



Antimicrobial Resistance: Agricultural Perspectives

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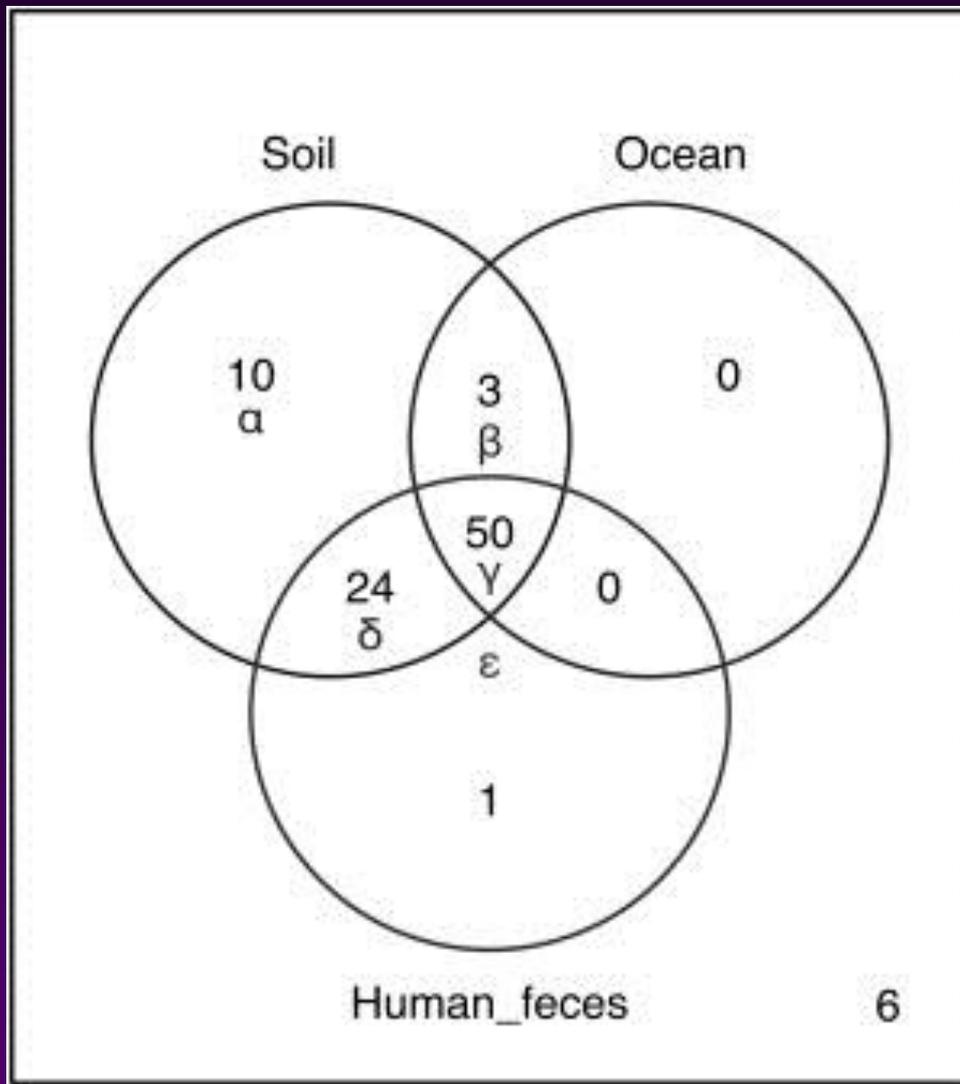
Pssst! Hey kid! Wanna be a Superbug...?
Stick some of this into your genome...
Even penicillin won't be able to harm you...!



It was on a short-cut through the hospital kitchens that Albert was first approached by a member of the Antibiotic Resistance.

SOIL AS A SOURCE OF ANTIMICROBIALS

- Penicillin discovered by Alexander Fleming in 1929 (*Penicillium*)
- Streptomycin discovered by Selman Waksman in 1943 (*Streptomyces*)
- 50% of all known antibiotics derived from the Genus *Streptomyces*



Common ARGD Class between Four Different Environmental Clusters Based on Roche 454 Data Sets Numbers inside each circle intersection indicate the number of common resistance classes between environmental data sets.

