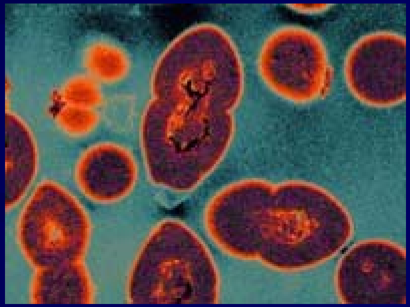
Antibiotic use in food animals

what effects for people?

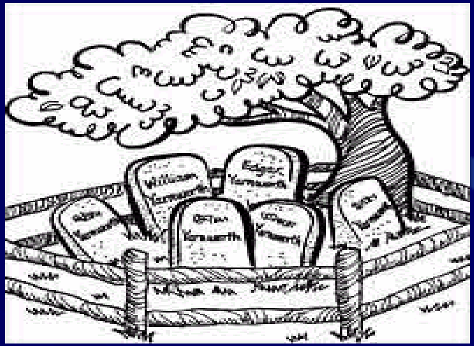
Peter Collignon
Director, Infectious Diseases and Microbiology,
The Canberra Hospital.
Professor, Canberra Clinical School,
Australian National University

Resistance is a growing problem

- Most bacteria
  - Staphylococcus
  - Pneumococcus
  - Enterococcus (VRE)



- Some no therapy, for most therapy difficult and expensive
  - Staph aureus and Enterococcus
  - Pseudomonas, Acinetobacter
  - Salmonella
  - E.coli



- Most of resistance problem is from human medical activity but some from animals – usually via food

Resistance;
the bugs are smart

- breakdown or inactivate the antibiotic
- barriers; stop it getting into the bacteria
- **bacteria change the goal posts**
  - altered targets, receptors

Antibiotic resistant bacteria do NOT stay quarantined to one area.

Nor do the genes that encode this resistance.

Antibiotic resistance is worse in developing countries; China

- MRSA
  - 82% if hospital acquired *S.aureus*
  - 22% if community acquired
- E.coli (community)
  - 60% resistant to fluoroquinolones
  - 56% gentamicin resistant
  - 29% ceftriaxone resistant

Li, Weinstein et al. Beijing 1998-1999 Zhonghua Yi Xue Za Zhi; 2001; Li, Yu et al. Infection. 2001

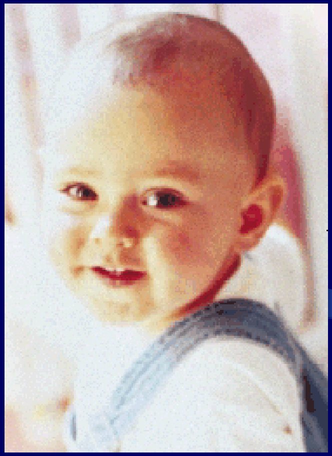
Resistance is proportional to use

- When you use it, you loose it!

- The more you use then the more resistance
  - cross resistance an issue
  - low dose and topical lead to more resistance
  - Volumes are most important

- Need to maintain "last line" or "critically important" antibiotics

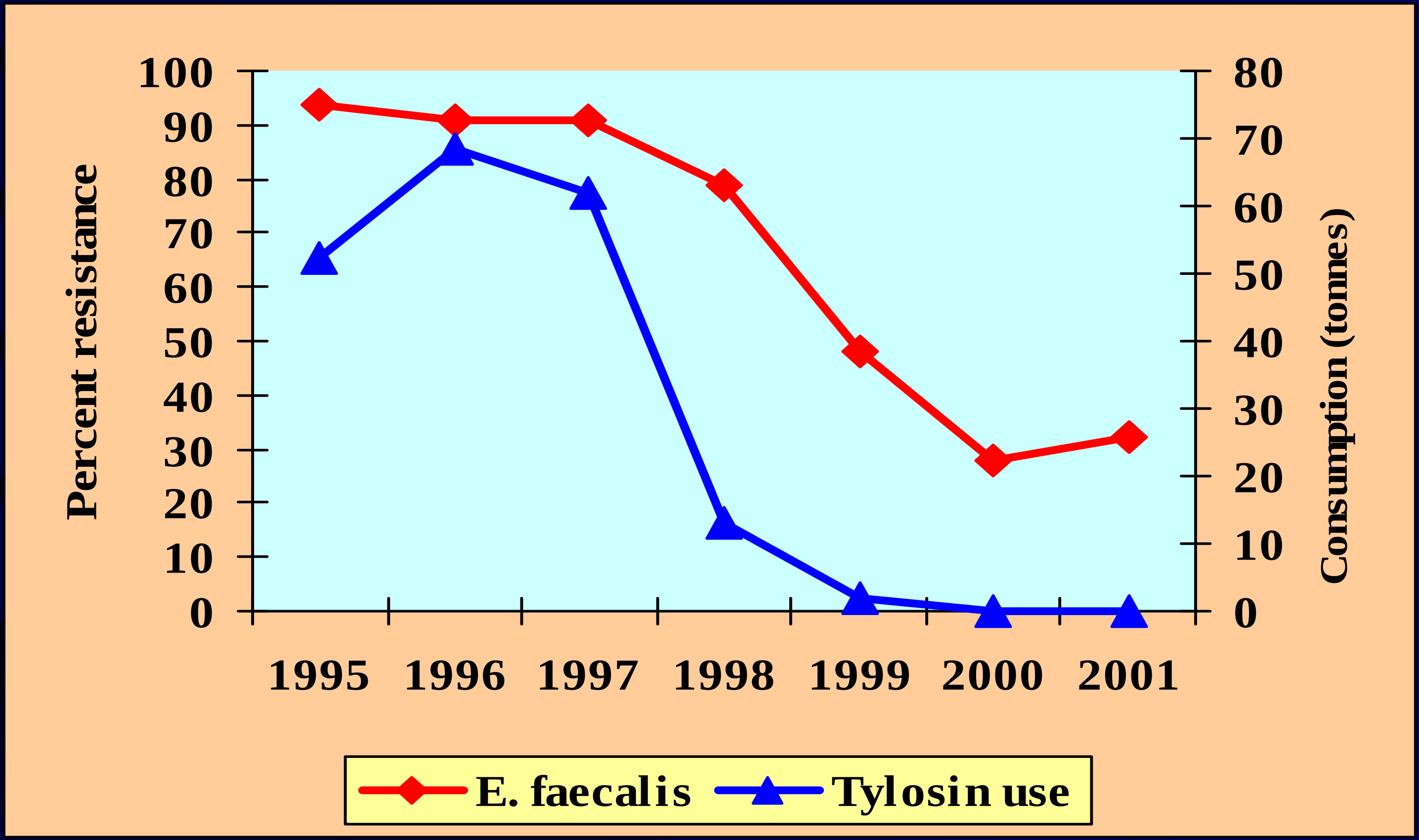
Pneumococcal resistance in Children



- Canberra prospective study
  - 461 children followed for over 2 years
- More antibiotics, the more resistance
  - overall 13.6% pen resistant
  - If betalactam OR 2.03
  - if both pen and ceph OR 4.67
  - but dropped with time (6 months OR 1 again)
- 4% increased risk of carriage for each day of betalactam therapy

Nasrin D, Collignon PJ, Roberts L et al. BMJ 2002:324:28-30

Trends in tylosin use for growth promotion and erythromycin resistance (pigs)



Enterococcus faecalis isolated from pigs at slaughter from 1995 to 2001

(WHO 2003; Aarestrup et al 2001).

Antibiotic Resistance in the Wild
kangaroos vs people

• ampicillin	2.9%	vs	46%
• tetracycline	0.2%		28%
• chloramphenicol	0.4%		14%
• trimethoprim	0.2%		15%

- in Australia in people low levels of resistance to "critically important" antibiotics
  - cefotaxime, meropenem, naladixic acid, ciproxin, gentamicin (many antibiotics have restricted use)

Sherley M, Gordon DM, Collignon PJ. Variations in antibiotic resistance profile in Enterobacteriaceae isolated from wild Australian mammals.Environ Microbiol. 2000 Dec;2(6):620-31.

Why an interest in agriculture?

- Huge volumes used for growth promotion
  - two thirds of all antibiotics used in world are used in agriculture – most still growth promotion
- Genetic engineering
  - which maintains antibiotic resistance genes in plants in wide scale production
- “Critical” antibiotics for people used
  - ceftiofur (3rd and 4th generation cephalosporin)
  - avoparcin (vancomycin)
  - enrofloxacin (ciprofloxacin)

Use of antibiotics in animals

- therapeutic
  - sick animals
- prophylaxis
  - prevent infection
  - metaphylaxis
- growth promotion
  - weight gain
  - feed efficiency

Huge volumes of antimicrobials used

– more in animals than people

- likely two thirds of total world use of Antibiotics

- In Australia (20 million people)
  - Animals >500,000 kg
  - People 300,000 kg
  - Ratio 1.6

- In Denmark 2006 (5 million)
  - Animals 116,500 kg
  - People 47,500kg
  - Ratio 2.4

Huge volumes still used for “growth promotion”

- In Australia (and elsewhere)
  - Almost half animal usage 233,000 kg
- This remains their “official” registration
  - despite pleas by industry that being really used for other purposes
- Disease prevention
  - Metaphalaxis
- Don’t work or only marginal efficacy
  - Only major benefit is 1% less feed intake
  - About the same cost at the drug

High FQ resistance in China 2004

JOURNAL OF CLINICAL MICROBIOLOGY, Aug. 2004, p. 3483–3489 Vol. 42, No. 8
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.8.3483–3489.2004

Characterization of Multiple-Antimicrobial-Resistant *Escherichia coli* Isolates from Diseased Chickens and Swine in China

Hanchun Yang,[1,2] Sheng Chen,[2] David G. White,[3] Shaohua Zhao,[3] Patrick McDermott,[3] Robert Walker,[3] and Jianghong Meng[2*]

