The Why for Surveillance and the Antibiogram?

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WHY?

Surveillance – keeping track or microorganisms

Antibiograms – keeping track of resistance

Together – epidemiology

Infection Prevention

Antimicrobial Stewardship

Antimicrobial Resistance Trends in the Greater Metropolitan Area of Phoenix, AZ

	% of Isolates	
	then (1978)	now (2010)
MRSA	0	55-65
VRE	0	25-45
Pneumococcus (Pen NS)	0	20-35
ESBLs	0	<2-7
KPCs	0	2-8
Erythro-R Pertussis	0	1 patient
MDROs	NA	increasing

Percent Resistance of Major Gram-Negative Pathogens to Selected Antimicrobics (BGSMC)

	% Resistance							
	E. coli		Kleb		Enterob		P. aerug	
	'00	'10	'00	'10	'00	'10	'00	'10
Agent	(633)	(213)	(168)	(144)	(107)	(73)	(306)	(274)
Cefepime	<1 →	13	<1 →	17	00 →	00	07 →	41
Pip/tazo	01 →	21	03 →	23	29 →	18	14 →	35
Imipenem	00	00	00 →	08	00	0	11 →	35
Genta	03 →	18	06 →	10	20	07	25 →	47
Tobra	02 →	22	06 →	17	06 →	07	18	14
Amikacin		02		13		00		17
Levoflox	01 →	33	01 →	19	15	07	28 →	45

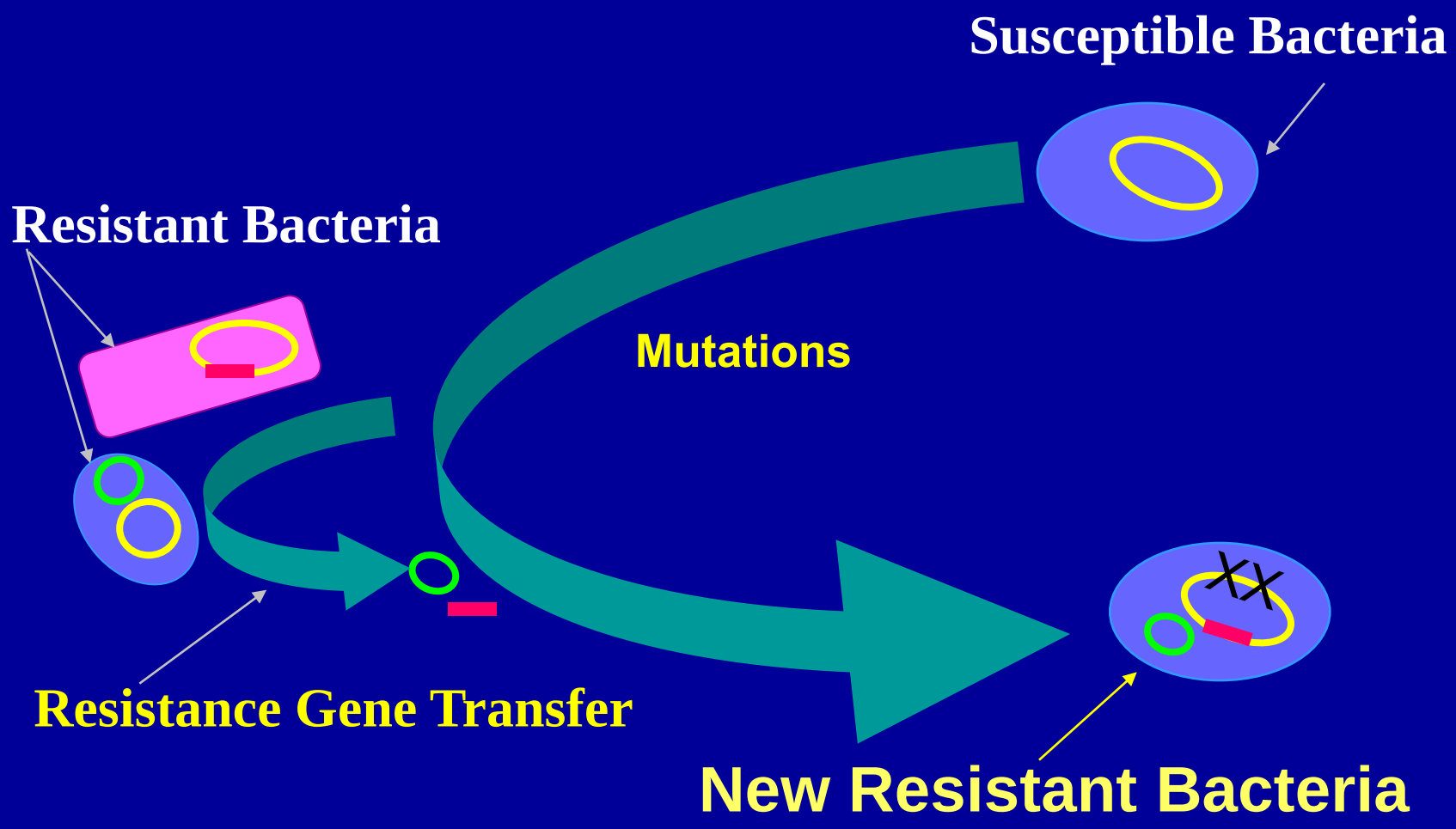
2010 numbers are for second half of year