Joseph Nesme , Sébastien Cécillon , Tom O. Delmont , Jean-Michel Monier , Timothy M. Vogel , Pascal Simonet

Large-Scale Metagenomic-Based Study of Antibiotic Resistance in the Environment

Current Biology, Volume 24, Issue 10, 2014, 1096 - 1100
<http://dx.doi.org/10.1016/j.cub.2014.03.036>

IMPACT OF SOIL DERIVED NATURAL PRODUCTS ON HUMAN HEALTH

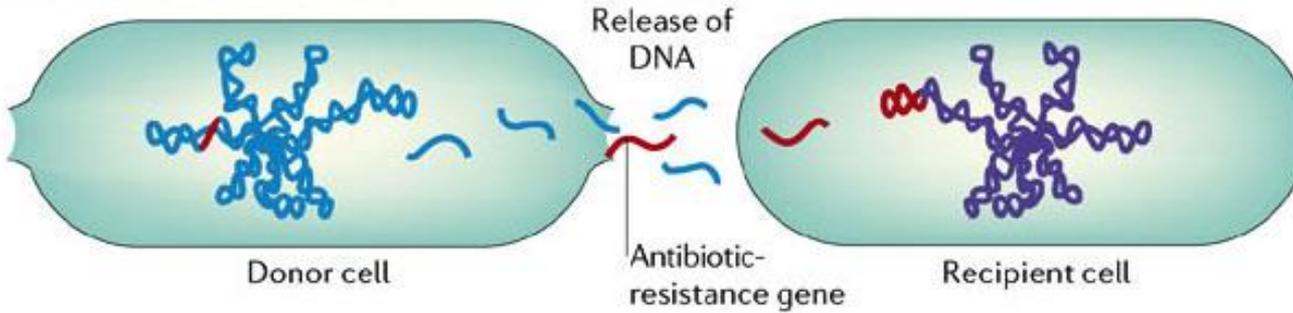
Item	Extent %	Reference
Prescription drugs	40	Strobel and Daisy, 2003
New chemical products registered by U.S. Food and Drug Administration	49	Brewer, 2000
Approved drugs between 1989 and 1995	60	Grabley and Thiericke, 1999
Approved cancer drugs between 1983 and 1994	60	Concepcion et al., 2001
Approved antibacterial agents	78	Concepcion et al., 2001

Why Antimicrobials

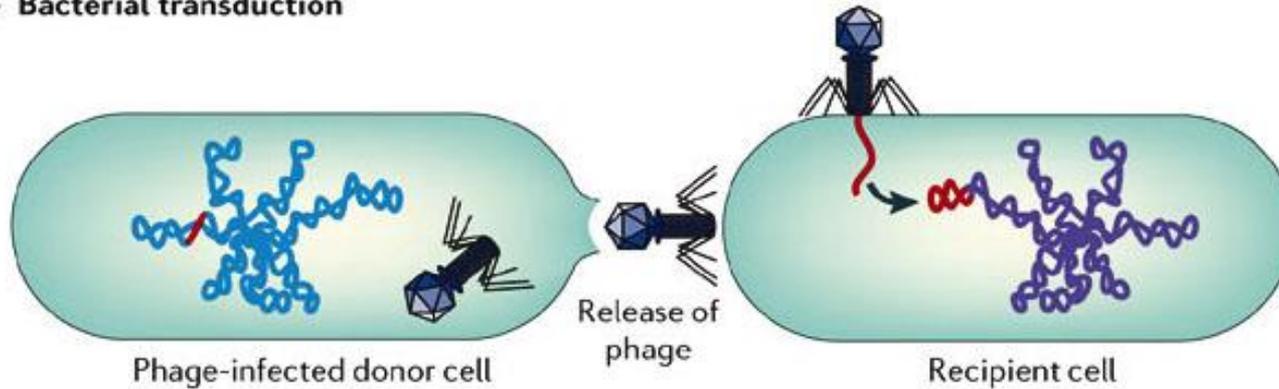
- Antibiotics are produced by certain bacteria and fungi to eliminate other microbes that compete for limited resources in the soil.
- For the antibiotic producing organisms to benefit, however, they must have some means to be resistant to the antibiotic.
- Bacteria, are very adept at acquiring foreign genes;
 - over time, some bacteria that do not produce antibiotics have acquired the genes necessary for antibiotic resistance.

