

IMED• Vienna • November 2016

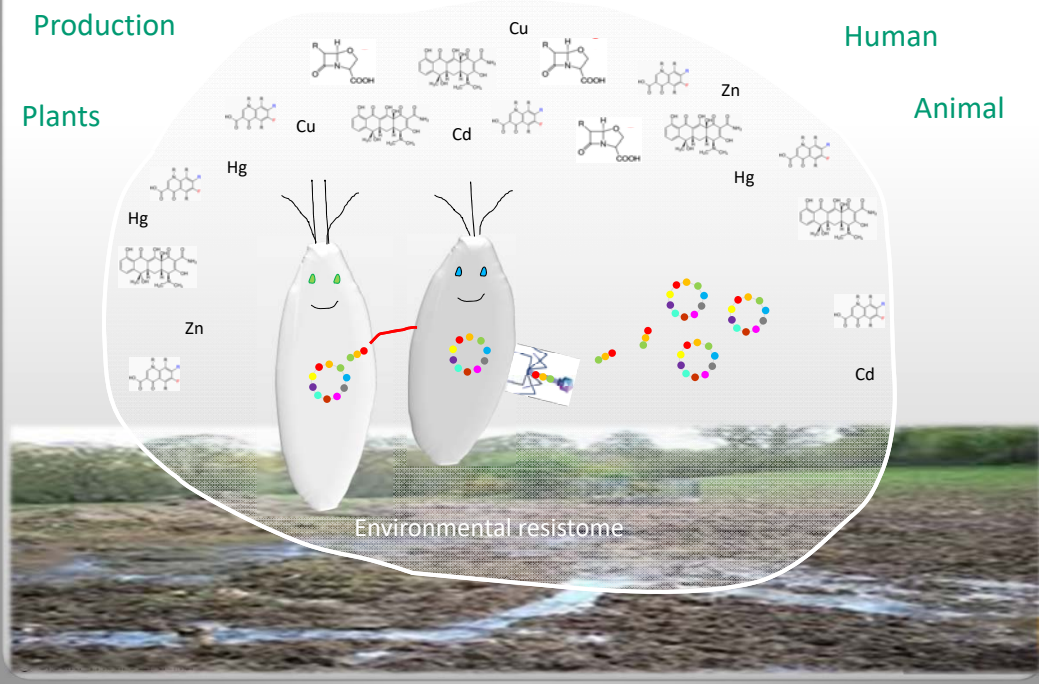
Ecology and Environmental Drivers of Antimicrobial Resistance