China Agricultural University, Beijing, China,[1] and Department of Nutrition and Food Science, University of Maryland, College Park,[2] and Division of Animal and Food Microbiology, Office of Research, Center for Veterinary Medicine, U.S. Food and Drug Administration, Laurel,[3] Maryland

Antimicrobial resistance. Most *E. coli* isolates recovered from diseased chickens and swine were resistant to multiple classes of antimicrobials (Table 1). The majority of isolates were resistant to tetracycline (98%), sulfamethoxazole (84%), ampicillin (79%), streptomycin (77%), and trimethoprim-sulfamethoxazole (76%). Resistance to chloramphenicol among the swine isolates (63%) was significantly higher ($P < 0.05$) than resistance among chicken isolates (24%). Surprisingly, all *E. coli* isolates, regardless of their animal origin, were resistant to the quinolone antimicrobial nalidixic acid. Due to the high

China Poultry Resistance (2005)

Table 1. Antimicrobial resistance phenotypes of chicken *E. coli* isolates

Class and/or antimicrobial	% Resistant strains (n = 70)
Phenicols	
Chloramphenicol	79
Florfenicol	29
Beta-lactams	
Ampicillin	83
Ceftiofur	7
Oxytetracycline	100
Aminoglycosides	
Gentamicin	44
dihydrostreptomycin	42
Amikacin	12
Potentiated sulfonamides	
Trimethoprim-sulfamethoxazole	100
Fluoroquinolones	
Enrofloxacin	83
Ciprofloxacin	81

J. Vet. Sci. (2007), **8**(3), 243–247

JOURNAL OF Veterinary Science

Antimicrobial susceptibility and molecular detection of chloramphenicol and florfenicol resistance among *Escherichia coli* isolates from diseased chickens

Xin-Sheng Li[1,†], Gui-Qin Wang[2,†], Xiang-Dang Du[1,*], Bao-An Cui[1], Su-Mei Zhang[1], Jian-Zhong Shen[2]

[1]*College of Animal Husbandry and Veterinary Science, Henan Agricultural University, Zhengzhou 450002, P.R. China*
[2]*Department of Pharmacology and Toxicology, College of Veterinary Medicine, China Agricultural University, Beijing 100094, P.R. China*

Swann Principles (UK 1969)

Only use growth promoters if

- Little or no application as therapeutic agents in humans or animals

- will not impair the efficiency of prescribed therapeutic antibiotics through the development of resistant strains

- have economic value in livestock production under farming conditions

Antibiotic Resistance

in Bacteria Isolated From Poultry

A report for the Rural Industries Research and Development Corporation

by Mary D Barton and Jodi Wilkins

2001

Table 11: Distribution of antibiotic resistance in *E coli*

E coli Antibiotic Sensitivity Results							
		Lab A Samples			Lab B Samples		
Antibiotic	**Conc**	**Total**	**No. Resistant**	**%**	**Total**	**No. Resistant**	**%**
	ug/ml	**Organisms**	***E coli***	**Resistant**	**Organisms**	***E coli***	**Resistant**
Ampicillin	8	182	96	**52.7**	47	36	**76.6**
Ampicillin	32	182	69	**37.9**	47	20	**42.6**
Augmentin	8	182	6	**3.3**	47	0	**0**
Augmentin	32	182	0	**0**	47	0	**0**
Cepthalothin	8	182	35	**19.2**	47	3	**6.4**
Cephalothin	32	182	9	**4.9**	47	0	**0**
Ciprofloxacin	1	182	0	**0**	47	0	**0**
Ciprofloxacin	4	182	0	**0**	47	0	**0**
Flavophospholipol	64	182	161	**88.5**	47	44	**93.6**
Gentamicin	4	182	3	**1.6**	47	1	**2.1**
Gentamicin	16	182	0	**0**	47	1	**21**
Lasalocid	4	182	182	**100**	47	47	**100**
Neomycin	6	182	13	**7.1**	47	3	**6.4**
Neomycin	25	182	12	**6.6**	47	1	**2.1**
Spectinomycin	16	182	22	**12.1**	47	13	**27.7**
Spectinomycin	64	182	16	**8.8**	47	11	**23.4**
Streptomycin	4	182	87	**47.8**	47	22	**46.8**
Streptomycin	16	182	61	**33.5**	47	16	**34**
Tetracycline	4	182	158	**86.8**	47	39	**83**
Tetracycline	16	182	107	**58.8**	47	25	**53.2**
Trimethoprim	8	182	84	**46.2**	47	17	**36.2**
Trimethoprim	16	182	84	**46.2**	47	17	**36.2**

Australian poultry

Enterococcus 2001 Barton and Wilkins

Table 17: Sources of *Enterococcus* spp isolates of major interest

	Lab A	%	Lab B	%
Samples tested	1168		118	
Total enterococci isolated	200	17.1	70	59
Vancomycin sensitive enterococci	95	8.1	66	55.9
Total VRE isolated	105	9	4	3.4
E faecium	102	8.7	17	14.4
E faecalis	9	0.8	39	33.1

There was a higher isolation rate of enterococci generally from the Laboratory B samples which may reflect some multiplication in transit to Adelaide. Most of the isolates were vancomycin sensitive, with only 3.4% vancomycin resistant. More than twice as many *E faecalis* as *E faecium* were present in the Laboratory B samples.

Almost equal proportions of vancomycin sensitive and vancomycin resistant enterococci were isolated from the Laboratory A samples. In contrast to the Laboratory B samples, *E faecium* was much more common than *E faecalis*: the isolation rate of *E faecium* to *E faecalis* was 11:1.

Australian poultry - Campylobacter

2001 Barton and Wilkins

Table 25: Antimicrobial resistance patterns in *Campylobacter* spp

Campylobacter Antibiotic Sensitivity Results									
		Lab A Samples				Plant C Samples			
Antibiotic	Conc	No. Resist	% Resist	No. Resist	% Resist	No. Resist	% Resist	No. Resist	% Resist
		C.jejuni	*C. jejuni*	*C. coli*	*C. coli*	*C.jejuni*	*C.jejuni*	*C. coli*	*C. coli*
		Total No. 18		Total No. 23		Total No. 113		Total No. 49	
Ampicillin	33ug	11	61.1	8	34.8	57	50.4	17	34.7
Erythromycin	78ug	2	11.1	4	17.4	3	2.7	2	4.1
Gentamicin	40ug	0	0	0	0	1	0.9	1	2
Lincomycin	19ug	5	27.8	7	30.4	4	3.5	2	4.1
Neomycin	120ug	0	0	0	0	0	0	1	2
Tetracycline	10ug	4	22.2	7	30.4	17	15	8	16.3
Tylosin	150ug	2	11.1	4	17.4	5	4.4	2	4.1
Ceftazidime	30ug	9	50	16	69.6	11	9.7	2	4.1
Ciprofloxacin	10ug	0	0	0	0	1	0.9	2	4.1
Clindamycin	25ug	1	5.6	1	4.3	1	0.9	1	2

What about Genetic engineering?

- Resistance genes left in plant material
  - Needlessly - e.g. beta-lactamase
- Genes should not transfer to bacteria
  - but UK study worrying
- Low chance of gene transfer to bacteria
  - But what if the animals receiving the “genes” are also on continuous antibiotics!

Plant genes transfer to bacteria (GM food)

- A recent study by the U.K. Food Standards Agency (FSA 2002) tracked what happens in the human gastrointestinal system. Their results were controversial and their conclusions are now hotly contested.

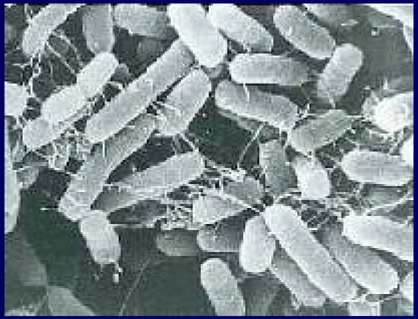
- Seven volunteers all of whom had an ileostomy.
  Fed a single meal consisting of a burger and a milkshake, both of which contained GM soya.
  After the meal the colostomy contents examined and bacteria cultured
  In three of the seven human volunteers a herbicide resistance gene from the GM soya was detected in their intestinal bacteria.

- Therefore Genes DO transfer from plants into bacteria even thought this is NOT supposed to happen

“Critically important” antibiotics for human health - used often and inappropriately

- 3^{rd} and 4^{th} generation cephalosporins
  - ceftiofur
- Glycopeptides
  - avoparcin (vancomycin)
    - VRE and maintain VRE with other ABs
- Fluoroquinolones
  - enrofloxacin (ciprofloxacin)
    resistant salmonella, campylobacter and E.coli
    - Major problem in US and Asia
    - Not Australia because NEVER approved in food animals
- Injected into eggs!
    - ceftiofur, gentamicin

Quinolone and 3rd Generation cephalosporin resistance



- salmonella spp.
  - in industrialized countries most via the food chain from animals
  - USA, UK, Europe, Denmark
- campylobacter spp (ciproxin).
  - in industrialized countries most via the food chain from animals
  - USA, UK, Europe. Denmark
  - other factors (e.g. tourists but…)