How transferred

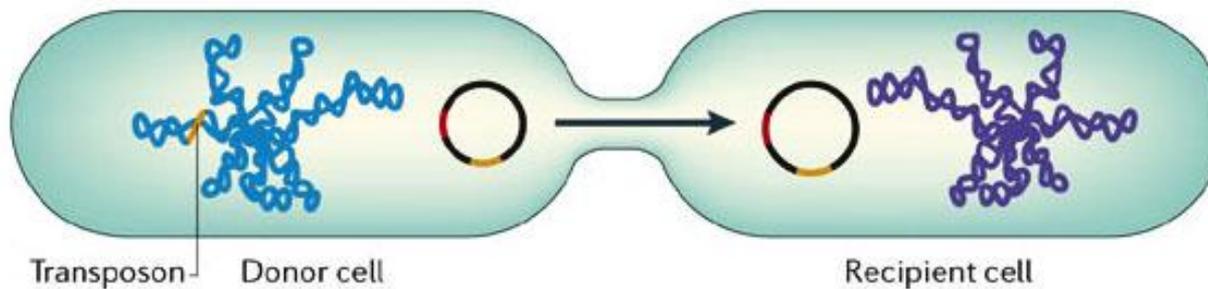
a Bacterial transformation



b Bacterial transduction



c Bacterial conjugation



Antibiotics in Agriculture

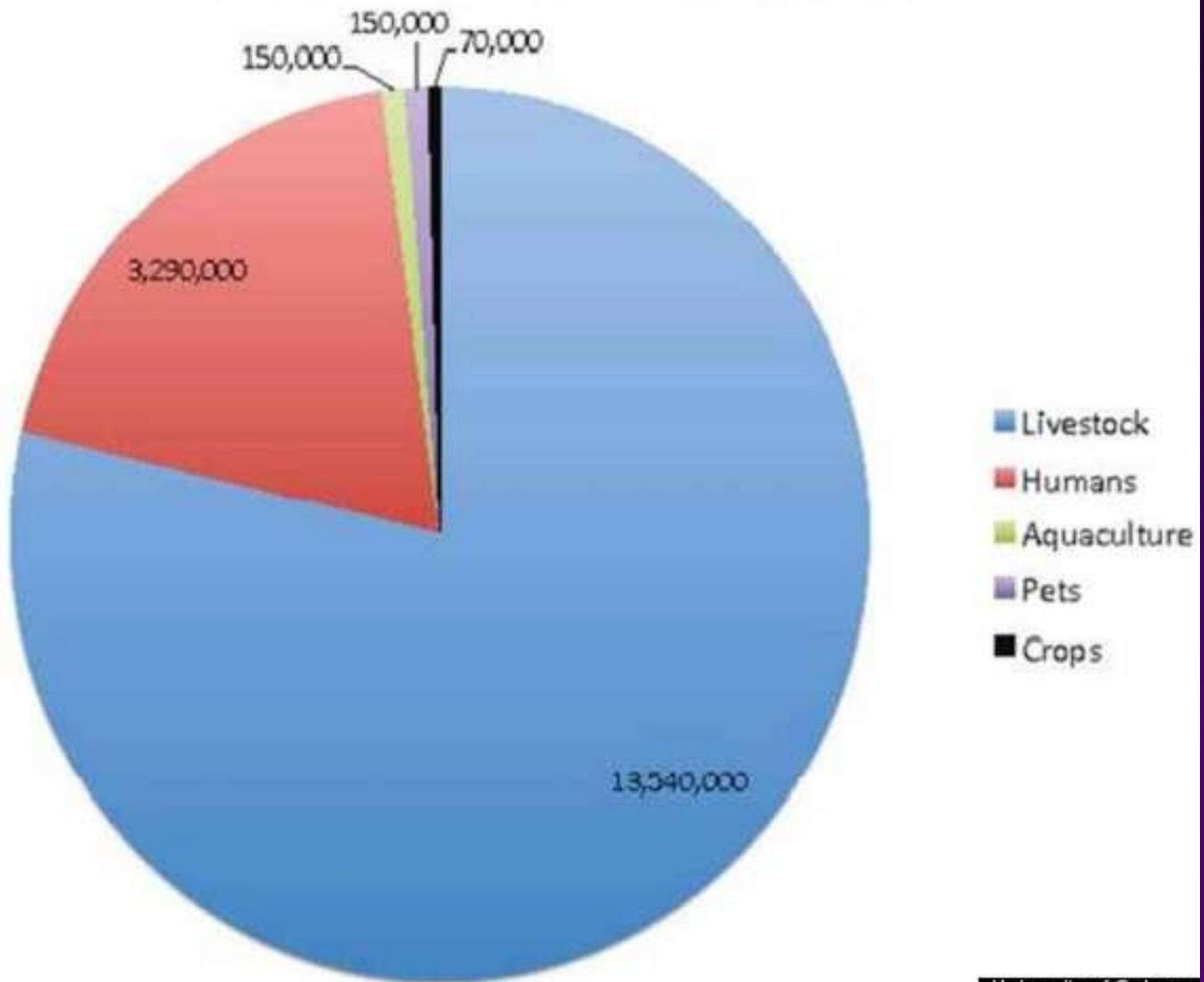
- Treatment of disease
- Prevention of disease
- Control of disease
- Improved feed efficiency
- Improved rate of gain

