Environmental pollution with antibiotics–health implications beyond drug-resistant infections

Antibiotic stewardship
California Council on Science and Technology
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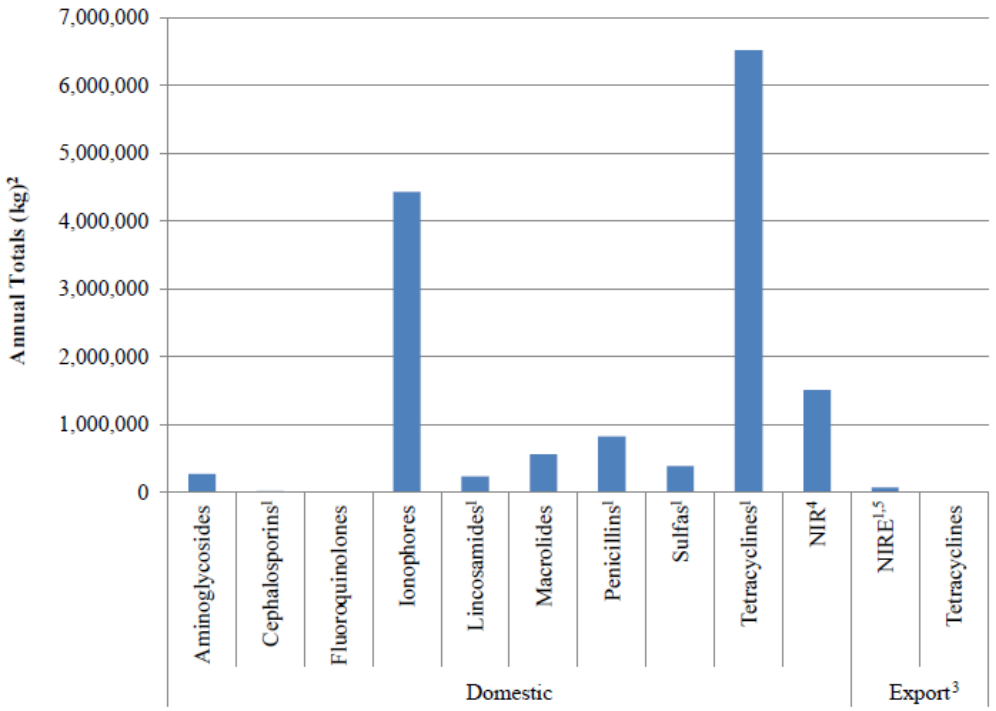
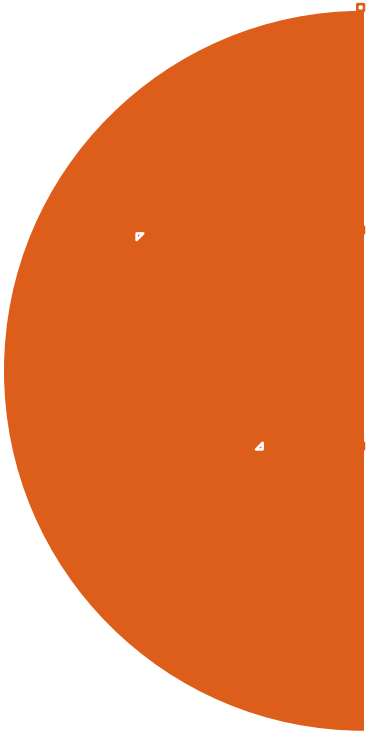
Antimicrobial agents used in food-producing animals actively marketed in 2013 (Summary Report, FDA, April 2015)



	Drug Class	Annual Totals (kg)[2]
Domestic	Aminoglycosides	270,342
	Cephalosporins[1]	28,337
	Fluoroquinolones	15,099
	Ionophores	4,434,657
	Lincosamides[1]	236,450
	Macrolides	563,251
	Penicillins[1]	828,721
	Sulfas[1]	384,371
	Tetracyclines[1]	6,514,779
	NIR[4]	1,512,547
	Subtotal	***14,788,555***
Export[3]	NIRE[1,5]	70,385
	Tetracyclines	6,927
	Subtotal	***77,312***
	Grand Total	***14,865,867***

Antimicrobial agents used in food-producing animals actively marketed in 2013 (Summary Report, FDA, April 2015)



14,865,867 kg of antibiotics for food-animal use marketed in 2013.