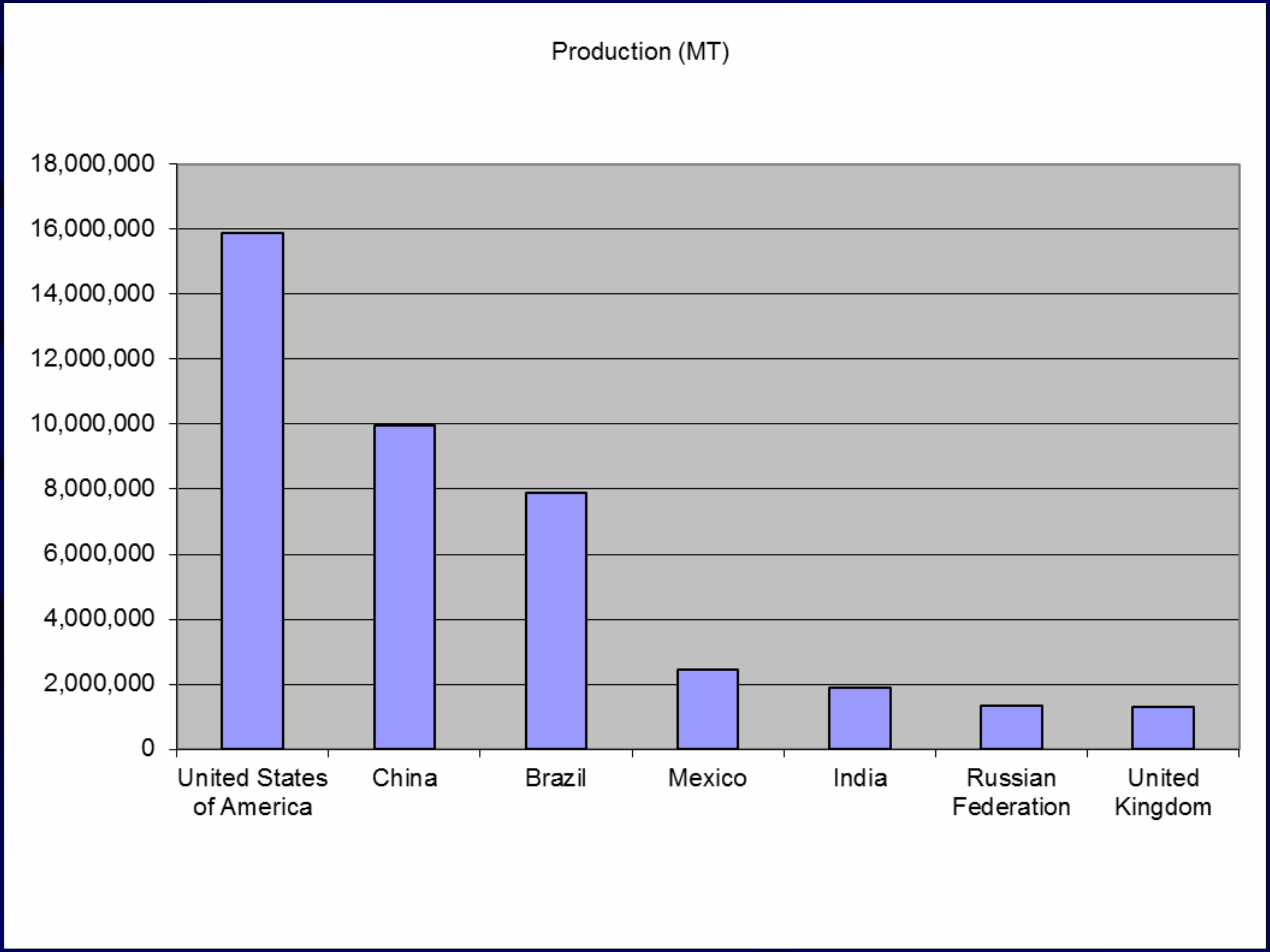
- E.coli
  - how much through food?

Ceftiofur (3rd gen cephalosporin)

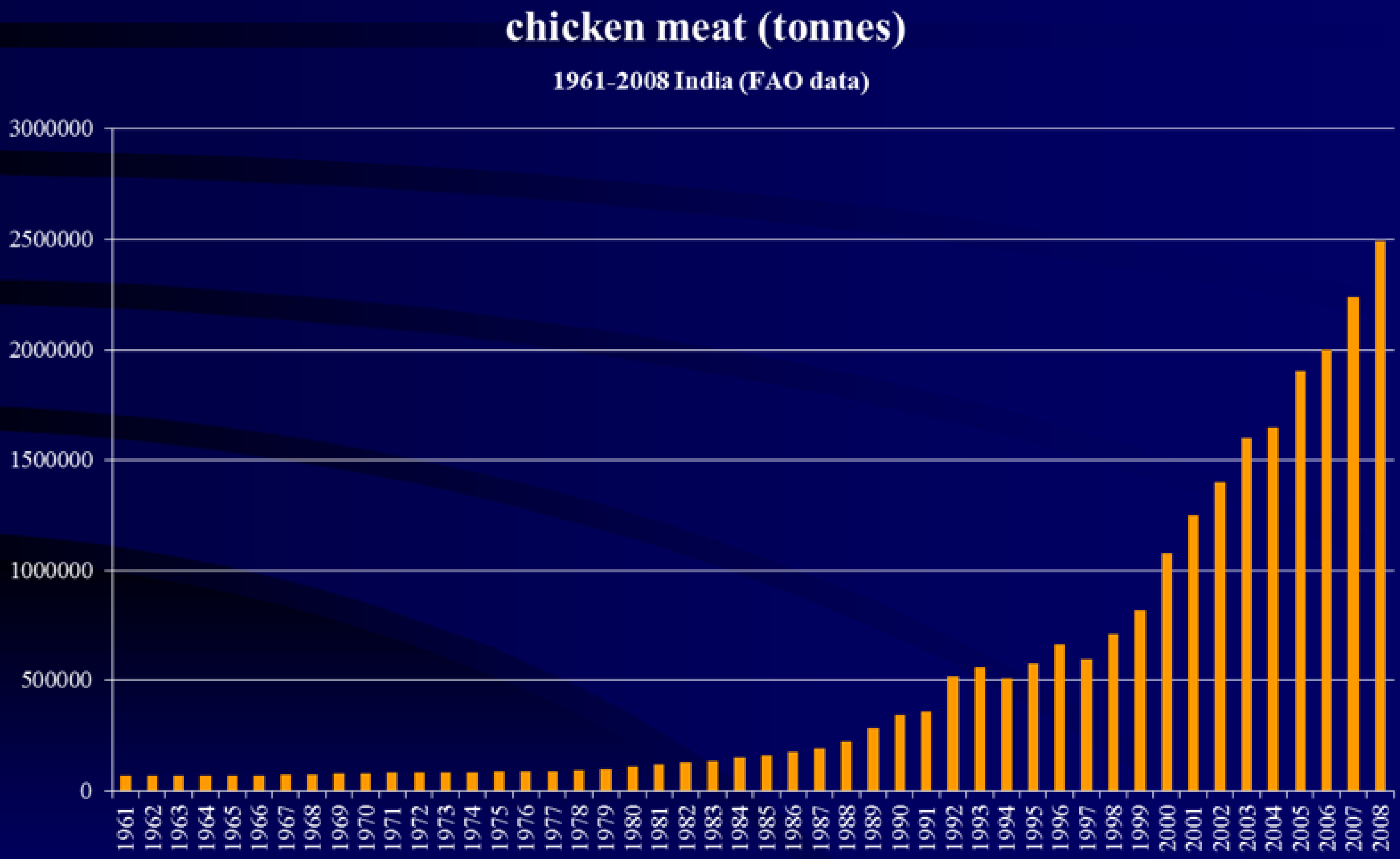
Mass injection of Ceftiofur

Mass exposure of poultry

International poultry production 2007



Poultry production increasing (India)



3rd generation cephalosporin resistance

- Ceftiofur (and others)
- Extended-spectrum beta-lactamase (eg CMY-2) are increasingly isolated from humans, animals, foods, and environmental sources
- The conjugative plasmid containing the cmy-2 gene can be transferred not only from the donor E. coli to Salmonella but also to other E. coli present in the intestinal tract.
- A nationwide surveillance for antimicrobial susceptibility in Escherichia coli strains isolated from food-producing animals in Japan was conducted from 1999 to 2002. CTX-M-type producing, and CMY-2 producing.
- Identification and expression of cephamycinase bla(CMY) genes in Escherichia coli and Salmonella isolates from food animals and ground meat.

Antimicrob Agents Chemother. 2001 Dec;45(12):3647-50.

Appl Environ Microbiol. 2005 Mar;71(3):1184-92.

Antimicrob Agents Chemother. 2005 Aug;49(8):3533-7.

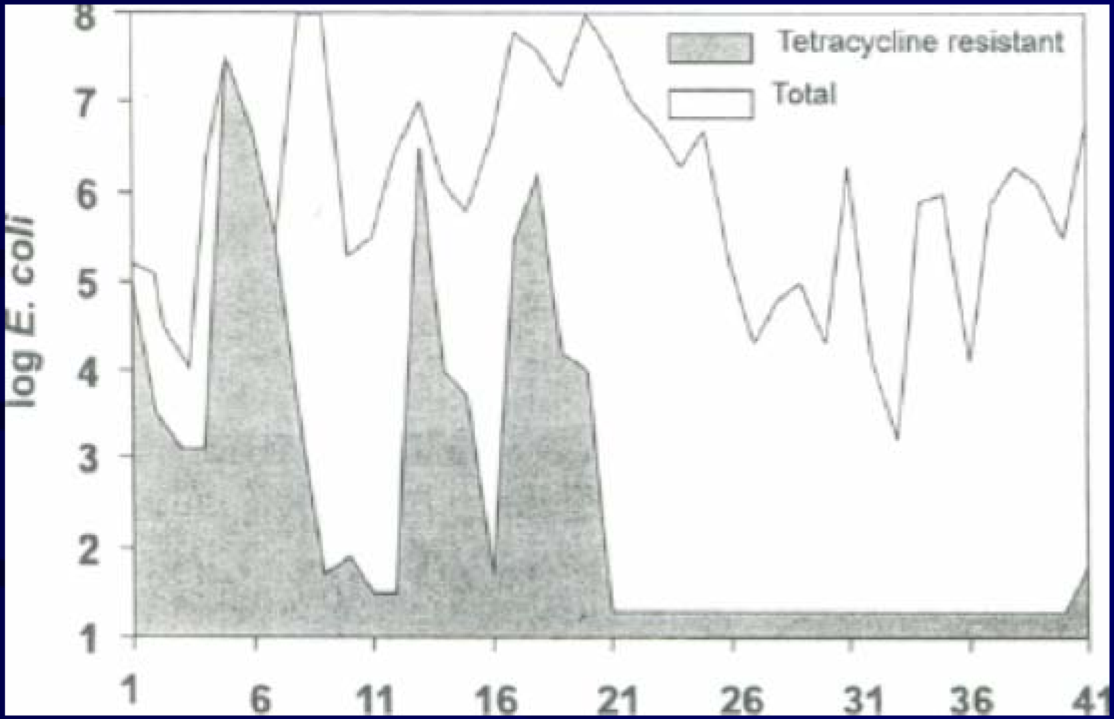
Quinolone resistance

- In Australia fluoroquinolones NOT approved for livestock use
    - <1% resistance in human E.coli (1998, 863 isolates, AGAR). In 2004 still low but 3.4% (596 isolates).
    - nil in food isolates (2007)
    - restricted human use of these antibiotics
- In Spain
    - in children, 22% ciprofloxacin resistant
    - in chickens, 90% resistant
- USA tried to stop use (ended in court!)
    - Bayer fought poultry ban for years