- In the U.S. 60 to 80% antibiotics used in animal production
- >80% of antibiotics excreted in manure
- AR manures increase AR levels in soils
 - How long?

Antimicrobials in crops

- Streptomycin and oxytetracycline
- Fruit Crops
 - Apple, Nectarine, Peach, Pear
- Vegetables
 - Bean, Celery, Pepper, Potato
- Horticultural Crops

Estimated US antibiotic use (annual kgs, approx)



Which agricultural antibiotics have a real possibility to impact human health?

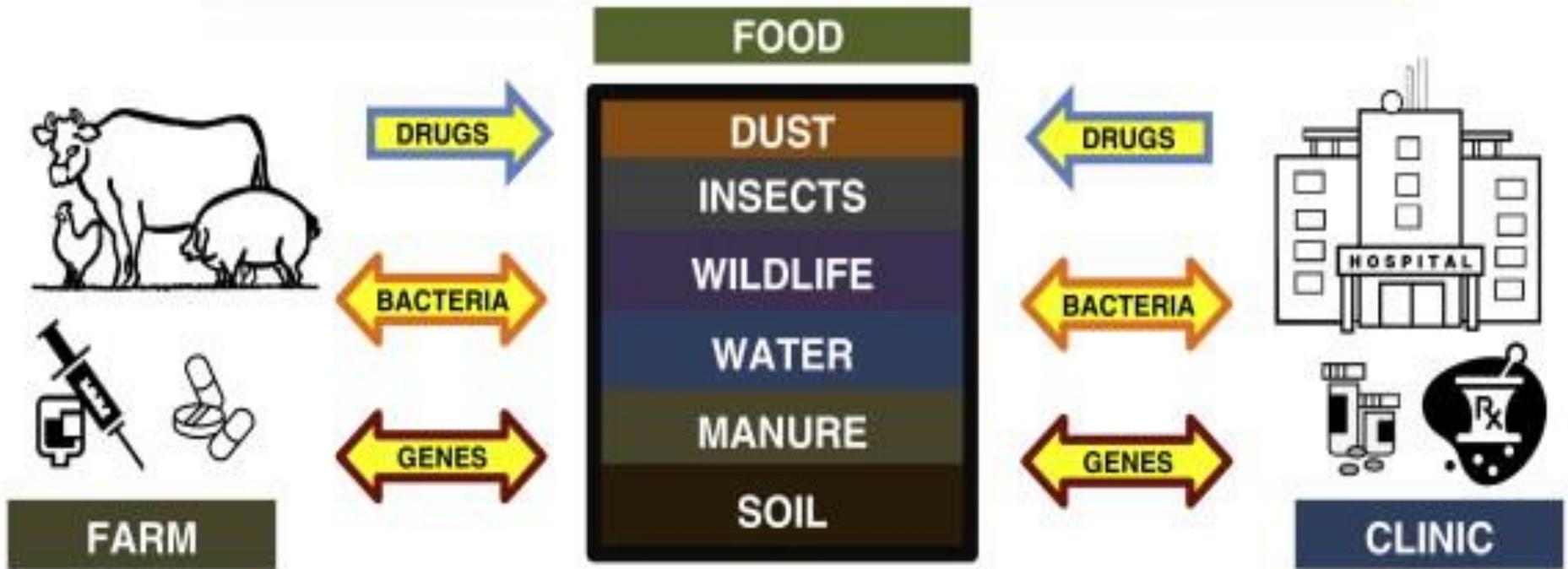
- Veterinary drug information
- Information from CDC prioritized list of bacteria posing antibiotic resistance threats
- Information regarding the ecology of pathogens