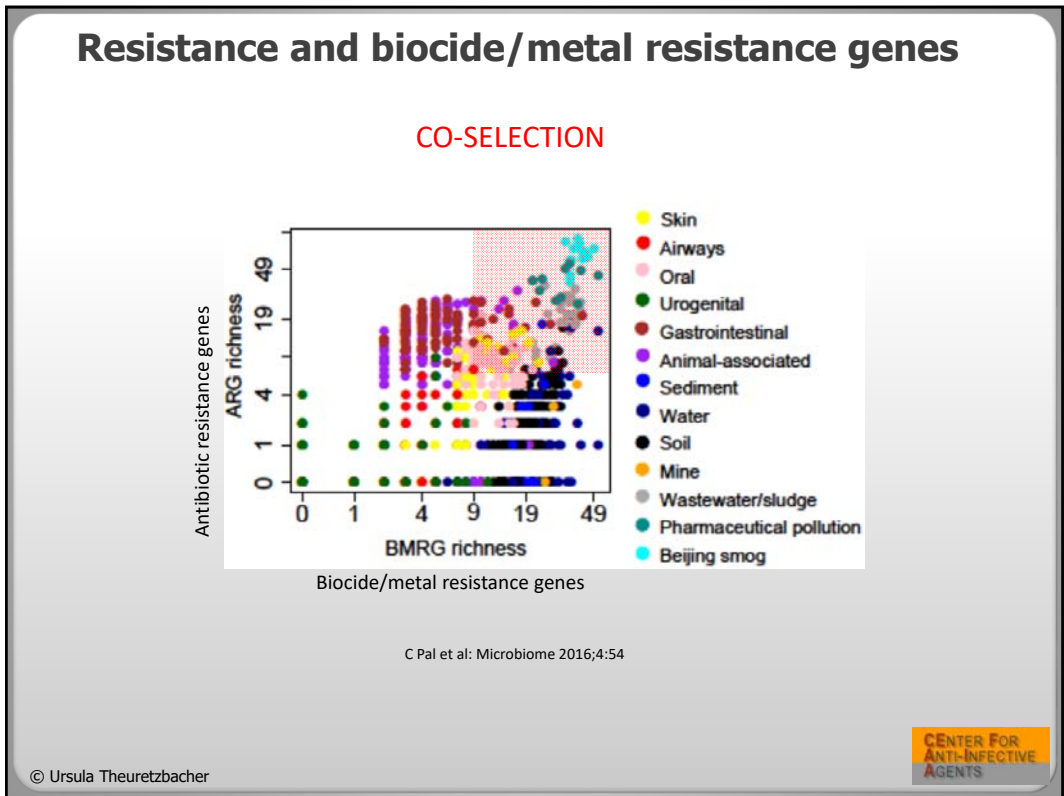
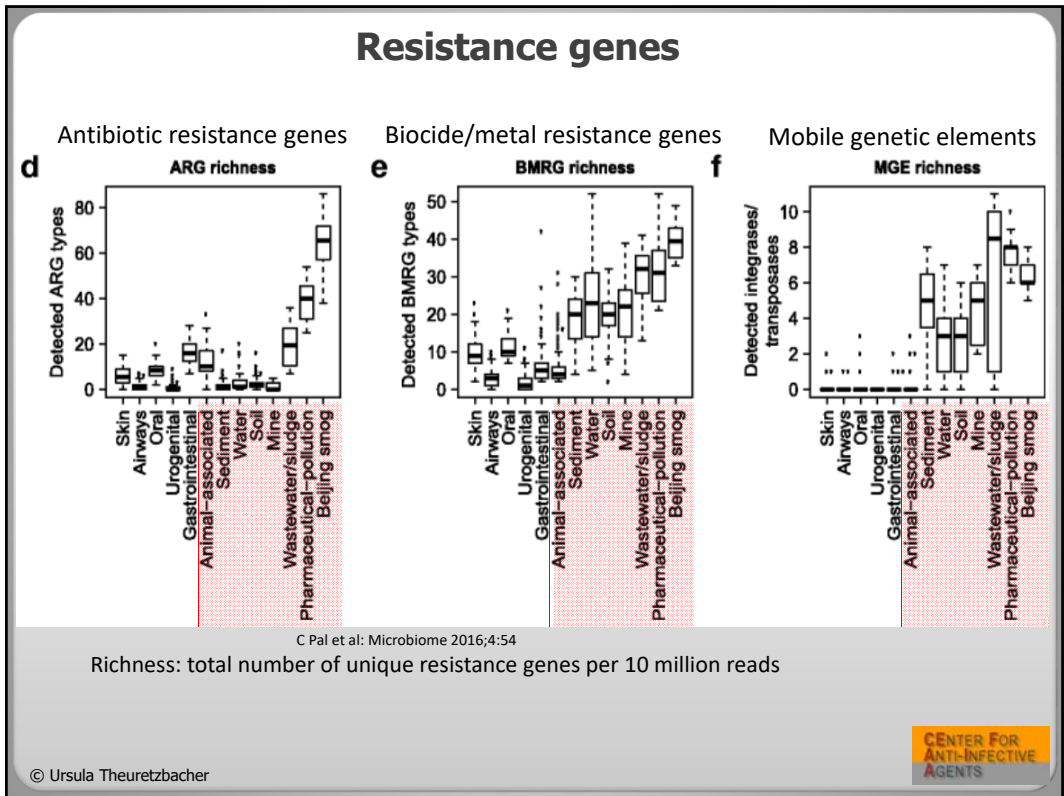
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Resistant bacteria, antibiotic resistance genes, selective agents in the environment





Resistance hot spots

- Effluents from production sites
- Water contaminated with effluents from livestock farm or aquaculture
- Animal manures from live stock farms
- Sewage sludge recycled onto agricultural land
- Hospital wastewaters
- Incompletely treated urban wastewaters
- Recycled drinking water

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Waste-water treatment plants

- Effluent contain antibiotics in high concentrations
- Example: Bulk drug manufacturing facilities near Hyderabad
 - Ciprofloxacin: 45 kg of API per day
 - Sampled strains: 86% resistant to ≥ 20 antibiotics
 - Class 1 and/or class 2 integrons in 95% of strains
- Example: Drug manufacturing facilities in China
 - 275kg of the antibiotic oxytetracycline per day into the Xiao River, higher concentrations than therapeutic