Bacteria of most concern

- Almost all via food
  - Salmonella
  - Campylobacter
- How much via food?
  - E.coli
  - Enterococcus
- New problem
  - ?S.aureus (MRSA)

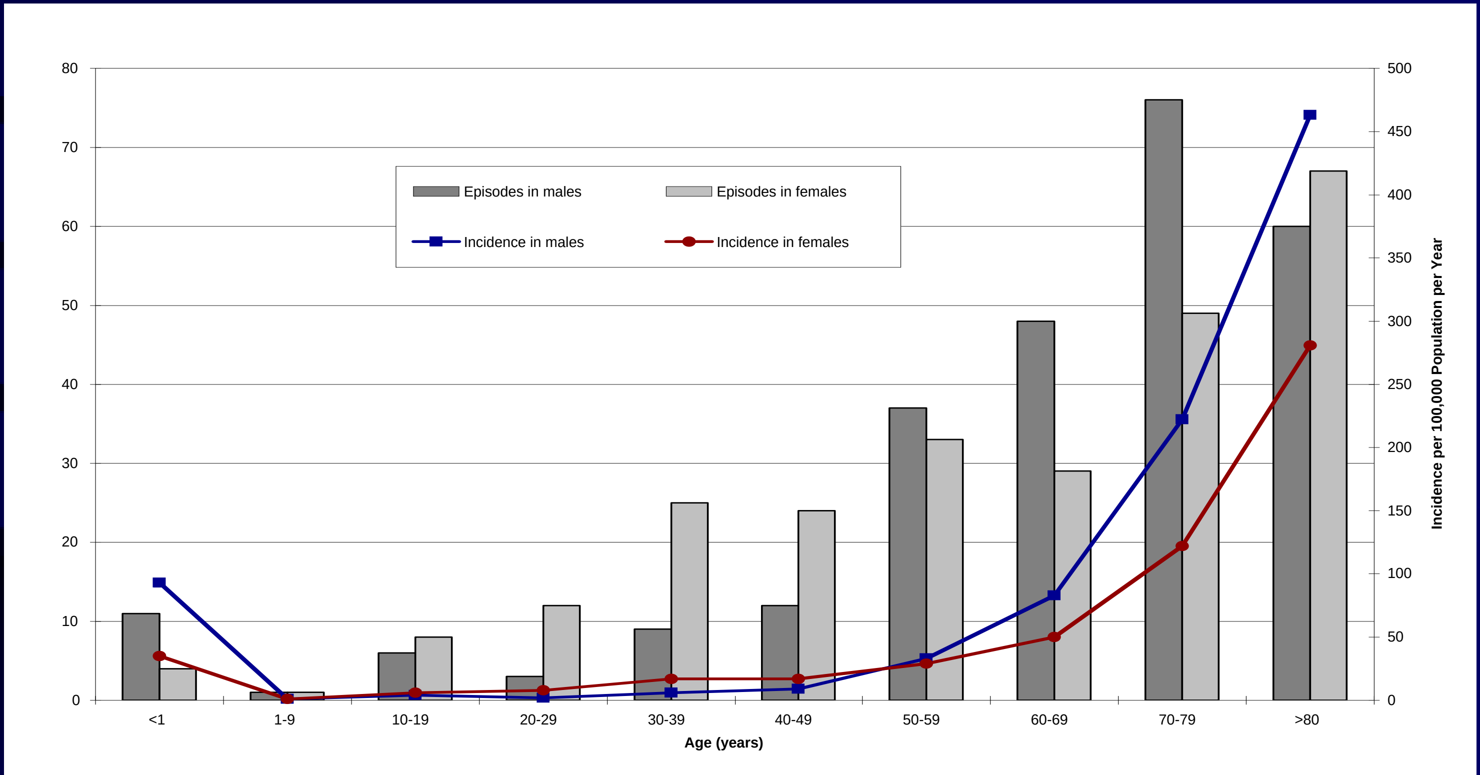
Many resistant bacteria are ingested



- A study of tetracycline-resistant E.coli in which volunteers were given sterile food for 20 days after a control period of 21 days showed that most came from food (Corpet 1988, 1993).

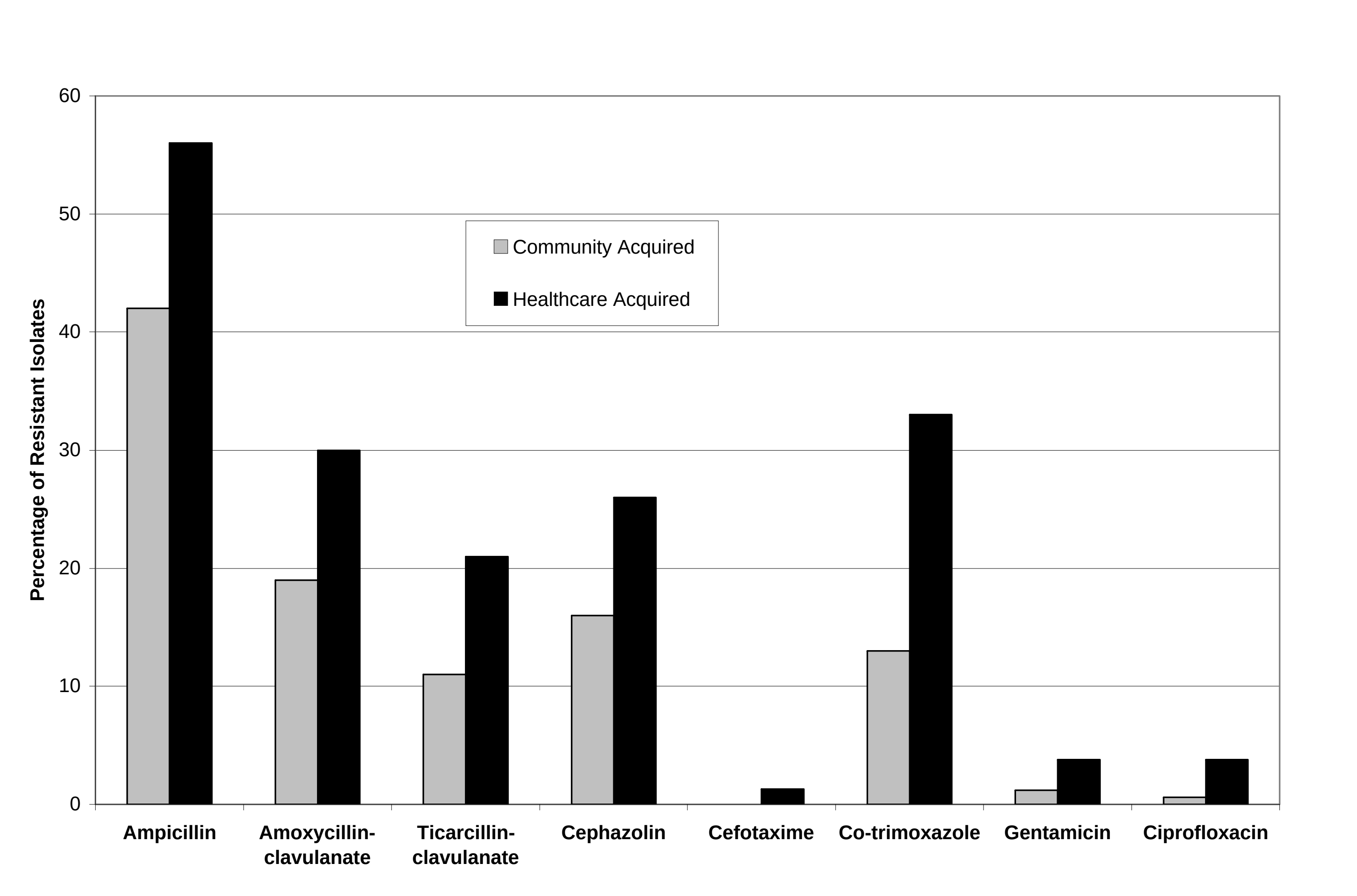
Number of Episodes and Incidence of *E.coli* Bacteraemia in Residents of Canberra, 2000-2004.

