted to the clinical microbiology laboratory at the Walter Reed National Military Medical Center (WRNMMC) have been tested for resistance to colistin by Etest. Here we report the presence of *mcr-1* in an *E. coli* strain cultured from a patient with a urinary tract infection (UTI) in the United States. The strain was resistant to colistin, but it remained susceptible to several other agents, including amikacin, piperacillin-tazobactam, all carbapenems, and nitrofurantoin (Table 1).

E. coli MRSN 388634 was cultured from the urine of a 49-year-old female who presented to a clinic in Pennsylvania on 26 April 2016 with symptoms indicative of a UTI. The isolate was forwarded to WRNMMC, where susceptibility testing indicated an ESBL phenotype, and *mcr-1* was detected by real-time PCR (6). Whole-genome sequencing (WGS) of MRSN 388634 was performed using a PacBio RS II system and a MiSeq benchtop sequencer.

TABLE 2 Characteristics of plasmids in *E. coli* MRSN 388634

Plasmid name	Size (kb)	Inc[a]	Copy no.[b]	Antibiotic resistance genes[c]
pMR0516mcr	225.7	F18:A-:B1	2	*strA*, *strB*, $bla_{CTX-M-55}$, bla_{TEM-1B}, ***mcr-1***, *sul2*, *tet*(A), *dfrA14*
pMR0416ctx	47	N	1	*aac(3)-IVa*, *aph(4)-Ia*, $bla_{CTX-M-14}$, *fosA3*, *mph*(A), *floR*, *sul2*

[a] Data represent plasmid incompatibility (Inc) group designations, as determined by Plasmid Finder version 1.2 (10).
[b] Data represent average numbers of copies per cell, normalized to the chromosomal read coverage.
[c] The gene of interest is indicated in bold.

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TABLE 1 Antibiotic resistance profile of MRSN 388634

Antibiotic(s)	MIC(s) (μg/ml)[a]
Amikacin	≤8, S
Amoxicillin/clavulanate	16/8, I
Ampicillin	>16, R
Aztreonam	>16, R
Cefazolin	>16, R
Cefepime	>16, R
Ceftazidime	>16, R
Ceftriaxone	>32, R
Ciprofloxacin	>2, R
Colistin	4, R
Ertapenem	≤0.25, S
Gentamicin	>8, R
Imipenem	≤0.25, S
Levofloxacin	>4, R
Meropenem	≤0.25, S
Nitrofurantoin	≤16, S
Piperacillin-tazobactam	4/4, S
Tetracycline	>8, R
Tobramycin	>8, R
Trimethoprim-sulfamethoxazole	>2/38, R

[a] MICs were determined using BD Phoenix (BD Diagnostics Systems, Hunt Valley, MD, USA) with panels NMIC/ID 133, except for colistin, for which determinations were performed using Etest and manual broth microdilution; both gave MICs of colistin of 4 μg/ml. R = resistant, I = intermediate, and S = susceptible, based on CLSI guidelines (except for colistin, where EUCAST breakpoints are used).

Real-time PCR for detection of plasmid-mediated polymyxin resistance (*mcr-1*) from cultured bacteria and st

Séverine Bontron[1], Laurent
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*Corresponding author.

J Antimicrob Chemother
doi:10.1093/jac/dkw192

Detection of the plasmid-mediated colistin-resistance gene *mcr-1* in clinical isolates and stool specimens obtained from hospitalized patients using a newly developed re

R. H. T. Nijhuis[1]*, K
A. Van Essen-Zand
and J. Gooskens[1]

J Antimicrob Chemother
doi:10.1093/jac/dkw074

Emerging plasmid-encoded colistin resistance: the animal world as the culprit?