98% over-the-counter!

17% increase from 2009 to 2013

1929

On the Antibacterial Action of Cultures of a Penicillium, with Special Reference to Their Use in the Isolation of B. influenzae

A. FLEMING

1940

Penicillin as a Chemotherapeutic Agent

E. CHAIN, H. W. FLOREY, A. D. GARDNER, N. G. HEATLEY, M. A. JENNINGS, J. ORR-EWING, AND A. G. SANDERS

Alexander Fleming, receiving Nobel Prize in Physiology and Medicine, 1945; shared with Howard Florey and Ernst Boris Chain

USE OF SULFASUXIDINE, STREPTOTHRICIN, AND STREPTOMYCIN IN NUTRITIONAL STUDIES WITH THE CHICK*

By P. R. MOORE, A. EVENSON, T. D. LUCKEY, E. McCOY, C. A. ELVEHJEM, AND E. B. HART

(From the Departments of Biochemistry and Agricultural Bacteriology, College of Agriculture, University of Wisconsin, Madison)

(Received for publication, June 27, 1946)

SundayReview | Opinion

The Fat Drug

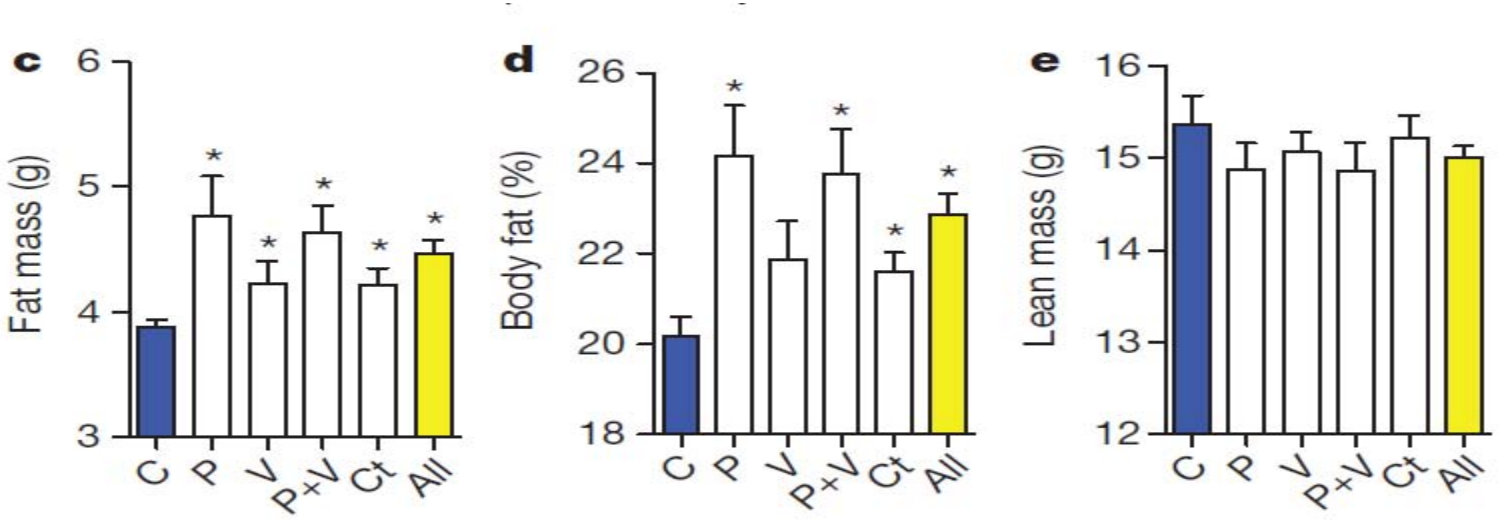
New York Times

Pagan Kennedy

March 8, 2014

Body mass changes in mice fed low-dose antibiotics

(Cho I et al, Nature 2012)



C: control; P: penicillin; V: vancomycin; Ct: chloramphenicol

Exposure to antibiotics in 1st 2 years of life in human infants

(Trasande L et al, International Journal of Obesity 2012)