Antimicrobial Resistance Mutations

- Production of inactivating enzymes
- Change in antimicrobial target
- Porin channels (block entry through outer)
- Efflux (active bilge pump)

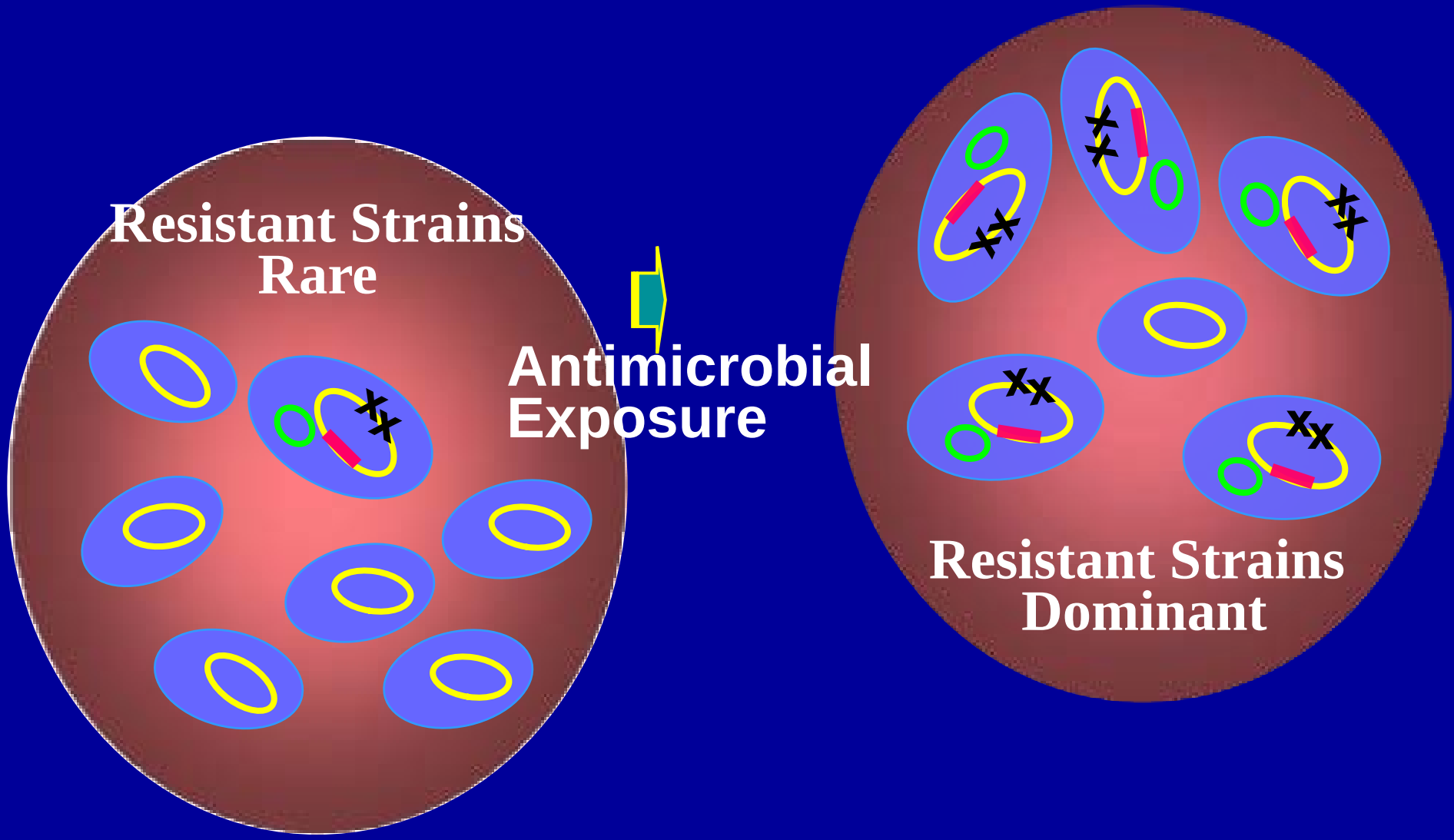
a: Jacoby et al. *N Engl J Med*. 2005;352:380-391. b: Villar et al. *JAC*. 1997;40:365-70.c: Rice et al. In *Man Clin Micro.* 2007, Chap 71. d: Moore et al.*AAC*. 1984;26:539-545. e: Li et al. IJAA. 2005;5:11-25.f: Piddock. *Clin Micro Rev*. 2006;19:382-402.