(28 per 100,000 per year)

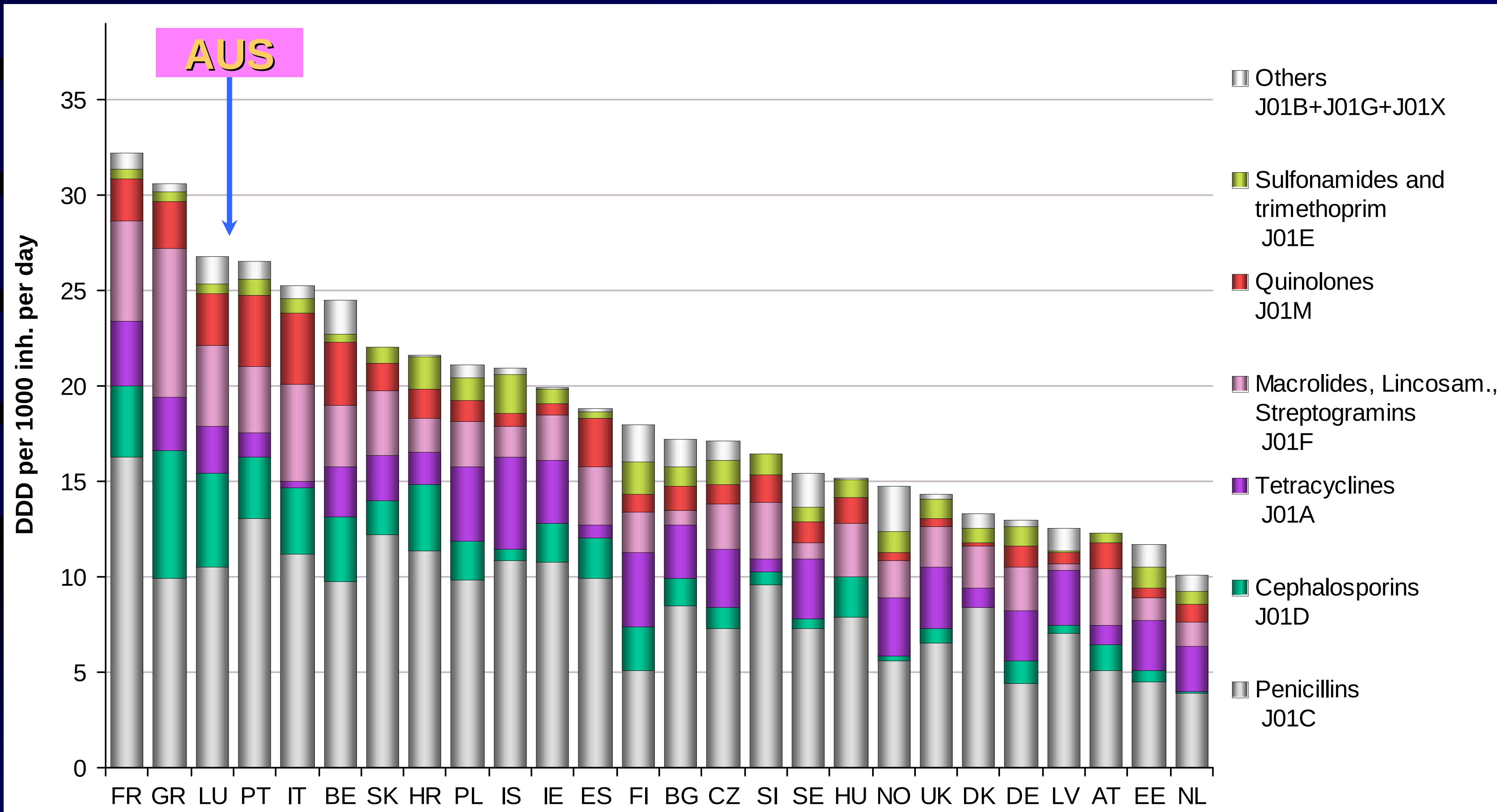


Kennedy KJ, Roberts JL, Collignon PJ. .Escherichia coli bacteraemia in Canberra: incidence and clinical features. .Med J Aust. 2008 Feb 18;188(4):209-13.

Antibiotic Resistance of *E.coli* Bacteremia Isolates (Canberra)

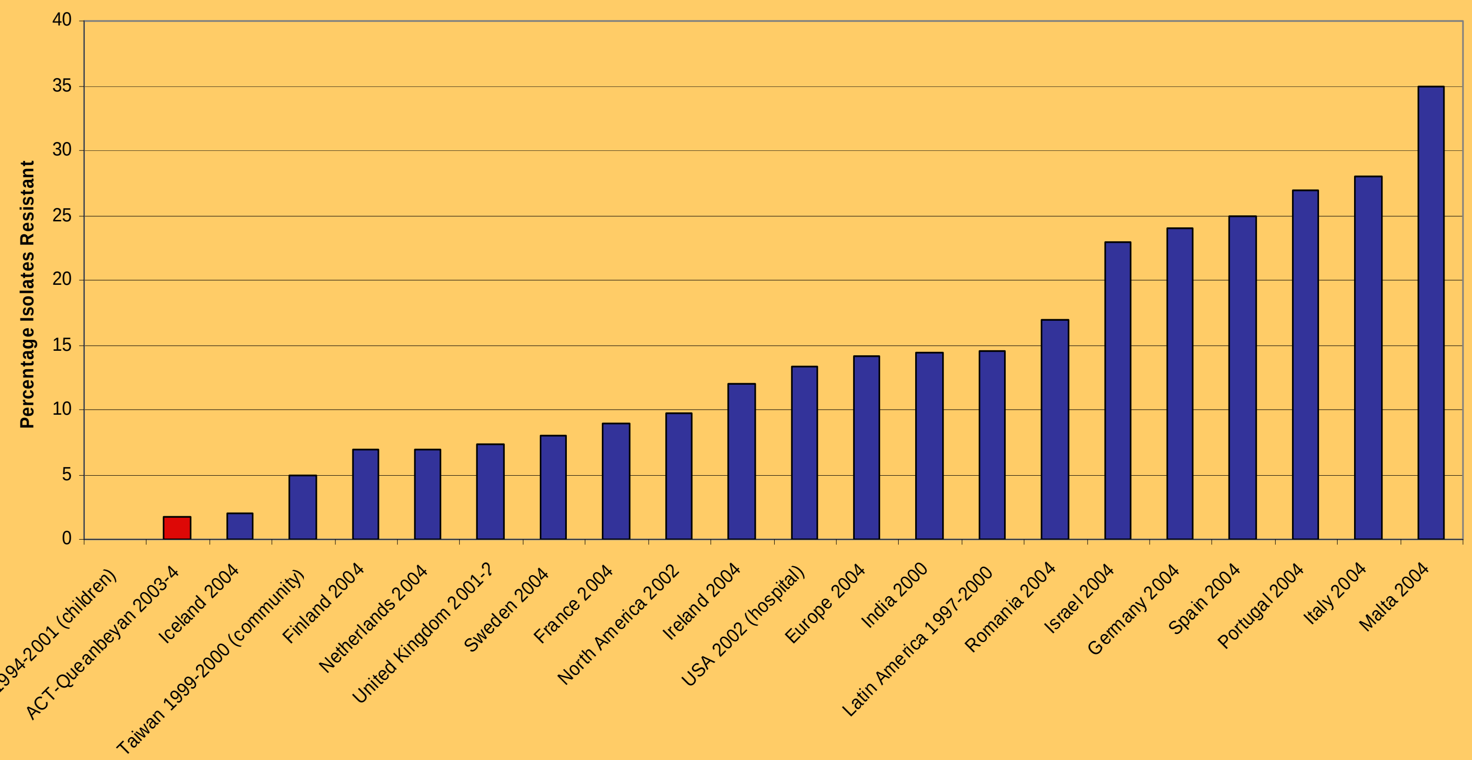


Total Outpatient antibiotic use in 26 European countries in 2002



Source: ESAC Website

Resistance Rates of Invasive E.coli Isolates to Ciprofloxacin



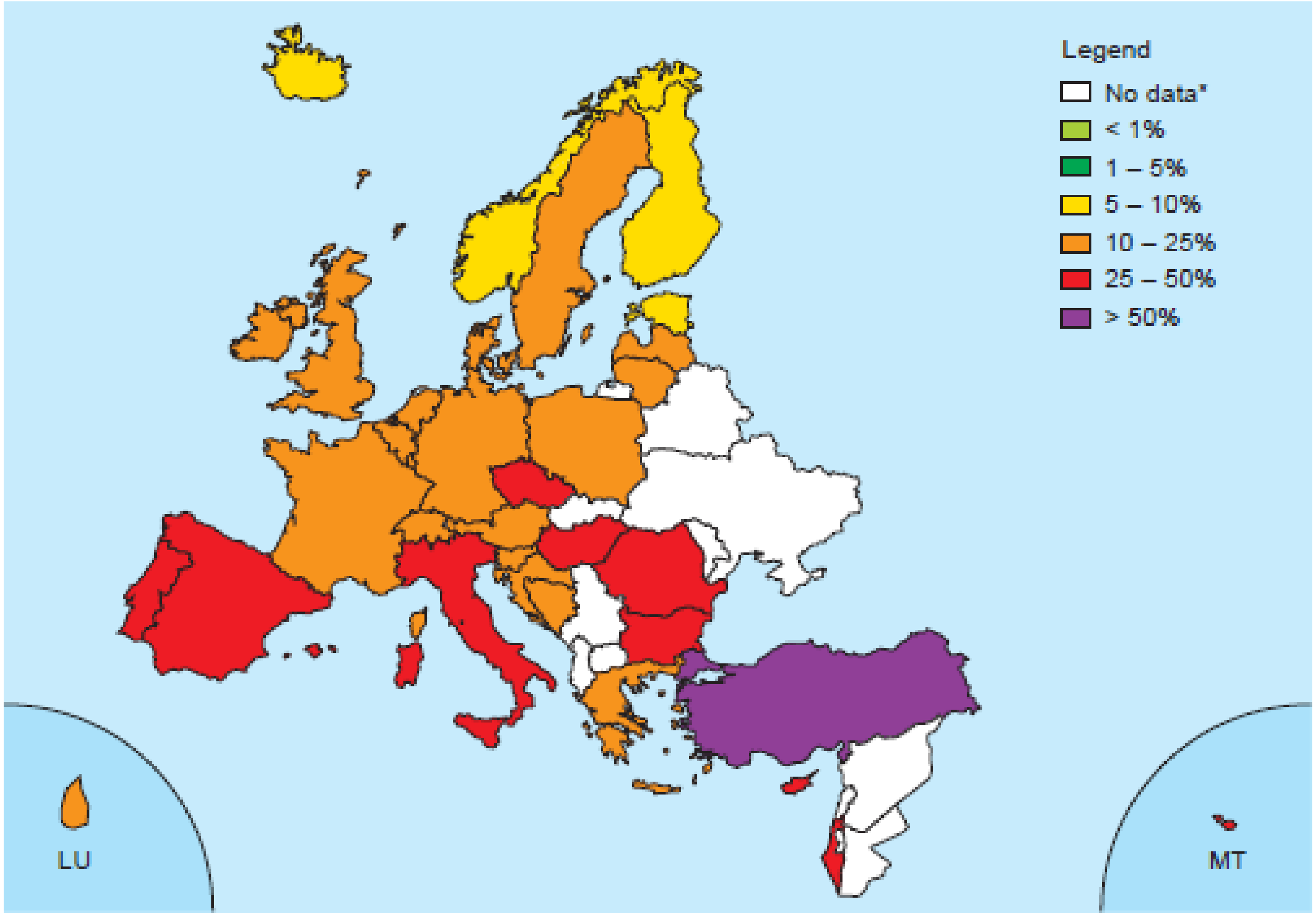


Figure 5.15. *Escherichia coli*: proportion of invasive isolates with resistance to fluoroquinolones in 2008.