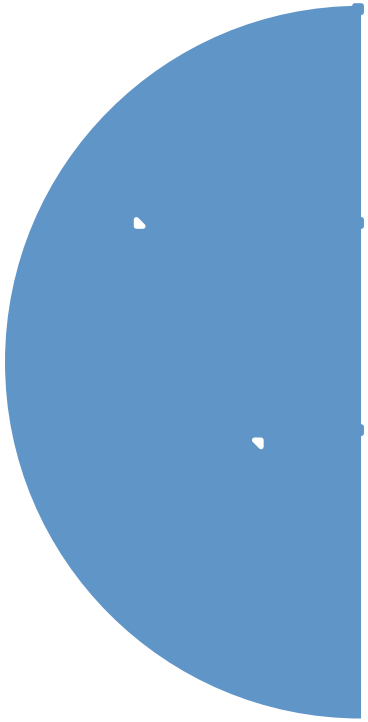
11,532 children born at ≥2500 g in Avon, UK (1991-92)

Exposures to antibiotics (6 months, 6–14 months, 15–23 months)

BMI at 6 weeks, 10 months, 20 months, 38 months and 7 years

Exposure to antibiotics in 1st 2 years of life in human infants

(Trasande L et al, International Journal of Obesity 2012)



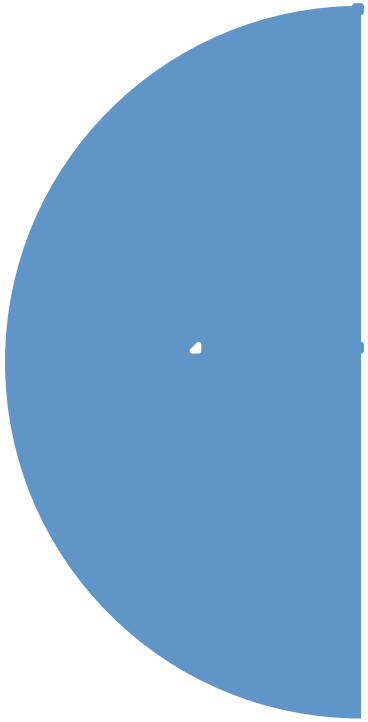
Antibiotic exposure during 6 months associated with increased body mass at 10-38 mos

Exposure during 15- 23 months associated with increased BMI at 7 years of age

No association for exposure during 6-14 months

Childhood antibiotic use and obesity

(Schwartz BS et al, Int J Obesity, 2015 (in press))



Electronic records of 163,820 healthy children aged 3-18 years

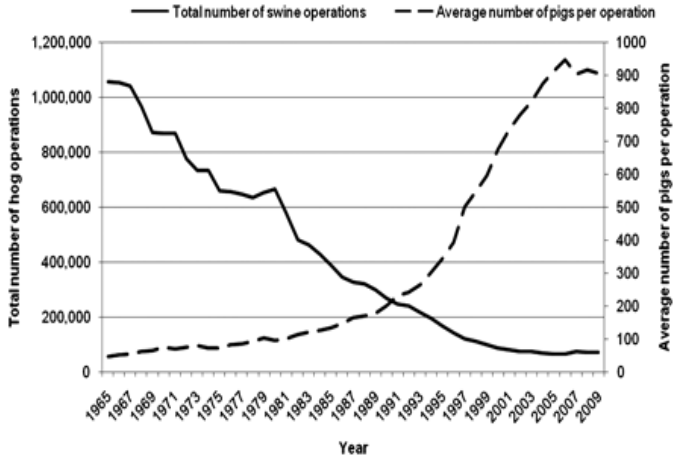
Antibiotic use may influence weight gain throughout childhood.

Quantity of antibiotics released into the environment

- 75% antibiotics used for growth promotion not absorbed by the animal body
- Released in manure and urine
  - Swine: 280 million tons of fresh manure (2002)
  - Chicken: 460 million tons (2006)
  - Cow: 2.6 million tons (2007)

- **Therefore: 2-18 million pounds of antibiotics released into the environment each year by animal waste alone!**

Concentrated Animal Feeding Operations (CAFOs)