Emergence of Antimicrobial Resistance



CDC Web Site

Selection for Antimicrobial-Resistant Strains



ESKAPE or "ESCAPE" Organisms

Proposed revisions capture more pathogens

E - *Enterococcus faecium*

S - *Staphylococcus aureus*

C - *Clostridium difficile*

A - *Acinetobacter baumannii*

P - *Pseudomonas aeruginosa*

E - *Enterobacteriaciae* …..Kleb in the enteric group

Peterson LR. Clin Infect Dis 2009;49:992

Development and Spread of Antimicrobial Resistance

Resistance may develop and spread due to :

- **Organisms surviving in GI tract and plasmid transfer, etc.**
- **Poor infection control practices**

Normark J Inteern Med 2002;252:91-106

Factors in the Emergence of Antimicrobial Resistance

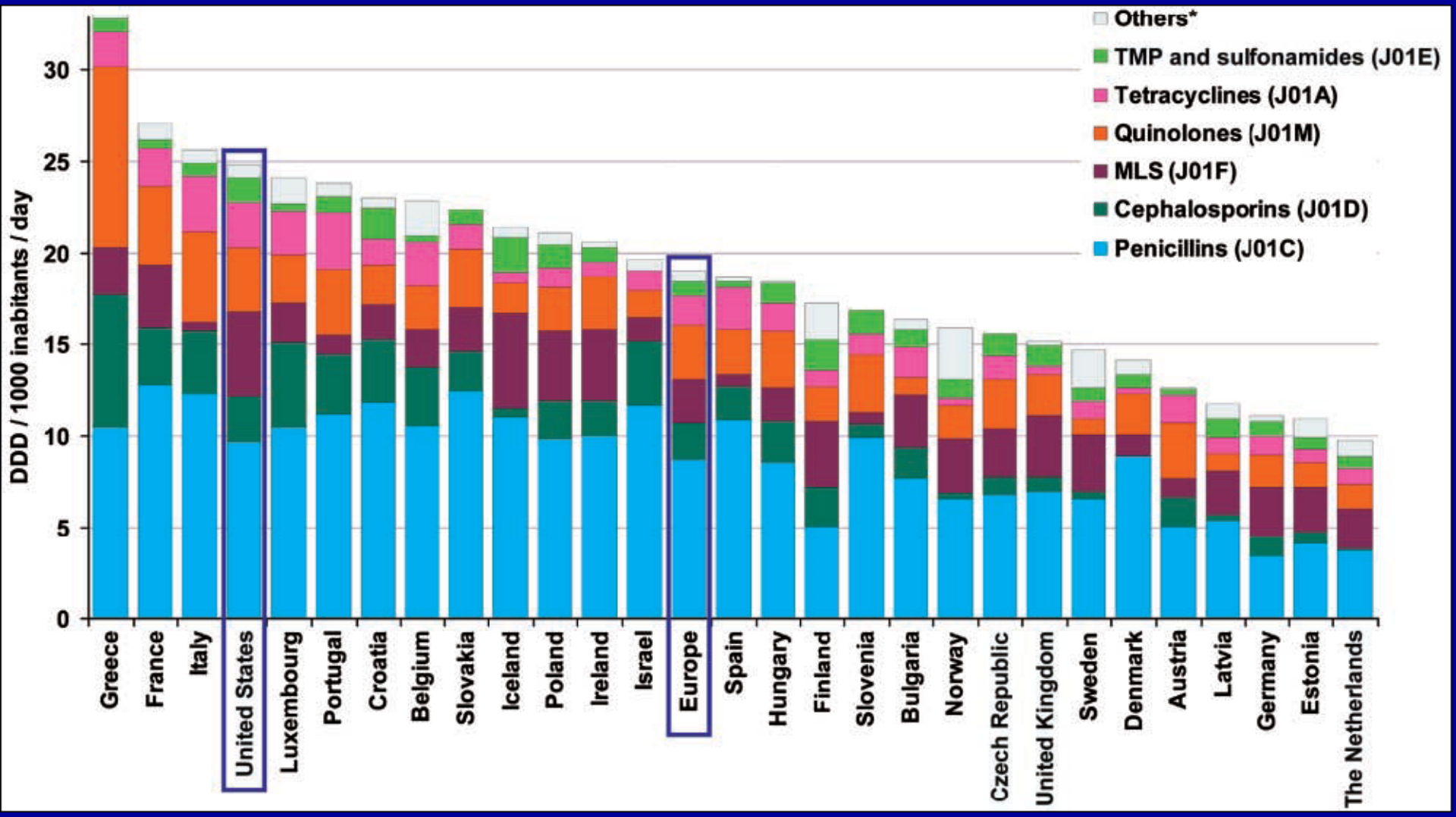
Zinner et al, Clin Infect Dis, 33:S3, 2001