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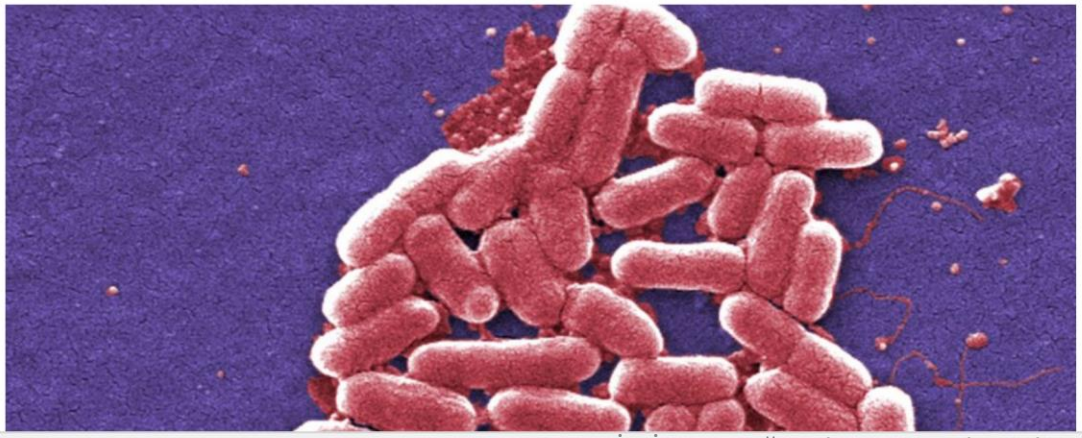
NATIONAL GEOGRAPHIC

GERMINATION *A Blog by Maryn McKenna*

Why It's Crucial the New Superbug Was in a Urinary Tract Infection

POSTED WED, 06/1/2016



ABOUT MARYN

Maryn McKenna is an award-winning journalist and the author of two critically acclaimed books, **Superbug** (2010) and **Beating Back the Devil** (2004). She writes for Wired, Scientific American, Slate, Nature, the Atlantic, the Guardian and others, and is a Senior Fellow of the Schuster Institute for Investigative Journalism at Brandeis University.

At Germination, she'll explore public health, global health, and food production and policy: ancient diseases, emerging infections, antibiotic resistance, agricultural planning, foodborne illness, and how we'll feed an increasingly crowded world.

More of her work is at **MarynMcKenna.com**, and she lives on Twitter at **@Marynmck**.

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http://phenomena.nationalgeographic.com/2016/06/01/its-crucial-the-new-superbug-was-in-a-urinary-tract-infection/

WIRED

That New Superbug Was Found in a UTI and That's Key

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THE WOMAN HARBORING *E. coli* resistant to colistin did not know it, and it's only luck that we do. Her doctor would have never prescribed that last-resort antibiotic for a routine urinary tract infection—it can cause serious kidney damage. But her doctor did take a urine sample, which ended up at the Walter Reed National Military Medical Center, where researchers had recently started testing for colistin resistance. The test came back positive. Then came scary headlines about a new superbug in the US.

Superbugs are bacteria with genetic mutations that let them survive humanity's harshest weapons in germ warfare: antibiotics. The gene behind this *E. coli's* colistin resistance is called mcr-1. It first emerged last year when Chinese researchers found it in samples from hospital patients and raw pork. Why pork? Colistin's serious side effects mean it's no longer used as a human antibiotic in many countries. But in China, farmers have been adding it by the pound into feed to fatten animals up.

https://www.wired.com/2016/05/new-superbug-found-uti-thats-key/

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Science News

from research organizations

First discovery in United States of colistin resistance in a human E. coli infection

Date: May 26, 2016

Source: The U.S. Military HIV Research Program (MHRP)

Summary: The Multidrug Resistant Organism Repository and Surveillance Network at the Walter Reed Army Institute of Research characterized a transferrable gene for colistin resistance in the United States that may herald the emergence of truly pan-drug resistant bacteria.