WHO drugs of importance in U.S. cattle, swine, and poultry

WHO drugs	# Drugs on list	#given to livestock	# administered to livestock only
	250	39	17

CDC Threat List 2013	Drugs of concern in human medicine that are also used in food animals
Urgent Threats	
Clostridium difficile	Metronidazole
Drug-Resistant Neisseria gonorrhoeae	Azithromycin; Tetracycline
Serious Threats	
Multidrug-resistant Acinetobacter	Ampicillin; Polymyxin
Drug-resistant Campylobacter	Fluoroquinolones; Macrolides
Enterobacteriaceae	Cephalosporins; Penicillins
Drug-resistant Salmonella typhi	Azithromycin
Drug-resistant Shigella	Azithromycin
Methicillin-resistant Staphylococcus aureus	Cephalosporins; Gentamycin; Rifampicin
Drug-resistant tuberculosis	Amikacin; Fluoroquinolones; Rifampicin
Concerning Threats	
Erythromycin-resistant Streptococcus	Erythromycin

What are baseline levels of drugs, bacteria and genes?



Current Opinion in Microbiology

Movement of antibiotic resistance between farm and clinic. The environment is a reservoir of resistance, and a conduit of resistance between farm and clinic. Specific mechanisms of are transport remain uncertain.

Durso, L., and K. Cook. Current Opinion Microb. 19:37–44

- Antibiotic use enriches bacteria carrying antibiotic resistance genes (AR genes)
- Antibiotic resistant bacteria (AR bacteria) and AR genes from agricultural settings can be physically transferred to humans.
- However how and at what rate bacteria and genes move from animals to humans through agricultural systems (soil, water, wildlife, insects, dust, food,) remain to be determined.

- Results suggest that the concentration of bacteria with AR genes increases in soils where livestock congregate, but are effectively restricted to those areas by the presence of grass filter strips down-gradient.
- The concentration of AR genes remained elevated for two years after livestock were removed from the site.

- A challenge for evaluating benefits and risks of agricultural antibiotic use is that AR occurs naturally in the environment
- Efforts to reduce the impact of agricultural antibiotic use should focus on determining which types of agriculturally used AR are most important to human health

What are the needs

- Need accurate data on antimicrobial use in agriculture
- Need research on fate of antimicrobials in the environment
- To assess benefits and risks of antibiotic use in agriculture, need information on baseline and natural levels of resistance
- Fate of antibiotics in the environment
- Critical need for research on the ecology of antibiotic resistance to identify types of resistance that are:
 - ecologically relevant to agricultural systems,
 - microbiologically relevant
 - clinically relevant

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