Antibiotic Resistance: the Quintessential One Health Issue

Multiple disciplines
  Clinical, Environmental
  Policy
  Statisticians

Working locally, nationally, and globally

To attain health for people, animals, and the environment
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Closely linked – not by disease, but by resistance
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What is known? What is not known?
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Closely linked – not by disease, but by resistance
The ability of a bacterium to prevent an antibiotic from adversely affecting that isolate, strain, or group.

**Horizontal Gene Transfer** confers antibiotic resistance in response to selective pressure

**Clinical settings**
- High antibiotic dosages

Resistance – anthropogenic?
Antibiotic Resistant Bacteria

Earliest antibiotics: naturally produced (e.g., Penicillin)
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Resistant to macrolides, aminoglycosides

AND synthetics – e.g., quinolones
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Resistance genes evolved in absence of selective pressure from humans, but why??
Antibiotic Resistant Bacteria

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Environment has a role in emergence and spread

Case Study #1: Water Recycling
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Environmental Antibiotic Resistance

Agricultural and clinical use of antibiotics, up to 75% excreted unaltered or as metabolites
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Agricultural and clinical use of antibiotics, up to *75% excreted unaltered* or as metabolites

Only the most modern wastewater treatment plants are designed for selective removal of these micropollutants

Recycled wastewater

Biosolids
Environmental Antibiotic Resistance

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Recycled wastewater
Biosolids

Proposed that this is a “key source of resistance to the environment”
Does Recycled Municipal Wastewater Induce Antibiotic Resistance?
Gilbert Riparian Preserve

Created in 1986, seven recharge basins receive tertiary-treated recycled water.
Gilbert Riparian Preserve

Created in 1986, seven recharge basins receive tertiary-treated recycled water

Control site: agricultural irrigation retention pond
Field Sampling over Two Years

*Enterococcus* spp.

GI tracts of humans and animals; environmental persistence

Great capacity for gene transfer
Enterococcus spp.

GI tracts of humans and animals; environmental persistence

Great capacity for gene transfer

Emergence of multiple drug-resistant strains in clinical settings

Ideal bacterial group for investigating the ecology of resistance development
# High Level Antibiotic Resistance

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Multi-Antibiotic Resistance – “Superbugs”

![Graph showing the percentage of resistant isolates for different total numbers of antibiotics for reclaimed water recharge.]

- **0**
- **1 to 3**
- **4 to 6**
- **7+**

- **Reclaimed Water Recharge**
Multi-Antibiotic Resistance – “Superbugs”

![Graph showing the percentage of resistant isolates for different total numbers of antibiotics, comparing Reclaimed Water Recharge and Groundwater Recharge.]

- **Reclaimed Water Recharge**
  - Zero: 10%
  - 1 to 3: 60%
  - 4 to 6: 20%
  - 7+: 5%

- **Groundwater Recharge**
  - Zero: 5%
  - 1 to 3: 15%
  - 4 to 6: 40%
  - 7+: 10%
Multi-Antibiotic Resistance – “Superbugs”

![Graph showing antibiotic resistance](image-url)

- **Total Number of Antibiotics**
  - Zero
  - 1 to 3
  - 4 to 6
  - 7+

- **Resistant Isolates (%)**
  - 0
  - 10
  - 20
  - 30
  - 40
  - 50
  - 60
  - 70

- **Methods**
  - Reclaimed Water Recharge
  - Groundwater Recharge

- **Question Mark**
What Does This Mean?

Antibiotic resistance: “metabolically expensive”

Recycled Water, Biosolids = Adding Soil Carbon

McLain and Williams (2014) *Sustainability*, 6, 1313-1327
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Environmental complexity – not a direct cause/effect

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Pollution via Antibiotic Resistance Genes

Review

Urban wastewater treatment plants as hotspots for antibiotic resistant bacteria and genes spread into the environment: A review

L. Rizzo a, A, C. Manaia b, C. Merlin c, T. Schwartz d, C. Dagcot e, M.C. Ploy f, I. Michael g, D. Fatta-Kassinos g
Review

Urban wastewater as a source of antibiotic resistant bacteria: a systematic review
L. Rizzo, C. Ma, C. Murray

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Antibiotic resistance genes as an emerging environmental contaminant
Haley Sanderson, Colin Fricker, R. Stephen Brown, Anna Majury, Steven N. Liss
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Science of the Total Environment
Volume 447, 1 March 2013, Pages 345-360

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Environmental Science & Technology

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Cell-free DNA: A Neglected Source for Antibiotic Resistance Genes Spreading from WWTPs
Yan Zhang, Aolin Li, Tianjiao Dai, Feifei Li, Hui Xie, Lujun Chen, Donghui Wen

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¶ Zhejiang Provincial Key Laboratory of Water Science and Technology, Department of Environmental Technology and Ecology, Yangtze Delta Region Institute of Tsinghua University, Zhejiang Jiaxing 314050, China
Antibiotic Resistance Genes and “Cell-Free DNA”

Antibiotic Resistance Genes and “Cell-Free DNA”


- As much as 50% of total DNA was “free DNA”
- Quantified intact resistance genes by PCR, qPCR
What is KNOWN and What is UNKNOWN about Antibiotic Resistance in Environmental Bacteria?

It is ancient – studies need control sites
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Human activities are depositing trace levels of antibiotics and resistance genes into the environment
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Culturing studies do not show cause-and-effect
Case Study #2: Antibiotics in Animal Feed

USA Growth promotion – 34.3 million pounds in 2015 (7.7 million pounds for humans) – since 1940s
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EU – began weaning in 1997; ‘judicious use rules’ in 2006

Appropriate drug
Effective drug
At right dose
Correct length of time
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USA – FDA established rules aligning with EU in 2018

Aimed at controlling antibiotic resistant bacteria moving off farms
Case Study #2: Antibiotics in Animal Feed

Denmark* – 105 metric tons of antibiotics in 1996 for growth promotion; by 2000, nearly nil

*DANMAP (2001) Danish Veterinary Laboratory, Copenhagen
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Diminished resistance to multiple antibiotics in fecal enterococci

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Increase in human *Salmonella* infection and resistance

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Over the same time period in Denmark, MRSA infections are increasing (EU/USA trend)

Possibly related to international travel

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Increased use of therapeutic antibiotics for food animals (48 tons in 1996; 94 tons in 2001)

*DANMAP (2001) Danish Veterinary Laboratory, Copenhagen
Changing Practices – is it effective?

World Health Organization: “one of the most critical human health challenges of the next century”
Changing Practices – is it effective?

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One Health approach is required to address development and dissemination – need communication and collaboration between sectors
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Accurate assessments of environmental quality impacts – and accurate assessments of human health risk – increase in importance
Questions?

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https://twitter.com