* These countries did not report any data or reported less than 10 isolates.

Much more resistant E.coli via food chain than we think?

Antimicrobial Drug–Resistant *Escherichia coli* from Humans and Poultry Products, Minnesota and Wisconsin, 2002–2004

James R. Johnson,*† Mark R. Sannes,*†[1] Cynthia Croy,*† Brian Johnston,*† Connie Clabots,*†
Michael A. Kuskowski,*† Jeff Bender,‡ Kirk E. Smith,§ Patricia L. Winokur,¶#
and Edward A. Belongia**

Emer Infect Dis Vol. 13, No. 6, June 2007

Many drug-resistant human fecal *E. coli* isolates may originate from poultry, whereas drug-resistant poultry source *E. coli* isolates likely originate from susceptible poultry-source precursors.

Resistant E.coli in people similar to poultry isolates (US)

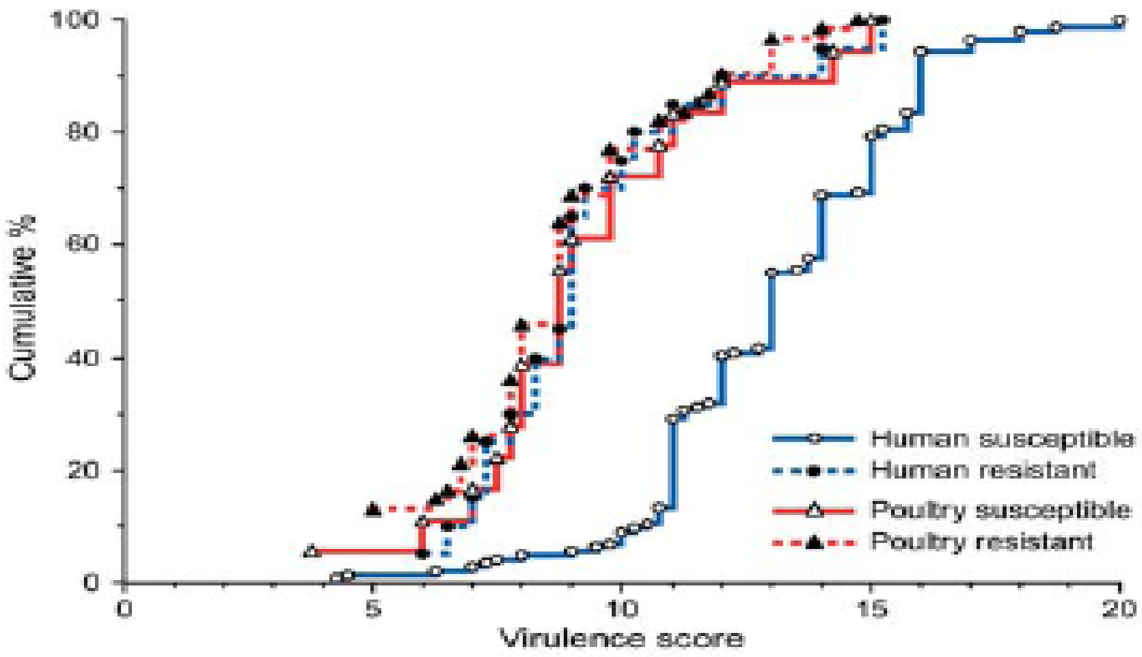


Figure 2. Distribution of virulence factor scores by source and resistance status among 243 extraintestinal pathogenic *Escherichia coli* isolates from human feces and poultry products, Minnesota and Wisconsin, 2002–2004. Resistant, resistant to trimethoprim-sulfamethoxazole, nalidixic acid (quinolones), and ceftriaxone or ceftazidime (extended-spectrum cephalosporins).

JOURNAL OF CLINICAL MICROBIOLOGY, Dec. 2004, p. 5767–5773 Vol. 42, No. 12
0095-1137/04/$08.00+0 DOI: 10.1128/JCM.42.12.5767–5773.2004

Emergence of Extended-Spectrum-β-Lactamase (CTX-M-9)-Producing Multiresistant Strains of *Salmonella enterica* Serotype Virchow in Poultry and Humans in France

François-Xavier Weill,[1*] Renaud Lailler,[2] Karine Praud,[3] Annaëlle Kérouanton,[2] Laëtitia Fabre,[1] Anne Brisabois,[2] Patrick A. D. Grimont,[1] and Axel Cloeckaert[3]

Imported chicken meat as a potential source of quinolone-resistant *Escherichia coli* producing extended-spectrum β-lactamases in the UK

Journal of Antimicrobial Chemotherapy, JAC Advance Access published online on January 25, 2008 .**R. E. Warren1,*, V. M. Ensor2, P. O'Neill1, V. Butler1, J. Taylor1, K. Nye3, M. Harvey3, D. M. Livermore4, N. Woodford4 and P. M. Hawkey2,3**

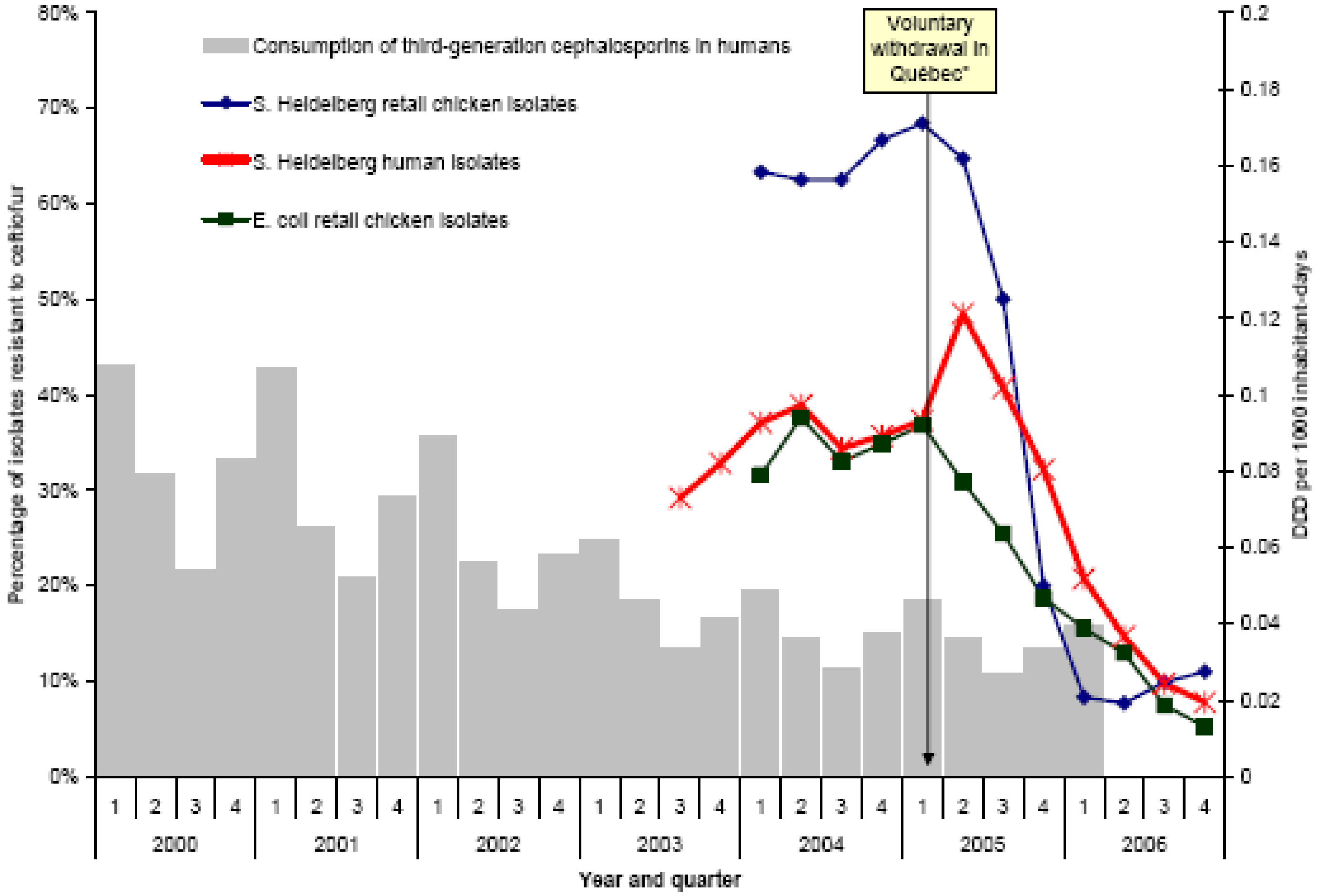
- Results: The country of rearing was identified from the packaging for 89 of 129 purchased samples. Only one of the 62 UK-reared chicken samples carried *E. coli* producing a CTX-M-1 enzyme, whereas 10 of 27 samples reared overseas had *E. coli* with CTX-M enzymes. Specifically, 4/10 Brazilian, 3/4 Brazilian/Polish/French, and 2/2 Dutch samples had *E. coli* with CTX-M-2 enzymes. Six of 40 samples for which the country of rearing was not known had producers of CTX-M enzymes, 5 of them with CTX-M-14.