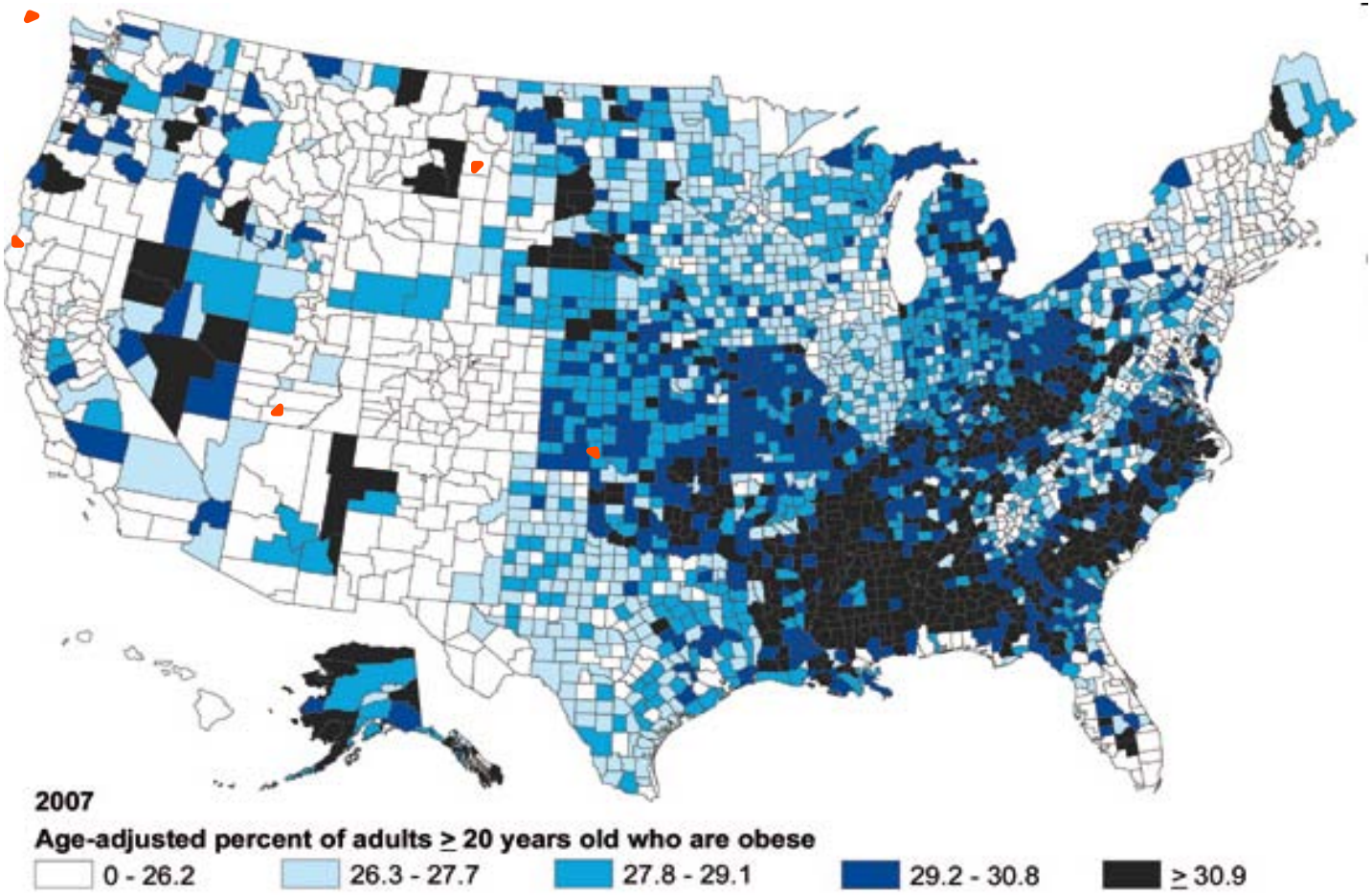


Manure disposal

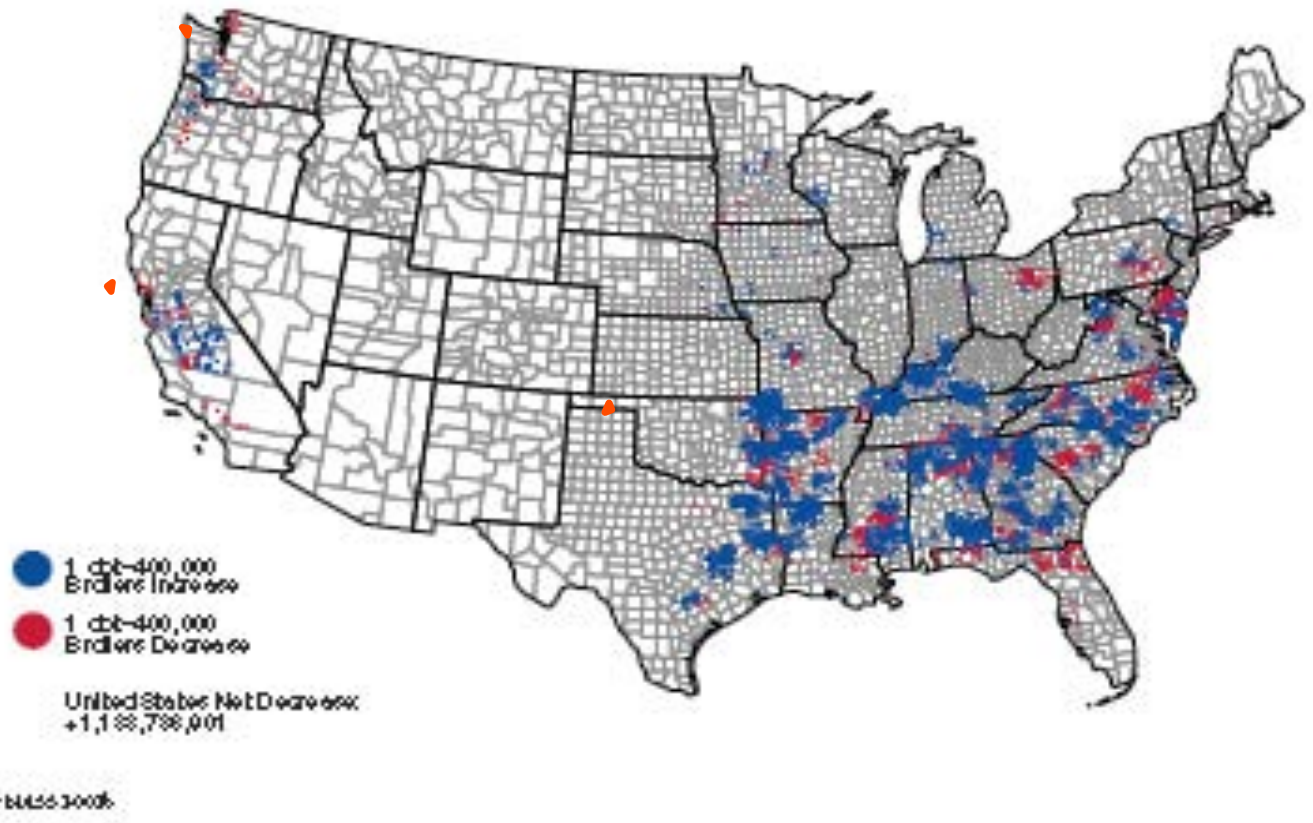
Figure 13.
CAFO Manure Pile
This enormous pile of manure was CAFO-generated
Photo credit: Courtesy of Factoryfarming.org.