Genetic determinants of resistance

- ease of occurrence (mutation rate)
- spread between organisms
- stability

- **Biology of the organism**
  - disease associations
  - asymptomatic carriage
  - transmissibility of organism

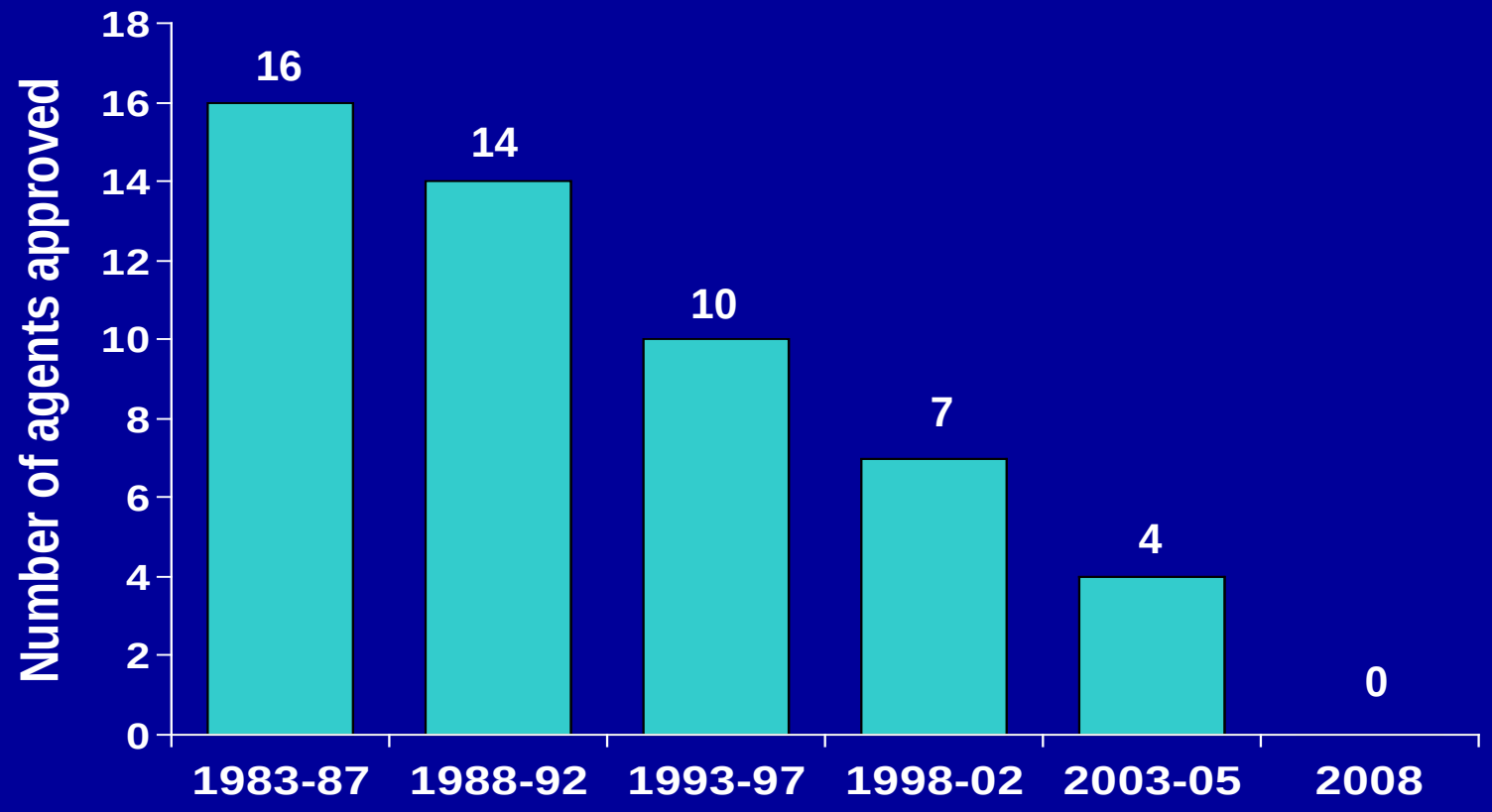
- **Selective pressure of antibiotic usage**
  - Inappropriate dosing (e.g. fluoroquinolones)
  - Pk/Pd at various sites (e.g. sweat, saliva, mucus membranes)