Link between ceftiofur resistance in human and chicken isolates: Canada

- In order to prevent and control *Escherichia coli* infections, some broiler chicken hatcheries in Canada used ceftiofur (extra-label use). Published information (Boulianne, 2005*1*) indicated that 100% of the Québec hatcheries surveyed were using ceftiofur in 2004 (in hatching eggs and/or day old chicks). CIPARS 2003 annual report highlighted higher rates of ceftiofur resistance in retail chicken and human isolates of *S*. Heidelberg.

- To address these public health concerns raised all broiler chicken hatcheries in Québec voluntarily stopped all use of ceftiofur in February 2005.

Figure 1. Past three quarters moving average of the percentage of isolates resistant to ceftiofur for retail chicken *E. coli*, retail chicken and human clinical *S. Heidelberg* isolates, and quarterly human consumption of 3rd generation cephalosporins dispensed at retail pharmacies (*IMS² Health*) in Québec.



Journal of Antimicrobial Chemotherapy (2006) **58**, 211–215
doi:10.1093/jac/dkl211
Advance Access publication 23 May 2006

JAC

Extended-spectrum β-lactamase-producing Enterobacteriaceae in different environments (humans, food, animal farms and sewage)

Raúl Jesús Mesa[1,2], Vanessa Blanc[2], Anicet R. Blanch[3], Pilar Cortés[2], Juan José González[4], Susana Lavilla[4], Elisenda Miró[1], Maite Muniesa[3], Montserrat Saco[5], MªTeresa Tórtola[2,4], Beatriz Mirelis[1,2], Pere Coll[1,2], Montserrat Llagostera[2,6], Guillem Prats[2,4] and Ferran Navarro[1,2]*

Results: An ESBL-producing Enterobacteriaceae prevalence of 1.9% was observed in human infections. A cross-sectional survey of human faecal carriers in the community showed a general prevalence of 6.6% with a temporal distribution. High use of antibiotics in winter coincided with a lower prevalence in carriers. ESBL-producing Enterobacteriaceae were detected in the five samples of human sewage, in samples from 8 of 10 pig farms, 2 of 10 rabbit farms, from all 10 poultry farms and in 3 of 738 food samples studied. Faecal carriage of ESBL-producing Enterobacteriaceae was detected in samples from 19 of 61 food-borne outbreaks evaluated. All food-borne outbreaks were due to enteropathogens. The prevalence of carriers in these outbreaks ranged from 4.4% to 66.6%.

Conclusions: This widespread occurrence of ESBL-producing Enterobacteriaceae suggests that the community could act as a reservoir and that food could contribute to the spread of these strains.

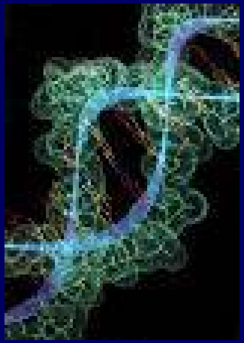
Table B. **Occurrence of resistance to antimicrobials in *Escherichia coli* from food products (percent resistant isolates)*** (Sources: The Community Summary Report on Trends and Sources of Zoonoses, Zoonotic Agents, Antimicrobial Resistance and Foodborne Outbreaks in the European Union in 2005 and national reports)

Country	Year	Food type	Number of isolates	Reported resistance (%)											Data source
				Ampicillin	3rd gen cephalosporin	Chloramphenicol	Ciprofloxacin-/Enrofloxacin	Nalidixic acid	Gentamicin	Neomycin-/Kanamycin	Streptomycin	Sulphonamides	Tetracycline	Trimethoprim	
Austria	2003	beef	40	2	-	2	2*	5	0	0	12	-	12	2	Ramost 2003
Belgium	2005	beef	238	13	2	4	1	2	-	-	12	19	16	11	Zoonoses report 2005
Denmark	2004	beef	196	8	0	1	0*	0	0	2	9	7	9	4	DANMAP 2004
The Netherlands	2005	beef	34	12	3	3	9*	3	0	0	-	15	12	12	MARAN 2005
Norway	2005	beef	90	3	0	0	0	0	0	0	10	3	2	3	Zoonoses report 2005
Austria	2003	poultry	34	26	-	0	30*	32	4	0	35	-	38	18	Ramost 2003
Belgium	2005	broiler	148	37	3	7	3	28	-	-	24	37	39	25	Zoonoses report 2005
Denmark	2004	broiler	216	15	0	<1	0*	6	0	0	1	15	9	3	DANMAP 2004
The Netherlands	2005	poultry	115	54	11	8	30*	33	4	12	-	50	47	43	MARAN 2005
Austria	2003	pork	56	16	-	12	4*	4	0	2	54	-	55	12	Ramost 2003
Belgium	2005	pork	86	10	-	7	1	2	-	-	19	15	21	15	Zoonoses report 2005
Denmark	2004	pork	178	15	0	2	0*	2	2	3	13	18	26	10	DANMAP 2004
The Netherlands	2005	pork, organic	155	16	1	6	0*	0	4	38	-	27	38	17	MARAN 2005
Germany	2005	mixed meat	50	2	0	0	0	-	0	0	10	14	12	4	Zoonoses report 2005
Portugal	2005	cheese	33	30	0	3	6	-	36	42	91	-	58	-	Zoonoses report 2005
Non-EU countries															
Canada QC	2003	broiler	112	50	33	18	0*	1	18	11	48	43	57	-	CIPARS 2003
Canada; ON	2003	broiler	136	35	18	5	2*	2	7	9	32	24	51	-	CIPARS 2003
Canada QC	2003	pork	61	20	2	10	0*	0	2	3	28	31	48	-	CIPARS 2003
Canada ON	2003	pork	91	20	2	8	0*	0	1	6	17	30	55	-	CIPARS 2003
Canada QC**	2003	beef	84	7	0	1	1*	1	1	2	2	7	19	-	CIPARS 2003
Canada ON**	2003	beef	100	8	2	2	0*	0	0	2	6	14	23	-	CIPARS 2003

* cut-off of >0.06 i.e. the same as for DANMAP has been used to define resistance for the compilation of this table; ** ON = Ontario, QC = Quebec

The gene is the clone for VRE

(not the enterococcus)



- Genes highly conserved
    - transposons; vanA and vanB
- great variation in types of enterococci
    - even in one individual patient with time
- not a “safe sex” gene
    - promiscuous
    - easily transmitted from enterococcus to enterococcus
    - In USA (2002) dialysis patient, transfer from VRE to MRSA

Industry perspective

- Not a problem
  - agriculture is being unfairly targeted because of medical misuse of antibiotics
- Antibiotics not really growth promoters
  - disease prevention
  - “digestion enhancers”
  - environmentally beneficial (greenhouse effect)
  - the world will starve without them
  - animal welfare will suffer
- bankrupt our agriculture sector
  - trade

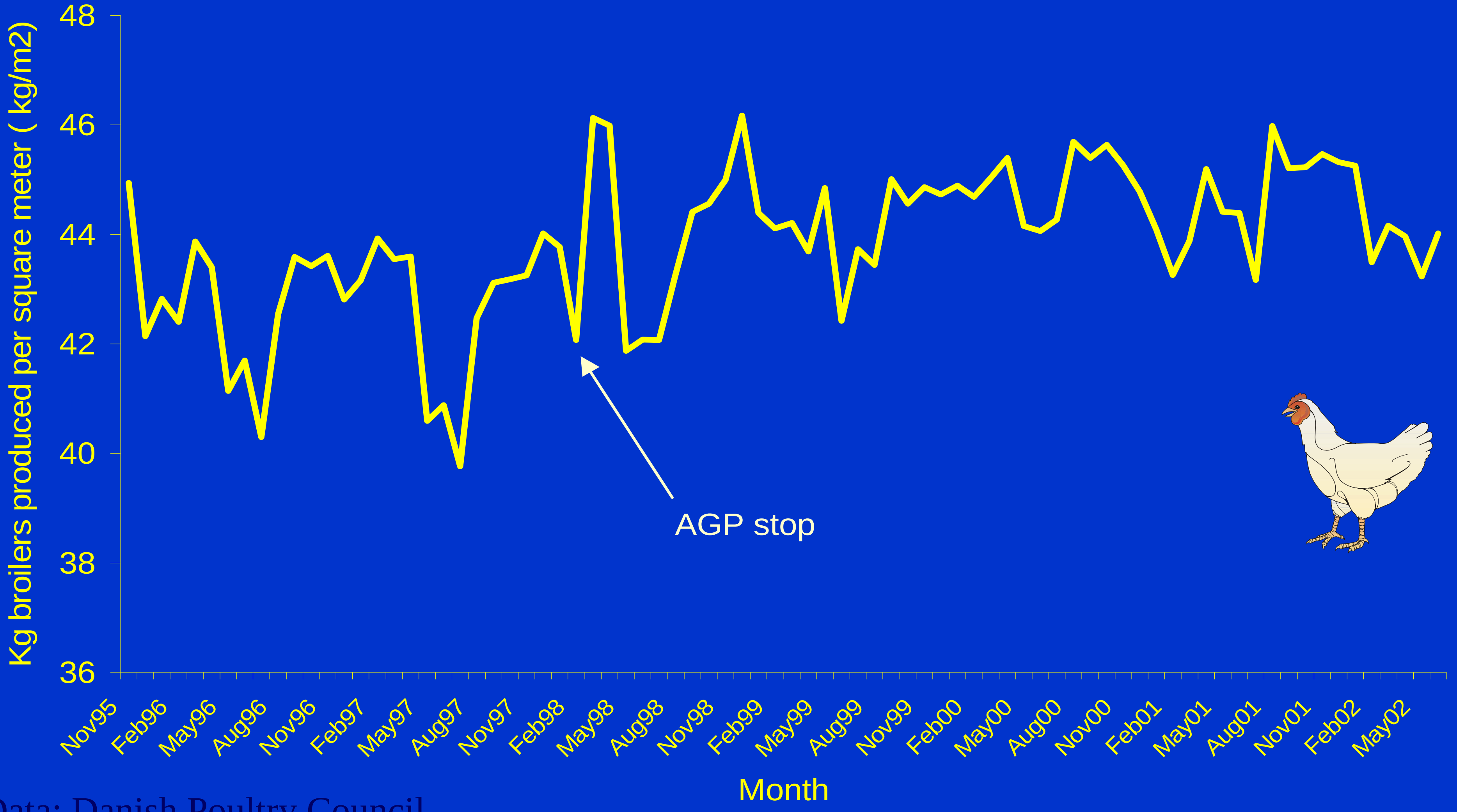
Industry arguments

- The world will end if we do not use antibiotics !
  - People will starve
  - Farmers go broke
  - Consumers worse off
- Animals will suffer
  - animal welfare