roguehealthandfitness.com

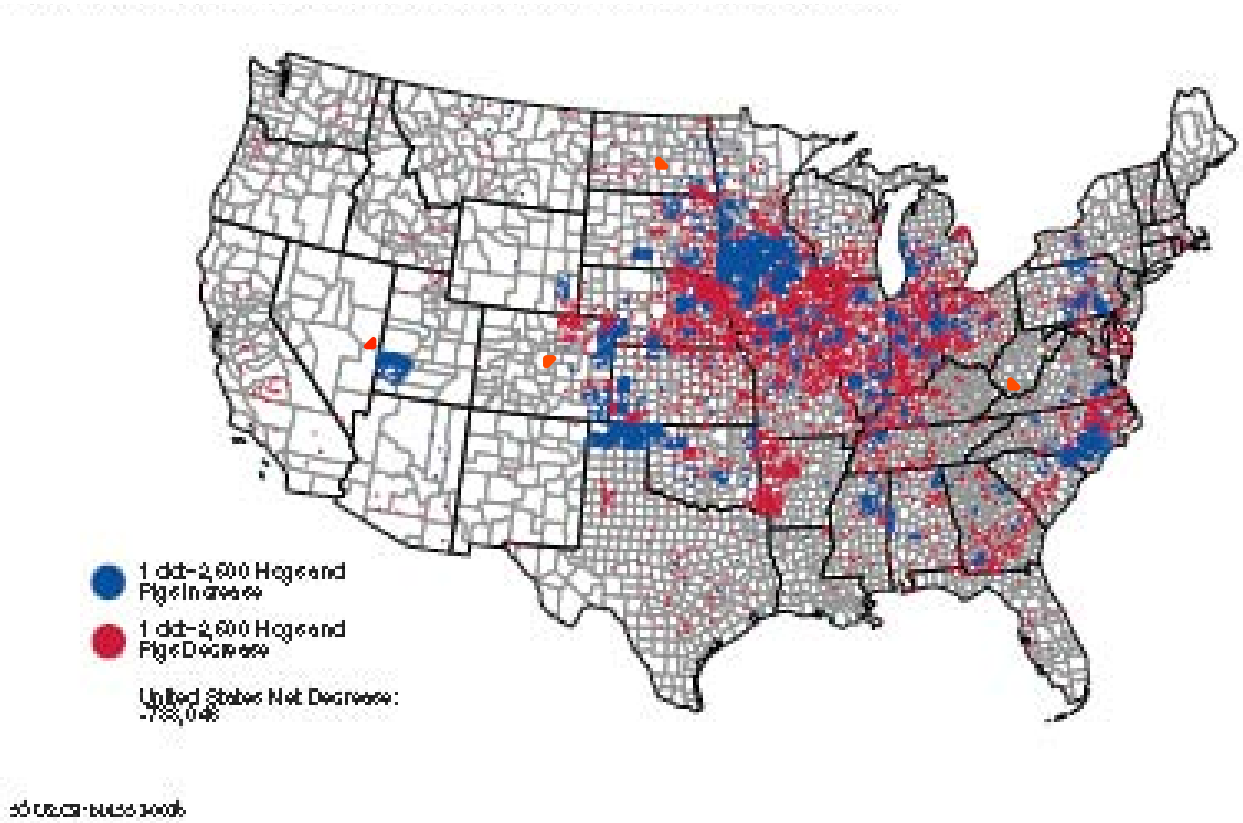
BMI by counties, USA, 2007



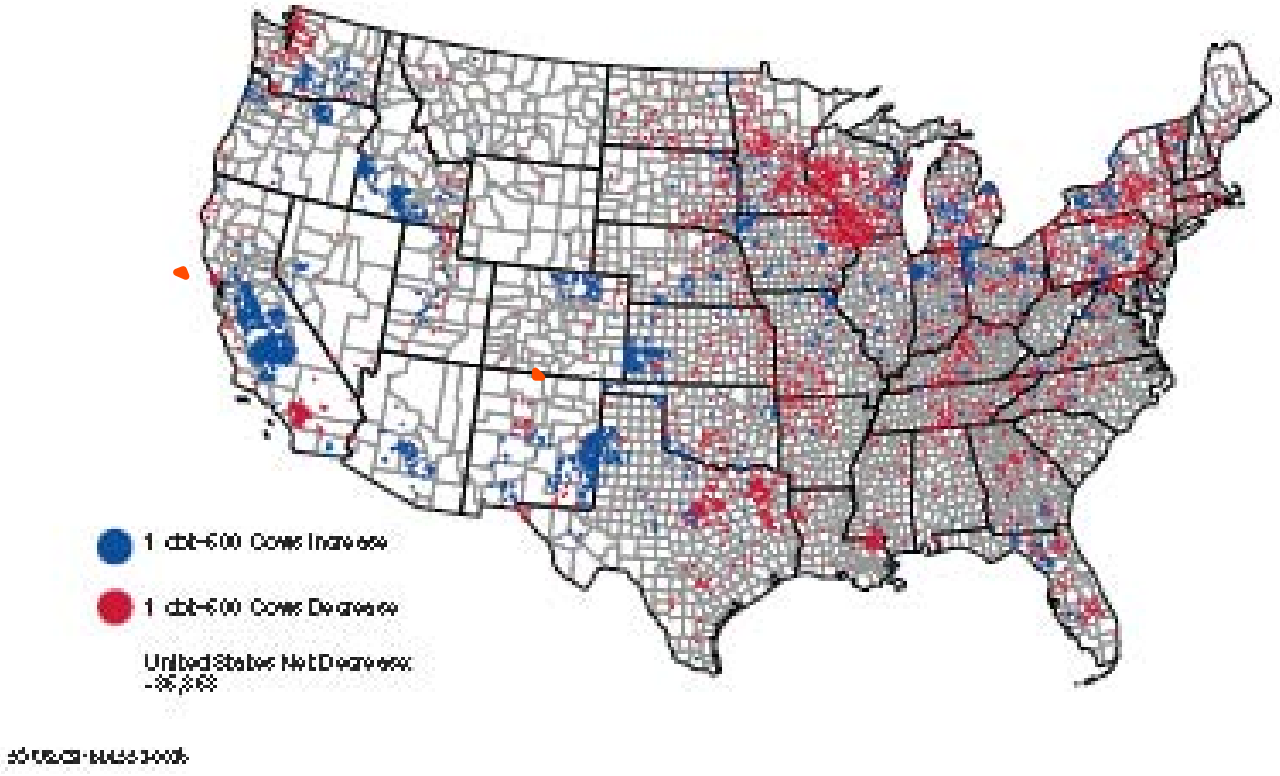
Geographic concentration of broiler production by counties, USA, 1997-2002



