The emerging threat of multi-drug resistant microorganisms
Emerging crisis

“Without urgent, coordinated action by many stakeholders, the world is headed for a post-antibiotic era, in which common infections and minor injuries which have been treatable for decades can once again kill…”

- Dr. Keiji Fukuda, WHO Assistant Director-General for Health Security, 2014
The WHO priority list

<table>
<thead>
<tr>
<th>PRIORITY: CRITICAL</th>
<th>PRIORITY 2: HIGH</th>
<th>PRIORITY 3: MEDIUM</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acinetobacter baumannii carbapenem-resistant</td>
<td>Enterococcus faecium vancomycin-resistant</td>
<td>Streptococcus pneumoniae penicillin-non-susceptible</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa carbapenem-resistant</td>
<td>Staphylococcus aureus methicillin-resistant vancomycin-intermediate and resistant</td>
<td>Haemophilus influenzae ampicillin-resistant</td>
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<tr>
<td>Enterobacteriaceae carbapenem-resistant, ESBL-producing</td>
<td>Helicobacter pylori clarithromycin-resistant</td>
<td>Shigella spp. fluoroquinolone-resistant</td>
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<td>Campylobacter spp. fluoroquinolone-resistant</td>
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<td>Salmonellae fluoroquinolone-resistant</td>
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<td></td>
<td>Neisseria gonorrhoeae cephalosporin-resistant fluoroquinolone-resistant</td>
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</tbody>
</table>

Source: WHO

But also, e.g., Malaria (protozoan), HIV & influenza (viral), TB (mycobacterial), Candida (fungal)
# Levels of drug resistance

## Categories

- **Multidrug-resistant (MDR):** acquired non-susceptibility to at least one agent in three or more antimicrobial categories

- **Extensively drug-resistant (XDR):** non-susceptibility to at least one agent in all but two or fewer antimicrobial categories

- **Pandrug-resistant (PDR):** non-susceptibility to all agents in all antimicrobial categories

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**FIG. 1.** Diagram showing the relationship of MDR, XDR and PDR to each other.

But see, e.g., de Kraker et al. (2016). Will 10 Million People Die a Year due to Antimicrobial Resistance by 2050?
Impacts on medical practice

- Organ transplants
- C-sections
- Joint replacement
- Chemotherapy
- Childbirth

Total Artificial Heart

Human Heart

Source: SynCardia Systems, https://commons.wikimedia.org/wiki/File:Graphic_of_the_SynCardia_temporary_Total_Artificial_Heart_beside_a_human_heart.jpg

Source: Blausen Medical Communications, https://commons.wikimedia.org/wiki/File:Hip_Replacement.png

Total Hip Replacement
Plague in Florence, 1348. L. Sabatelli.
First antibiotics

- 1907: Salvarsan (arsphenamine), anti-syphilis
- From ~1932: sulfonamides (sulfa)
- 1942: Penicillin (first natural antibiotic)
Emergence of AMR

What is driving MDR emergence and risk?

- Use of antibiotics in medicine
- Use of antibiotics in food systems
- Human population growth/demographics
- Urbanization
- Antibiotic discovery void
Drivers: medical use

- Overprescription (duration)
- Inappropriate prescription (e.g., for viral infection or prophylaxis)
- Non-compliance or self-medication
- Nosocomial infection

CDC is working to reduce unnecessary antibiotic use

White House National Action Plan to Combat Antibiotic-Resistant Bacteria (CARB)

Goal: By 2020, reduce inappropriate outpatient antibiotic use by 50%

Find out when antibiotics are necessary.
Visit: http://www.cdc.gov/getsmart

Centers for Disease Control and Prevention
National Center for Emerging and Zoonotic Infectious Diseases
Drivers: food systems

- Up to 80% of antibiotics go to animals
- Little evidence of efficacy: up to 90% excreted
- Spread to humans through contact or ingestion
- Environmental contamination

RESISTANCE
- Animals can carry harmful bacteria in their intestines
  - When antibiotics are given to animals...
  - Antibiotics kill most bacteria
  - But resistant bacteria can survive and multiply

SPREAD
- Resistant bacteria can spread to...
  - Animal products
  - Produce through contaminated water or soil
  - Prepared food through contaminated surfaces
  - The environment when animals poop

EXPOSURE
- People can get sick with resistant infections from...
  - Contaminated food
  - Contaminated environment

IMPACT
- Some resistant infections cause...
  - About 1 in 5 resistant infections are caused by germs from food and animals
  - Source: Antibiotic Resistance Threats in the United States, 2013

Learn 4 steps to prevent food poisoning at www.foodsafety.gov

Learn more about antibiotic resistance and food safety at www.cdc.gov/foodsafety/antibiotic-resistance.html
Learn more about protecting you and your family from resistant infections at www.cdc.gov/drugresistance/protecting_yourself_family.html
Drivers: population/demographics

- Greater population = more opportunities for evolution of resistance and human-human transmission
- More elderly population = more opportunities for nosocomial spread
Drivers: urbanization

- Patterns of human-human (and sometimes human-animal) contact
- Density of people
- Health system structure and function
- Food system structure and function
Discovery void

- 40s-60s: “glory years of antibiotic discovery” (Hancock and Knowles 1998); numerous new classes of antibiotics
- Very little since; easy wins identified

Systems problems

- Characteristics
  - Detail and dynamic complexity
  - Multiple stakeholders
  - Multiple scales
  - Cross-sectoral/related to other problems
  - Resistance to change
  - Unanticipated outcomes

Source: http://www.innovationmanagement.se/2010/06/14/complexity-science-and-innovation/
Complexity drives outcomes

Any use of antimicrobials, however appropriate and conservative, contributes to the development of resistance”

- Review on Antimicrobial Resistance, 2014

Source: Newell and Siri, 2016. A role for low-order system dynamics models in urban health policy-making
Complexity and engagement

- Real systems have many parts
- Understanding parts ≠ understanding system
- Silos lead to restricted focus

Source: Cherau et al. (2017). Risk assessment for antibiotic resistance in South East Asia
Systems approaches

- Systems methods to:
  - Characterize and measure feedback
  - Identify leverage points for action
  - Forecast likely outcomes and compare policy scenarios

- Collaborative work (co-production of knowledge/ inter- and trans-disciplinarity / stakeholder involvement) to:
  - Improve communication
  - Provide more complete understanding of systems
  - Assess feasibility of actions
  - Promote stakeholder ownership
Solutions

- New antibiotic development
- Stewardship of existing antibiotics
  - Reduce use in animal husbandry
  - Reduce human-animal contact
  - Reduce inappropriate prescriptions
  - Improve diagnosis and treatment choice
  - Improve compliance
  - Prevent nosocomial infections
- Promote systemic change
  - Grow cross-sectoral communication
  - Highlight feedback narratives
  - Change incentives for all actors
  - Make correct action convenient
Thank you!

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