The bioethics around rapid diagnostics and the battle against antibiotic resistance

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Antibiotic resistance: the stats

- Antibiotic resistance develops when bacteria mutate upon being overexposed to antibiotics in people or animals.[1]

- According to the Centers for Disease Control, in the United States alone, drug resistant infections sicken 2.8 million people annually and are responsible for at least 35,000 deaths each year.[2]

- The United Nations has suggested that, if the problem is not soon addressed, antibiotic resistant infections could kill up to 10 million people globally by 2050.[3]

[1] Munthe, C. *et. al.* "Health-related Research Ethics and Social Value: Antibiotic Resistance Intervention Research and Pragmatic Risks." *Bioethics*. 33:335-342 (2019).

[2] "About Antibiotic Resistance." *The Centers for Disease Control*. Available at: https://www.cdc.gov/drugresistance/about.html

[3] Jacobs, A. "Doctors Heavily Overprescribed Antibiotics Early in the Pandemic." *The New York Times*. (June 4, 2020).

Overuse / misuse in humans: Failing to identify pathogens

*****According to studies, treatment decisions involving antibiotics, including whether to use an antibiotic, which antibiotic to use, and the appropriate duration of such use, are incorrect in 30 percent to 50 percent of cases.[4]**

- The overuse / misuse of antibiotics in this manner can give rise to the problem of antibiotic resistance.[5]
- In many cases, faulty clinical determinations can be attributed to the lack of available microbial testing. Healthcare providers are unable to properly identify and classify bacteria, thus impairing their ability to make clinically sound treatment decisions.[6]
- When healthcare providers use bacterial testing, they often rely upon culture testing, which can have a lengthy turnaround time and lead to delayed or incorrect treatment regimens.[7]

[4] Ventola, C.L. "The Antibiotic Resistance Crisis." *Pharmacy and Therapeutics*. 40:4:277-283 (2015).
[5] Ventola, C.L.
[6] Ventola, C.L.
[7] Parsonage, B., *et al*. "Control of Antimicrobial Resistance Requires an Ethical Approach." *Frontiers in Microbiology*. 8:2124 (November 2, 2017)

The fallout from a lack of rapid diagnostics

Therefore, when faced with the inability to rapidly identify pathogenic bacteria, the healthcare provider may:

1. prescribe an antibiotic when it is unwarranted (for a viral infection, for example);
2. prescribe an incorrect antibiotic;
3. prescribe a powerful, broad-spectrum ”catch all” antibiotic to cover the widest range of possible bacteria (when a simpler antibiotic would suffice);
4. delay administration of an antibiotic until culture or blood results are available;
5. withhold an antibiotic altogether (for fear of overprescribing antibiotics in general).

The lack of rapid diagnostics harms patients

*****In each of these scenarios, healthcare providers are harming their patients.**

- **Wrong antibiotic / delaying an antibiotic** = deterioration in the patient's present condition.
- **Wrong antibiotics / Broad spectrum antibiotics** = also increase risk of antibiotic resistance within the patient resulting in treatment failure in future infections.
- **Withholding antibiotic altogether to prevent resistance** = can lead to benign infections turning deadly. (Untreated bronchitis can rapidly progress to pneumonia. Untreated strep throat can lead to heart damage. A lingering urinary tract infection can induce sepsis).

Bioethical implications

*****The harm that results from improper antibiotic decision-making is violative of the bioethical duties that healthcare providers owe to their patients.**

- These include the duties of **beneficence** – to do good – to heal; and **non-maleficence** – the “do no harm” principle.

- The healthcare provider’s duty to respect the patient’s **autonomy** is likewise infringed.

  - Patients are owed the right to full **informed consent which includes the risks & benefits of a proposed treatment and of any alternatives.**

  - Yet, unbeknownst to patients, providers may be lacking info re: pathogens, and therefore of the risks/benefits and alternatives of treatment.

  - This results in patients relying on treatment plan to their detriment.

The need for rapid, point-of-care, diagnostics

***Rapid, point-of-care diagnostics, can help ensure that treatment decisions involving antibiotics are made with empirical data, rather than being an exercise in supposition.**

***This assists healthcare providers in upholding their bioethical duties to patients, while helping to combat the antibiotic resistance crisis.**

- Therefore, pharmaceutical/biotech industries should endeavor to develop accurate, rapid testing technology.
  - ***Bioethical consideration***: pharma/biotech have an obligation of **non-maleficence** to patient consumers in that they must ensure that rapid diagnostics do not sacrifice accuracy for speed = could also lead to harmful treatment decisions.

The social justice challenge

The development of rapid diagnostics is of critical importance – but there is a serious bioethical challenge for which we must prepare…

Potential challenge: *Rapid diagnostics may carry a higher price tag than current tests, such as routine cultures. This can present a problem with upholding the bioethical principle of* ***social justice.***

The principle of social justice requires *that all patients be treated equally.*

****All stakeholders must uphold the principle of social justice****

How can stakeholders uphold the principle of social justice?