Drugs	Levels in $\mu\text{g/l}$
Ciprofloxacin	28,000-31,000
Losartan	2,400-2,500
Cetirizine	1,300-1,400
Metoprolol	800-950
Enrofloxacin	780-900
Citalopram	770-840
Norfloxacin	390-420
Lomefloxacin	150-300
Enoxacin	150-300
Ofloxacin	150-160
Ranitidin	90-160

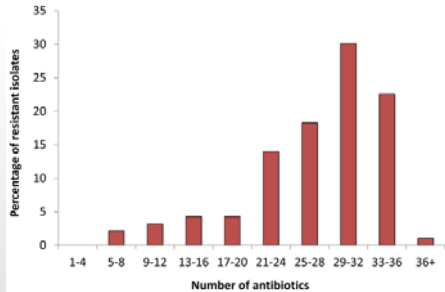
NP Marathe et al: PLoS ONE 8(10): e77310
 Larsson DG et al: J Hazard Mater. 2007;148(3):751-5

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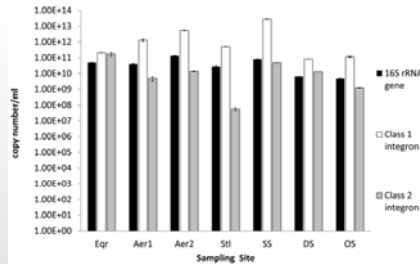
Resistance in a waste-water treatment plant

Patancheru, Hyderabad

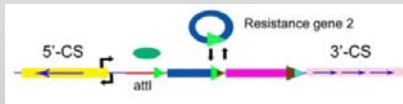
Multi-drug resistance



16S rRNA gene copy number and copy numbers of integron classes 1 and 2



Marathe NP et al. PLoS ONE 2013; 8(10): e77310

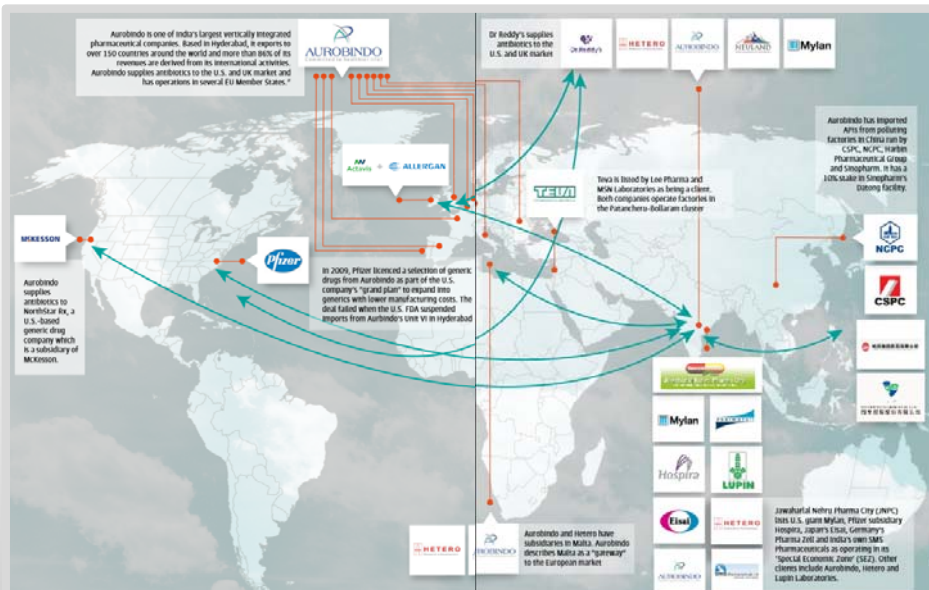


Y Deng et al: Ann Clin Microbiol Antimicrob. 2015; 14: 45.

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Pharmaceutical Pollution



Swedish investment bank Nordea, Responsible investment 2016: Impacts of Pharmaceutical Pollution on Communities and Environment in India

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Animal farming

Hot spots: Swine farms

- Complex mixture with high numbers of different growth-promoting chemicals, including antibiotics and metals
- Co-selection
- 149 unique microbial ARGs
- ARG highly enriched (about 200 fold, up to 121,000-fold, up to 19 unique *tet* genes in a single site)
- Mobile genetic (plasmids, integrases, and transposases)
- Transposases highly enriched (up to 90,000-fold)
- Horizontal gene transfer and resistance gene fixation in genome