The world will end if we do not use antibiotics (animal welfare)

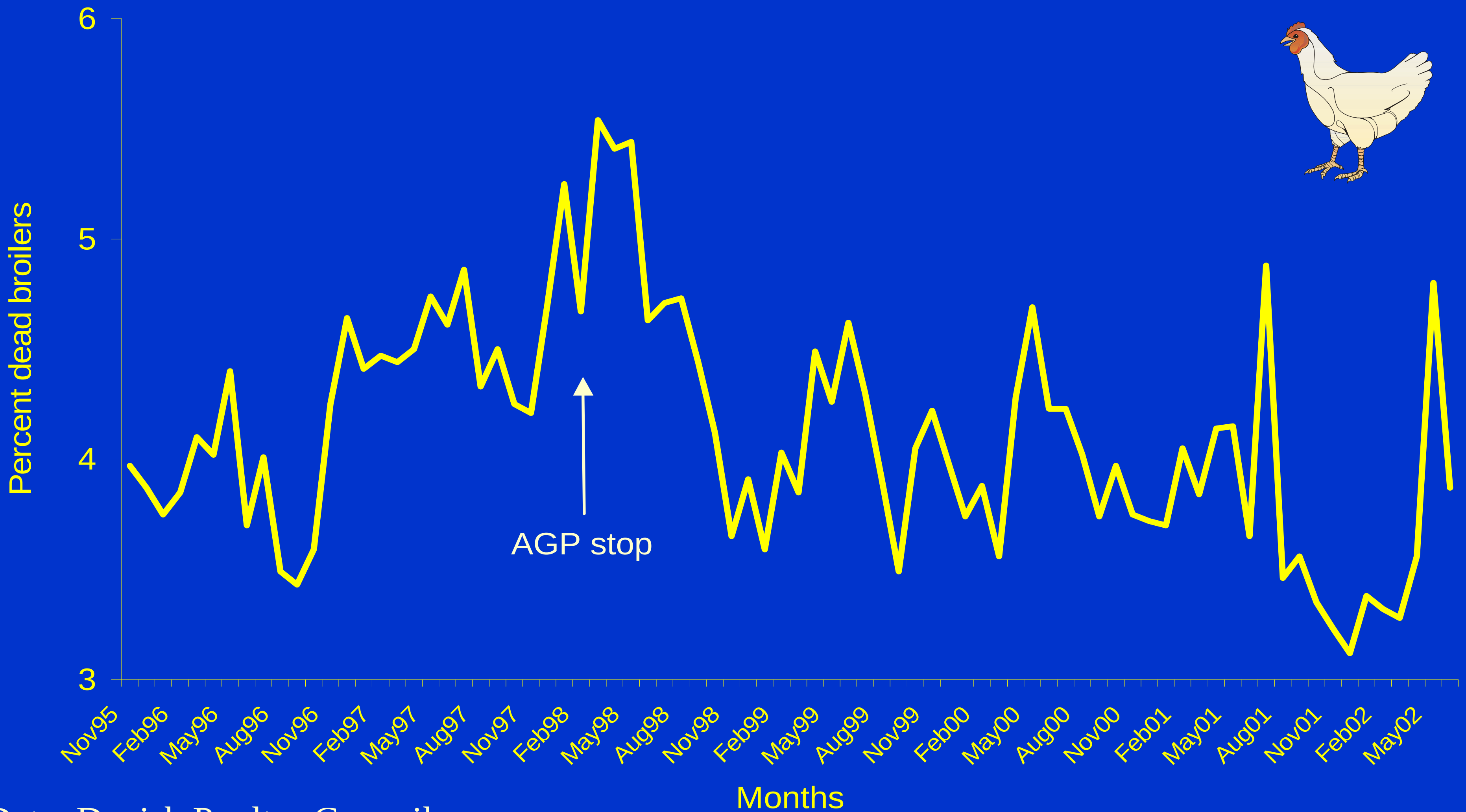
- Growth promoters
  - but Sweden, Denmark
- Prophylaxis
  - but EU
  - no improvement in mortality in manufactures own studies
- Therapy
  - quinolones (but Australia does not have it!)
  - ceftiofur

Mean kg broilers produced per m^2 November 1995 to June 2002



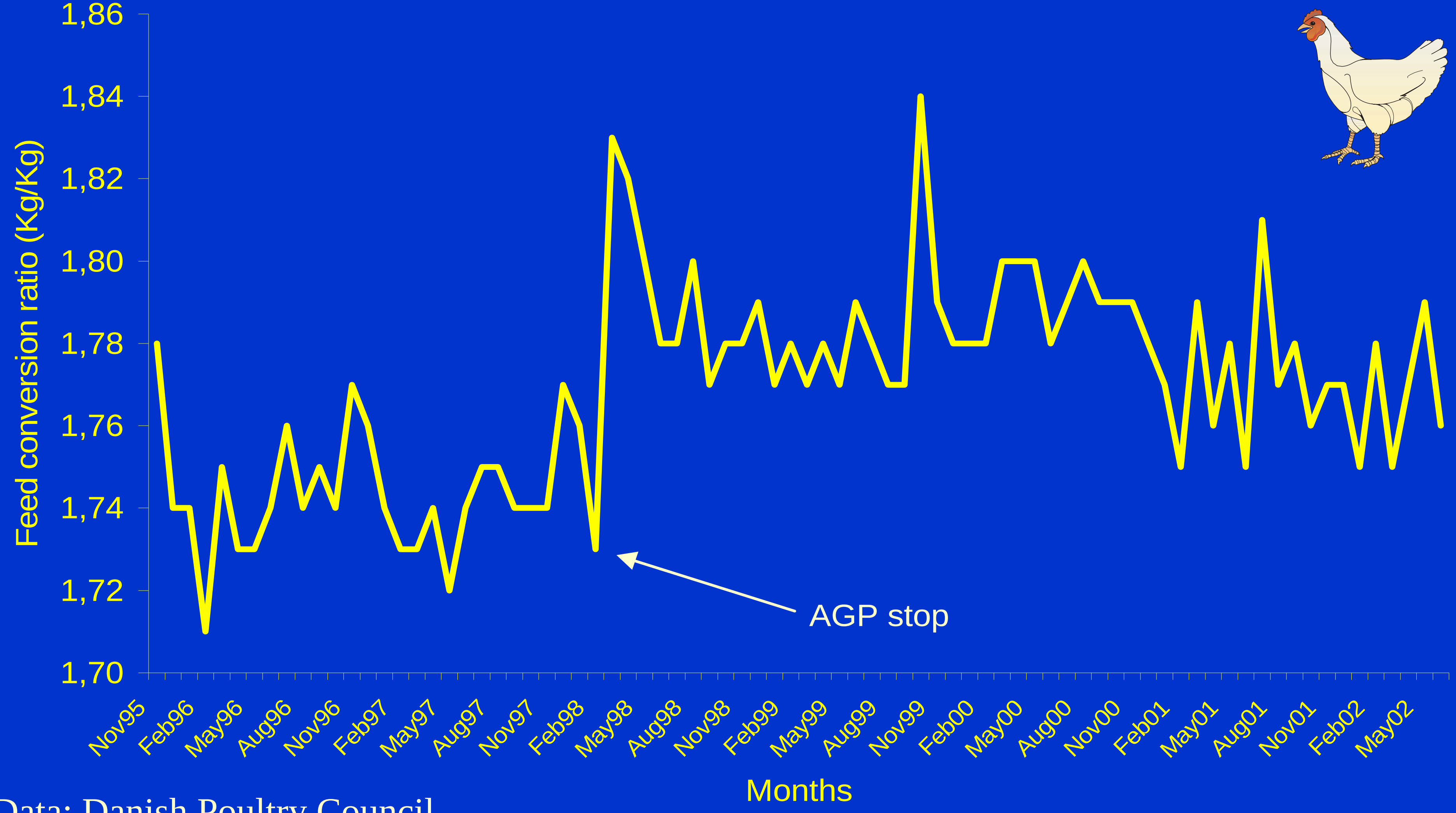
Data: Danish Poultry Council

Percent dead broilers in total November 1995 to June 2002



Data: Danish Poultry Council

Feed conversion ratio
November 1995 to June 2002



Data: Danish Poultry Council

International action

- WHO
- EU
- USA
- Australia; JETACAR

WHO
"Critically important" antibiotics

- Defined at Canberra and Copenhagen meetings
- Codex
  - International trade implications
  - Food safety
- FAO and OIE involvement

Therapy of sick animals is NOT an issue

- Sick animals can be treated with antibiotics
  - BUT not with “last line” or “critically important ”drugs
  - vets usually involved in therapy unlike growth promotion and prophylaxis

Prudent Antibiotic use in food production animals

- No antibiotic use as growth promoters
- Use antibiotics for prophylaxis sparingly
  - find alternatives; feed, vaccines etc
- Do not use "critically important" or "last line" human antibiotics for therapy
  - glycopeptides, fluoroquinolones, 3rd generation cephalosporins, new agents (linezolid)

Information about antibiotic use and resistance in food animals and aquaculture

- Often a Black Hole!
- We need transparent information AND better practices

We can get a “win-win” situation

- If substantially less antibiotic are used then
  - better human health (lower risk of resistant bacteria)
  - better market opportunities for our exports
  - less resistance when animals get sick
- Help if International rules harmonized
  - at least in major western trading blocks
  - happening anyway (USA and EU)