Geographic concentration of hog production sites by counties, USA, 1997-2002



Geographic concentration of dairy cows by counties, USA, 1997-2002



Obesity in human-companion animals

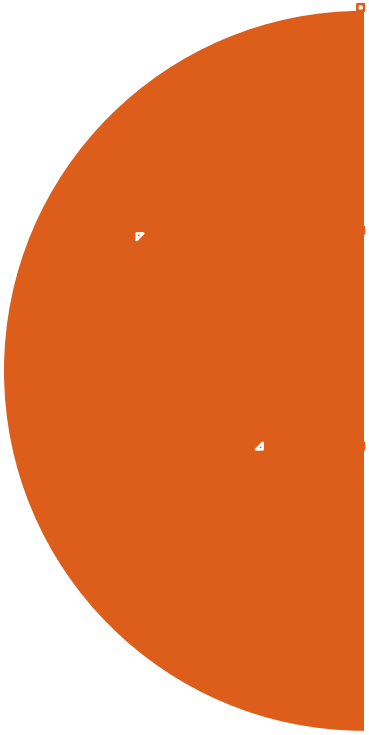
Source food	Antimicrobial agents found	Concentrations	Country
shrimp	Fluoroquinolones	0.1 to 1 ng/g	USA
salmon, trout, shrimp tissues	Fluoroquinolones	0.28 to 16 ng/g	Canada
swine, chicken, shrimp tissues	Fluoroquinolones	1-100 ng/g	China
Bob veal, heavy calves, heifers, market hogs, non-formula-fed veal, roaster pig, sows	Sulfonamides	0.1-1 ppm	USA
Bull meat	Moxidectin (milbemycin)	89.13 ppb	USA
Goat meat	Oxytetracycline	4.66 ppm	USA
Market hog, roaster pig meat	Carbadox	47-110 ppb	USA
Catfish, basa	Fluoroquinolones	1.9-6.5 ppb	China
Honey	Erythromycin	50-1776 ng/g	Turkey
Corn, green onion, cabbage	Chlortetracycline	2-17 ng/g	USA