- **Healthcare Providers (physicians, hospitals, etc.)**
  - ✓ Must offer life-saving diagnostics to all patients, regardless of ability to pay.
- **Pharma / Biotech**
  - ✓ Find ways to keep costs as low as possible to promote accessibility.
- **State and Federal Governments**
  - ✓ Special ethical obligation to help forestall the antibiotic resistance crisis to ensure the health of citizens. Should work towards subsidizing rapid tests (like with COVID-19 tests) to ensure they are available to all.
  - ✓ Must ensure that test are widely distributed and available – especially amongst healthcare providers in low-income communities.
- **Third Party Payors**
  - ✓ Ethical obligation to cover the costs of these diagnostics.
  - ✓ Rapid diagnostics should be regarded as routine tests rather than specialty tests, which can be excluded from coverage.
  - ✓ Failure of insurers to pay would be an unjustifiable interference with healthcare providers' ethical obligations to patients.
  - ✓ In any event, it's actually more cost-effective for insurers to pay, since tools will cut long-term costs by reducing patient morbidity and mortality.

Important to recognize other contributors to antibiotic resistance

- **Unregulated agricultural use of antibiotics in animals**
  - Approx. half of the world's consumption of antibiotics is for agricultural purposes.[8] In the US, only 20 percent of antibiotic sales are intended for human use, while the remaining 80 percent is for use in livestock.[9]
  - Antibiotics used for non-therapeutic purposes, such as for growth promotion and disease prevention in response to extremely overcrowded animal housing conditions.[10]
  - Antibiotics and their residues enter the food and water supply, making their way to people.[11]
  - There is no meaningful governmental regulations or monitoring around use of antibiotics in agriculture.[12]

*****Govt. (the FDA) has an ethical obligation to regulate and monitor such use for the safety of its citizens.**

- **Unregulated antibiotic prescriptions in developing nations**[13]
  - Antibiotic resistance is a global problem! There is spillover from other nations, as we saw with COVID-19.

[8] Littmann, J. *et al*. "The Ethical Significance of Antimicrobial Resistance." *Public Health Ethics*. 8:3:209-224 (2015).
[9] Chin, T. "Antibiotic Resistance." *Health Affairs*. (May 21, 2015); He, Y. "Antibiotic resistance genes from livestock waste: occurrence, dissemination, and treatment." *NPJ Clean Water*. 3:4 (2020).
[10] Manyi-Loh, C. "Antibiotic use in Agriculture and Its Consequential Resistance in Environmental Sources: Potential Public Health Implications." *Molecules*. 23:795 (2018); Duckenfield, J. "Antibiotic Resistance Due to Modern Agricultural Practices: An Ethical Perspective." *Journal of Agricultural and Environmental Ethics*. 26:333-350 (2013).
[11] He, Y. "Antibiotic resistance genes from livestock waste: occurrence, dissemination, and treatment." *NPJ Clean Water*. 3:4 (2020); Manyi-Loh, C. "Antibiotic use in Agriculture and Its Consequential Resistance in Environmental Sources: Potential Public Health Implications." *Molecules*. 23:795 (2018).
[12]. Reiley, L. "Some beef 'raised without antibiotics' tests positive for antibiotics in study." *Washington Post*. April 7, 2022; Richtel, M. "Tainted Pork, Ill Consumers and an Investigation Thwarted." *The New York Times*. August 4, 2019; "Questions and Answers: Summary Report on Antimicrobials Sold or Distributed for Use in Food-Producing Animals." *The Food and Drug Administration*. Available at: https://www.fda.gov/industry/animal-drug-user-fee-act-adufa/questions-and-answers-summary-report-antimicrobials-sold-or-distributed-use-food-producing-animals
[13] Manyi-Loh, C.; "Antibiotic Resistance - Key Facts." World Health Organization. Available at: https://www.who.int/news-room/fact-sheets/detail/antibiotic-resistance

Summary

- Rapid diagnostics will help healthcare providers mitigate improper treatment decisions which harm patients in violation of the bioethical principles.
- Stakeholders, including pharma / biotech, government, healthcare providers, and third party payors, have corresponding bioethical imperatives to create, distribute, utilize, and subsidize reliable, rapid, point-of-care diagnostics.
- Diagnostics must be justly distributed and financially accessible in conformity with the principle of social justice.
- We must simultaneously address the other causes of antibiotic resistance, such as antibiotic use in agriculture and unregulated use of antibiotics in developing nations.

As the World Health Organization has observed, the antibiotic resistance crisis may seem slow-moving and abstract compared to the COVID-19 pandemic.

However, antibiotic resistance is a growing concern for everyone around the globe and the problem demands our collective, focused attention.

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