Others*
TMP and sulfonamides (J01E)
Tetracyclines (J01A)
Quinolones (J01M)
MLS (J01F)
Cephalosporins (J01D)
Penicillins (J01C)
DDD / 1000 inabitants / day
0
5
10
15
20
25
30
Greece
France
Italy
United States
Luxembourg
Portugal
Croatia
Belgium
Slovakia
Iceland
Poland
Ireland
Israel
Europe
Spain
Hungary
Finland
Slovenia
Bulgaria
Norway
Czech Republic
United Kingdom
Sweden
Denmark
Austria
Latvia
Germany
Estonia
The Netherlands

Epidemiologic Distribution of Resistant Organism Groups

- Community-Associated
  - Individual cases (no previous association with health care)
  - Day-care centers (may have higher resistance risks)
  - Home-care (no previous association with health care)
- Health-Care Associated
  - Hospitals (wards, units)
  - Extended-care facilities (e.g. nursing home; chronic care facilities)
  - Dialysis centers
- Travel-associated (secondarily spread)

A Changing Landscape for Numbers of Approved Antibacterial Agents



Bars represent number of new antimicrobial agents approved by the FDA during the period listed.

Infectious Diseases Society of America. *Bad Bugs, No Drugs*. July 2004.
Spellberg B et al. *Clin Infect Dis*. 2004;38:1279-1286.
New antimicrobial agents. *Antimicrob Agents Chemother*. 2006;50:1912

Hospital and Societal Costs of Antimicrobial-Resistant Infections (ARI)

Attributable Medical costs … $18,588 - $29,069/pt

Excess LO …….. 6.4 - 12.7 days

Attributable mortality …… 6.5%

Societal cost …….. $10.7 – 15.0 million

Roberts, RR et. al. Clin Infect Dis 2009;49:1175

Cost of HAI vs Benefits of Infection Prevention to US Hospitals

Direct Medical Cost

Urban consumers:	$28.4 - $33.8 billion
Inpatient hospital services	$35.7 - $45 billion

Benefits of IP (with effectiveness adjustments)

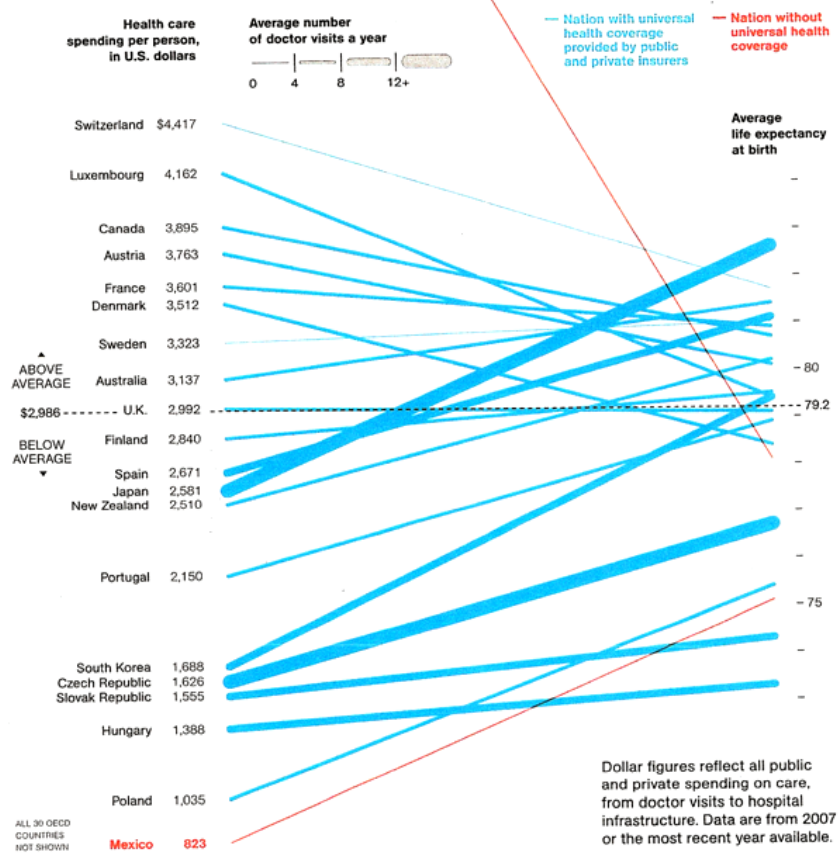
low (20% preventable)	$5.7 - $6.8 billion
high (70% preventable)	$25.0 - $31.5 billion