Water sources	Antimicrobials	Concentrations	Country
Pig farm waste water	Sulfonamides	20 µg/ml	Vietnam
Sewage samples	Cefalexin, Cefotaxime	>1 µg/ml	Hong Kong, Shenzhen
Swine farm lagoon	Chlortetracycline	68-1000µg/L	USA
Wastewater treatment plant effluent	Minocycline, Epitetracycline, Tetracycline, Doxycycline	95.8-915.3 µg/L	Portugal
Wastewater treatment plant final effluents	Erythromycin, Ciprofloxacin, Sulfamethoxazole, Tetracycline	0.08 µg/L, 0.118 µg/L, 0.243 µg/L, 0.151 µg/L	Canada
Wastewater	Chlortetracycline, Ciprofloxacin, Erythromycin, Sulfamethoxazole, Tetracycline, Trimethroprim	0.69 µg/L, 0.03-0.14 µg/L, 0.9-1.7 µg/L, 0.05-1.9 µg/L, 0.05-0.85 µg/L, 0.05-0.71 µg/L	USA
Cache-la-Poudre River	Macrolides	0.06-0.17 µg/L	USA
Wastewater	Sulfamethoxazole	232 - 9000 ng/L	Austria, Switzerland, USA, Spain, Germany
Elbe and Saal Rivers	Erythromycin, Sulfamethoxazole, Trimethroprim	30-70 ng/L, 30-70 ng/L, <30-40 ng/L	Germany
Po River	Macrolides	0.7-68.3 ng/L	Italy
Wastewater treatment plant effluents	Quinolones	40-580 ng/L	France, Italy, Sweden, Greece, Switzerland
Wastewater treatment plant effluent	Sulfamethoxazole, Trimethroprim, Efloxacin, Erythromycin	310-400 ng/L, 180-320 ng/L, 110 ng/L, 2.5 µg/L	USA, Germany
Rio Grande River	Sulfamethoxazole	300 ng/L	USA
Surface water	Erythromycin, Sulfamethoxazole	150 ng/L, 30 ng/L	Germany

Animal waste	Antimicrobials	Concentrations	Country
Cattle manure	Chlortetracycline	7.73 mg/L	USA
Cattle, turkey manure	Monensin	1-4.4 mg/L, 1.2-1.5 mg/L	USA
Swine manure	Chlortetracycline	27 mg/L	USA
Swine slurry	Tetracycline	5-24 mg/L	Germany
Others			
Hospital effluent sludge	Oxofloxacin, Ciprofloxacin	0.7-2.0 mg/kg	Sweden
Hospital effluent	Ciprofloxacin, ampicillin	0.7-124.5 μg/L, 20-80μg/L	Germany
Hospital effluent	Minocycline, Epitetracycline, Tetracycline, Doxycycline	8.1-531.7 μg/L	Portugal
Hospital effluent	Ciproflozacin, Metronidazole, Sulfamethoxazole, Trimethroprim, Doxycycline	3.6-101 μg/L, 0.1-90.2 μg/L, 0.4-12.8 μg/L, 0.6-7.6 μg/L, 0.6-7.6 μg/L	Sweden
Hospital effluent	Sulfamethoxazole, Trimethroprim, Ofloxacin, Ciprofloxacin, Lincomycin, Penicillin G	400-2100 ng/L, 2900-5000 ng/L, 25.5-35.5 μg/L, 850-2000 ng/L, 300-2000 ng/L, 850-5200 ng/L	USA
Dairy plant effluent	Lincomycin	700-6600 ng/L	USA

Fate of antibiotics in the environment

(Kummerer, K. J Antimicrob Chemoth 2003)



Quinolones: not degradable in soil sediments

- Sarafloxacin (fluoroquinolone used to prevent poultry disease): 1% degraded after 80 days.

Virginiamycin (used as growth promoter):

- long half life.

Cyclosporin A:

- several months in soil

Global consumption of antimicrobial agents by food animals (Boeckel et al, PNAS, 2015)

Global annual antimicrobial drug consumption

- Cattle: **45 mg/kg animal**
- Chicken: **148**
- Pigs: **172**

Predicted: 63,151 to 105,596 tons between 2010 and 2030.

1/3 of this increase expected to occur due to shift to intensive farming operations

chinesequiz.com

BRICS countries: increase will be 99%

- Asia: protein intake **7 grams/capita/day** in 1960; **25 grams/capita/day** in 2013

Current situation in China

150-000-200,000 tons of antibiotics used annually (Bu Q et al, J Hazard Mater 2013)

Pigs: generate 618 billion kg of manure/yr (Larson C et al. Science 2015)

Urine samples of 1064 school children in 3 sites in eastern China (Wang H et al, Env Sci Tech, 2015):

- Human use accounts for half of the total

www.nature.com

- Antibiotics detected: **macrolides, beta-lactams, tetracyclines, quinolones, sulfonamides (58%; 74% at one site!)**
- Antibiotics of veterinary use: 3; Human use: 4; Both: 11.
- More than 1 antibiotic: 20%

Antibiotic environmental pollution

Antibiotics: not officially recognized as a form of pollution

Health consequences of environmental antibiotics:

- Selection of drug-resistant pathogens
- ?Obesity epidemic
- Destruction of ecosystems (disruption of denitrifying microbes)

What should/could be done?