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FULL STORY

The Multidrug Resistant Organism Repository and Surveillance Network (MRSN) at the Walter Reed Army Institute of Research (WRAIR) characterized a transferrable gene for colistin resistance in the United States that may herald the emergence of truly pan-drug resistant bacteria.

https://www.sciencedaily.com/releases/2016/05/160526152033.htm

Felaketin ayak sesleri: Antibiyotik direnci

ntv.com.tr
8 Haziran 2016 Çarşamba , TÜLAY KARABAĞ

Sağlık

Geçtiğimiz günlerde ABD'de ortaya çıkan bir bakteriyi hiçbir ilaç öldüremedi. Yani antibiyotik direnci nedeniyle bakteriler artık tıbbın elindeki ilaçlara adeta 'kafa tutuyor'. Minik canlılardan yükselen bu sinyaller, insanoğlunu bekleyen felaketin 'ayak sesleri' olarak yorumlanıyor. Enfeksiyon Uzmanı Dr. Derin ise

KLİMİK Derneği Çalışma Grupları Olgu Tartışmaları: Antibiyotik Direnci: Şimdi Nasıl Tedavi Edelim, Yönetelim?

The Dangers of Hubris on Human Health

Humanity has always been under constant threat from infectious disease. Globally, we are getting better at monitoring signs of a health-related crisis and alerting each other

Challenges to human health never cease to evolve. Vaccines and antibiotics have helped us to survive leading causes of death from bygone eras, but we face rising rates of chronic illnesses such as heart disease, cancers and diabetes. Although recent pandemics, such as SARS, avian flu and swine flu, have been contained, they also show how easily deadly viruses can

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Sorun ne kadar büyük?

- *mcr-1* geninin plazmid ile taşınabiliyor olması diğer dirençli bakterilerle bu genin paylaşılabileceği ve tüm ilaçlara dirençli bakteri infeksiyonları ile karşı karşıya kalacağımızı gösterir


Memlekete gelen penisilin

Ankara 9 (Telefonla) — Son gönderde memlekete dokuz milyon ünitelik penisilin gelmiştir. Üç milyon üniteliği penisilin Kızılaya ayrılmış, geriyi Sıhhat Bakanlığı emrine verilmiştir.

TABLE 2: GOALS AND OBJECTIVES: Combating Antibiotic-Resistant Bacteria	
GOAL 1: Slow the Emergence of Resistant Bacteria and Prevent the Spread of Resistant Infections	
Objectives	
1.1	Implement public health programs and reporting policies that advance antibiotic-resistance prevention and foster antibiotic stewardship in healthcare settings and the community.
1.2	Eliminate the use of medically-important antibiotics for growth promotion in food- producing animals and bring other agricultural uses of antibiotics, for treatment, control, and prevention of disease, under veterinary oversight.
1.3	Identify and implement measures to foster stewardship of antibiotics in animals.
GOAL 2 : Strengthen National One-Health Surveillance Efforts to Combat Resistance Objectives	
2.1	Create a regional public health laboratory network to strengthen national capacity to detect resistant bacterial strains and a specimen repository to facilitate development and evaluation of diagnostic tests and treatments.
2.2	Expand and strengthen the national infrastructure for public health surveillance and data reporting, and wprovide incentives for timely reporting of antibiotic-resistance and antibiotic use in all healthcare settings.
2.3	Develop, expand, and maintain capacity in State and Federal veterinary and food safety laboratories to conduct antibiotic susceptibility testing and characterize select zoonotic and animal pathogens.
2.4	Enhance monitoring of antibiotic-resistance patterns, as well as antibiotic sales, usage, and management practices, at multiple points in the production chain for food animals and retail meat.
GOAL 3: Advance Development and Use of Rapid and Innovative Diagnostic Tests for Identification and Characterization of Resistant Bacteria	
Objectives	
3.1	Develop and validate new diagnostics—including tests that rapidly distinguish between viral and bacterial pathogens and tests that detect antibiotic-resistance—that can be implemented easily in a wide range of settings.
3.2	Expand availability and use of diagnostics to improve treatment of antibiotic-resistant infections, enhance infection control, and facilitate outbreak detection and response in healthcare and community settings.

Ne yapmalı?

- **İnfeksiyonu önle**
- **Laboratuvar tanısı**
- **Laboratuvar tanısını doğrula**
- **Çevre temizliği**
- **Sağlık otoritesini bilgilendir**
- **Gıda güvenliği**

Teşekkür ederim

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