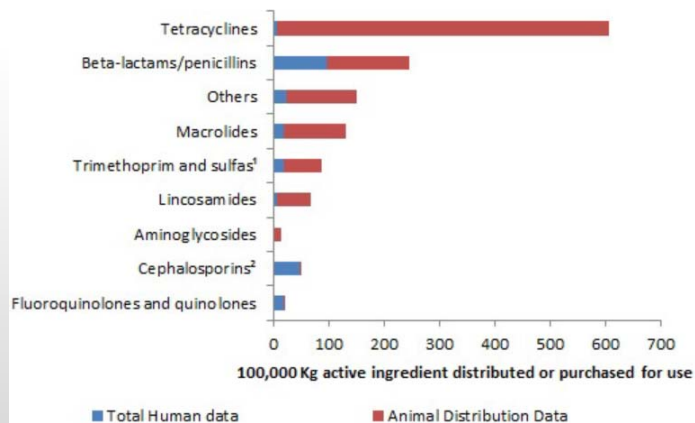
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Y-G Zhu et al: PNAS 2013, 2013, 110:3435-40



Antibiotics for use in animals and humans

Canada 2014



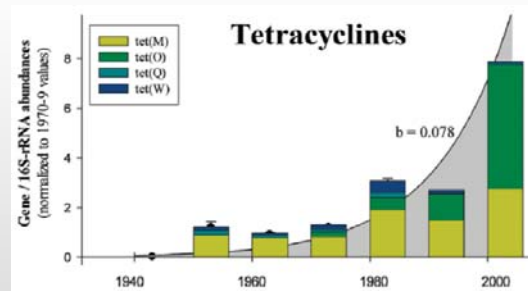
CCDR: Volume 42-11, November 3, 2016

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Soil

Quantitative changes in resistance



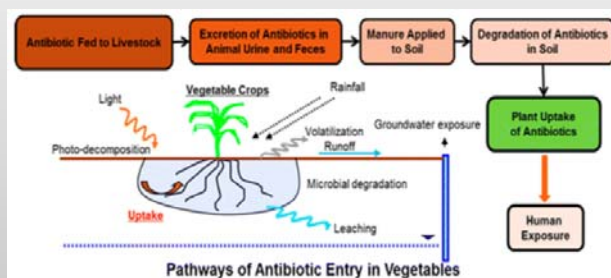
CW Knapp et al: Environmental science & technology 2010; 44 (2), 580-587

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Agriculture

- Antibiotic residues in surface soil:
 - Example: CFX, EFX and NFX means estimated: 107.3 μ g/kg, 17.4 μ g/kg and 57.1 μ g/kg, respectively. (Sci. Total Environ. 2012, 430 , 126–131)
- Antibiotics residues in plants via waste water irrigation
- Vegetables that were grown in manure-applied soil
 - Florfenicol, enrofloxacin, trimethoprim, and levamisole in their leaves or roots



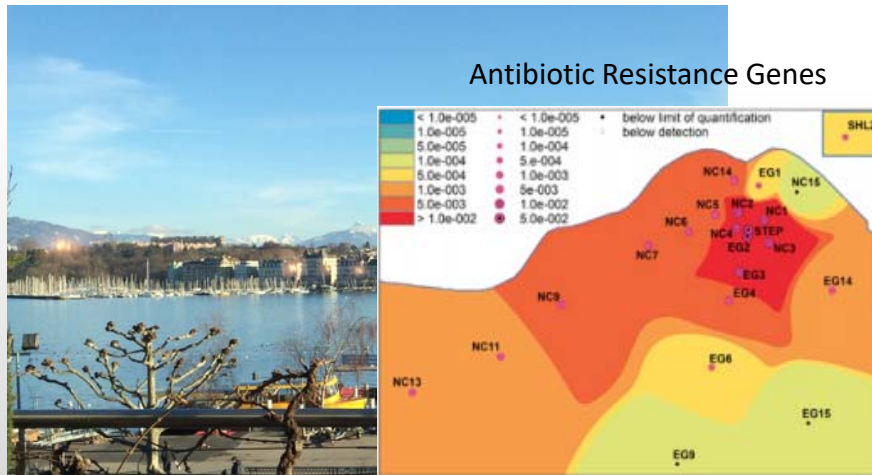
DH Kang et al: J. Agric. Food Chem., 2013, 61 (42), pp 9992–1000

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Hospital Wastewater

Lake Geneva



Czekalski et al: *ISME J* 2014;8:1381–90

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Resistance hot spots in the environment

"A dosed planet"

- Large amount of antibiotics resistance genes are disseminated into the environment
- Resistome and mobilome elements are not necessarily removed by water treatment
- Interactions between mobile elements
- Lateral transfer between pathogens, commensals, and environmental bacteria
- More research required
- Extensive global and national policies required

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