CDC Website, 2011

United States $7,290

HEALTH

The Cost of Care The United States spends more on medical care per person than any country, yet life expectancy is shorter than in most other developed nations and many developing ones. Lack of health insurance is a factor in life span and contributes to an estimated 45,000 deaths a year. Why the high cost? The U.S. has a fee-for-service system—paying medical providers piecemeal for appointments, surgery, and the like. That can lead to unneeded treatment that doesn't reliably improve a patient's health. Says Gerard Anderson, a professor at Johns Hopkins Bloomberg School of Public Health who studies health insurance worldwide, "More care does not necessarily mean better care." *—Michelle Andrews*



Dollar figures reflect all public and private spending on care, from doctor visits to hospital infrastructure. Data are from 2007 or the most recent year available.

GRAPHIC: OLIVER UBERTI, NG STAFF. SOURCE: "OECD HEALTH DATA 2009," ORGANISATION FOR ECONOMIC CO-OPERATION AND DEVELOPMENT

Healthcare Reform and CMS Oversight of HAI

- Cost expectations - how much and where to focus; how much can we afford and willing to spend?
- Clinical value – is there real value in what we do?
- Best practices - what are the best and are they supported by strong evidence based medical studies?
- Outcome studies - do practices meet expectations and provide clinical value?
- HAI burden, public and governmental scrutiny and focus on healthcare (State and Federal oversight and rule making)?

Need for Judicious Use of Antimicrobial Agents

- Antimicrobials misused every day (50% misuse in both in and outpatients; CDC)
- Misuse adversely affects patients and society
  - Used when not needed
  - Continued when no longer needed
  - Wrong dosage
  - Unnecessary broad spectrum
  - Wrong bug/drug combination
- Judicious use of antimicrobics improves patient outcomes and financial burden
- Improved use of antimicrobics is a Public Health imperative (AZ State has set up an HAI Committee with meetings open to the public)

(CDC Website, 2011)

CDC Program
Goals- Get Smart for Healthcare

- **Improve patient safety through better treatment of infections.**

- **Reduce the emergence of anti-microbial resistant pathogens and *Clostridium difficile*.**

- **Heighten awareness of the challenges posed by antimicrobial resistance in healthcare and encourage better use of antimicrobials as one solution.**

Support of Antimicrobial Stewardship

- ID Physician director, co-director or champion and ID-trained Pharmacist
  - Review susceptibilities
  - Look at Pk/Pd and optimize dosing
  - Recommend/educate as to 1st, 2nd, 3rd optimal empiric therapies for organism prevalent to institution and or location
- Clinical Microbiology
  - Timely pathogen ID and AST
  - AST reporting - CLSI/FDA standards, selective (cascading) reporting
  - Evaluation and interpretation of susceptibilities

Microbiology Laboratory Support

- The clinical microbiology service is an essential and integral part of organizational initiatives that underpin antimicrobial stewardship efforts.

- The establishment of best practice procedures for rapid microbiological evaluation is critical to delivering timely and accurate information.

- Intensive care units are an area of particular importance, as the control of resistance in these units can affect other areas of the hospital. The clinical microbiology service should therefore pay particular attention to services provided to these areas.

Microbiology Laboratory Support

- Can interpret isolate significance, provide antimicrobial susceptibility interpretation and provide antimicrobial management advice.

- Critical role to play in improving overall antimicrobial use through providing information, establishing guidelines and educating other hospital staff. One key strategy is the production of annual cumulative antibiograms to indicate susceptibility patterns for key pathogens.

- Provides surveillance data on resistant organisms for infection control purposes.

How is Resistance Defined?

- MIC determinations represent the most refined means of measuring in vitro antibacterial activity (reproducible ↑↑)
- CLSI establishes MIC breakpoints

→ MIC breakpoints (interpretive criteria)

- Susceptible (S)
- Intermediate (I)
- Resistant (R)

New CLSI 2010
Cephalosporin Interpretations for Enterics

- New breakpoints based on knowledge of:
  - PK/PD determinants of efficacy
  - Supplemental animal studies
  - MICs predict clinical outcomes better than resistance mechanisms

Steve Jenkins, Pro Statement on CLSI Ceph Interpretational Guidelines, ASM Web site, 2010

2011 - 6 month blood isolates only – 9 Banner hospitals combined

Organism (#)	AMP	AMOX/ CLAV	CEFAZOLIN	CEFTRIAX	CEFEPIME	GENT	TOBRA	AMIK
E.coli (533)	46	76	85	95	95	94	91	100
Klebsiella pneumoniae (145)	0	88	88	91	91	95	91	98
Enterobacter cloacae (58)	0	0	0	78	100	100	100	100
Ps. aeruginosa (87)	-	-	-	-	81	76	93	98
Proteus mirabilis (47)	60	70	72	98	98	94	94	100
Organism	CIPRO	LEVO	TRIM-SULFA	PIP/TAZO	IMIPENEM			
E. coli	78	78	66	NA	100			
K. pneumoniae	88	88	87	90	97			
E. cloacae	98	98	93	76	100			
P. aeruginosa	76	-	-	85	82			
Proteus mirabilis	57	57	51	NA	NA			

Combined Banner EDs Phoenix Area - 2011 Jan-June: all specimens

Organism (#)	AMP	AMOX/ CLAV	CEFAZOLIN	CEFTRIAX	CEFEPIME	GENT	TOBRA	AMIK
E.coli (4759)	50	79	86	96	97	92	91	100
Klebsiella pneumoniae (923)	0	95	95	97	97	98	97	99
Ps. aeruginosa (417)	-	-	-	-	86	75	91	94
Proteus mirabilis (329)	58	65	68	95	95	88	87	100
Enterobacter cloacae (120)	0	0	0	79	98	98	98	100
Organism	CIPRO	LEVO	TRIM-SULFA	PIP/TAZO	IMIPENEM	NITRO#		
E. coli	79	79	71	-	100	95		
Klebsiella pneumoniae	95	95	91	95	98	38		
P.aeruginosa	70	-	-	89	88	-		
P. mirabilis	55	55	57	95	-	0		
E. cloacae	92	92	89	82	99	27		

2010 Non–urine isolates Banner combined hospitals

Organism (#)	AMP	AMOX/ CLAV	CEFAZOLIN	CEFTRIAX	CEFEPIME	GENT	TOBRA	AMIK
E.coli (782)	46	76	84	95	96	92	90	100
Klebsiella pneumoniae (206)	0	90	90	94	94	97	93	97
Enterobacter cloacae (88)	0	0	0	92	100	100	98	100
Ps. aeruginosa (295)	-	-	-	-	85	80	93	93
Proteus mirabilis (113)	66	69	72	91	91	84	84	100
Organism	CIPRO	LEVO	TRIM-SULFA	PIP/TAZO	IMIPENEM			
E. coli	77	77	69	91	100			
K.pneumoniae	93	93	85	88	97			
E.cloacae	97	97	93	90	100			
P.aeruginosa	76	-	-	89	91			
Proteus mirabilis	64	64	66	92	84			

Banner Health System Emergency Departments 2001 to 2006 MRSA Trending

	2001	2002	2003	2004	2005	2006
Total Number of Wound Cultures Collected	334	434	490	865	2302	3062
Number of Cultures with MRSA	18	56	48	250	1093	1441
Percentage of Cultures with MRSA	5.4%	12.9%	20.0%	28.9%	47.5%	46.8%

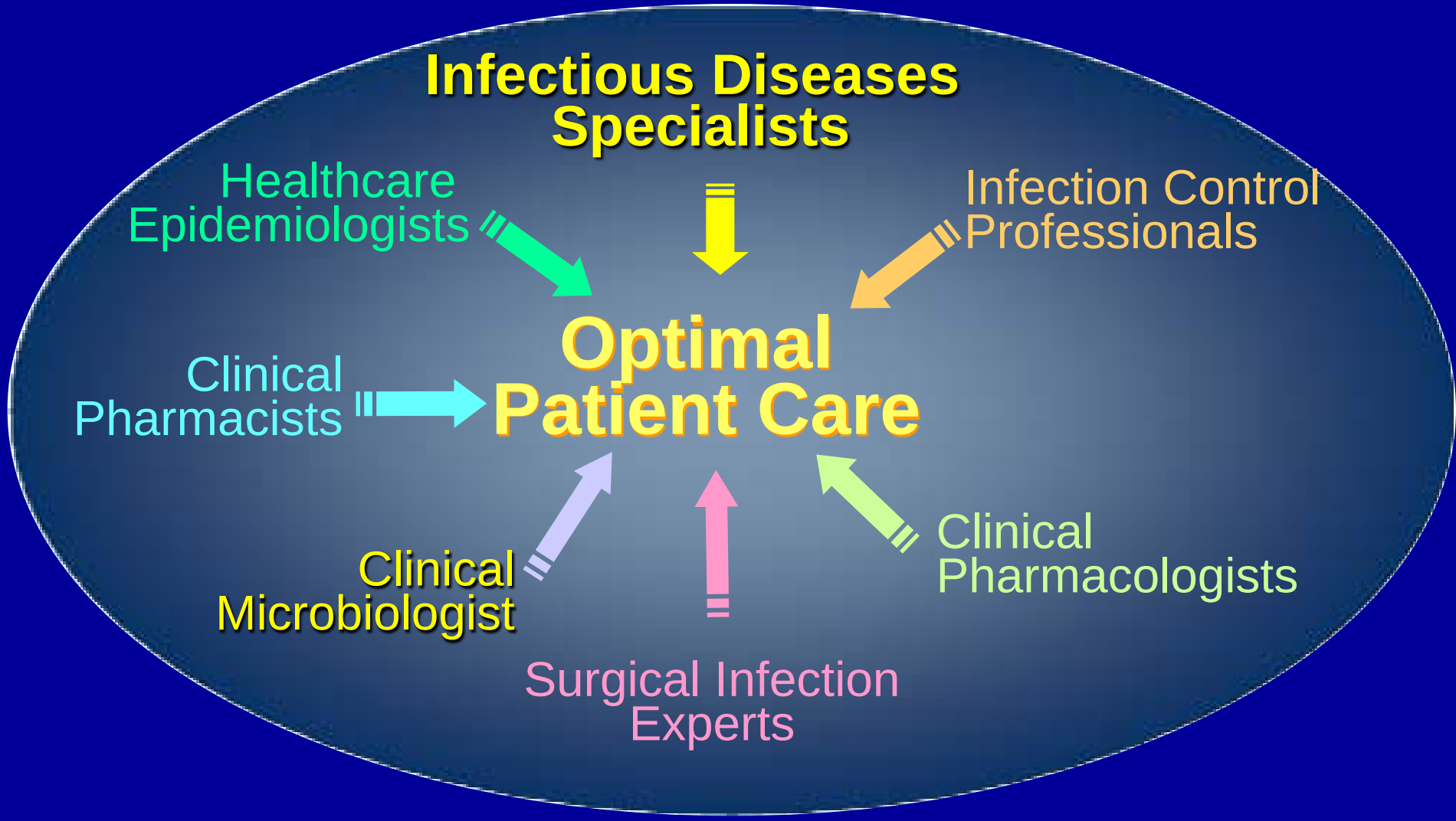
	2001	2002	2003	2004	2005	2006
Number of Hospitals included*	3	3	3	3	5	5

Streptococcus pneumoniae at Banner Health Phoenix Area Nov 2010-May 2011

Number of Isolates	Percent Penicillin* S Mening	Non-mening	Erythro Percent Susceptible	Clinda Percent Suscept	Levoflox Percent Susceptible	Ceftriaxone Percent Susceptible Mening	Non-mening
Blood and CSF							
160	77%	94%	74%	88%	100%	91%	97%
Respiratory							
131	56%	99%	63%	77%	97%	84%	99%

Combined Susceptible Antibiogram for Chronic/Long Term Care Facilities (Phoenix Metropolitan Area, 10/1/2009-4/1/2010)

Organism (#)	AMP	AMOX/ CLAV	CEFAZ	CEFTRI	CEFEP	GENT	TOBRA	AMIK
A. baumannii (78-119)	**0**	**1**	**0**	**0**	**1**	**24**	**30**	**47**
Klebsiella pneumoniae (95-96)	**0**	**54**	**51**	**63**	**63**	**79**	**52**	**80**
Ps. aeruginosa (385)	-	-	-	-	54	55	80	95
Proteus mirabilis (76 - 158)	**10**	**67**	**26**	**46**	**46**	**81**	**56**	**61**

Organism	CIPRO	LEVO	TRIM-SULFA	PIP/TAZ	IMIPEN
A. baumannii	**1**	**1**	**39**	**2**	**12**
K. pneumoniae	**59**	**59**	**45**	**65**	**85**
P. aeruginosa	**38**	**33**	na	70	54
P. mirabilis	**8**	**11**	**13**	**94**	na

Infectious Diseases Expert Resources