Antibiotic Disposal and Resistance in Our Water Systems

By: Gwen Maly, Robbie Gonzales, Marisa Perez, Ashley Glazener, and Phil Romero
Introduction

“Pharmaceuticals were first discovered in the environment around 30 years ago” (Garrison et al., 1976, Hignite and Azarnoff, 1977, Waggot, 1981).

Antibiotic resistance is now more of a problem than it ever has been, but why?

Improper disposal of antibiotics is one of the major players leading to a rise in resistant bacteria, especially in our water systems.
What is antibiotic resistance?

- Antibiotics are drugs that fight bacterial infections (CDC 2017).
- For example, the antibiotic cephalexin treats streptococcal bacterial infections.
- Antibiotic resistance occurs when the bacteria is not killed by the antibiotic and multiplies (CDC 2017).
- Antibiotic resistant bacteria have genes that allow the microbe to evade the drugs designed to kill it (Madigan et al. 2019).
- Resistance is most commonly found emerging from soils and waterways polluted with traces of antibiotics and traces of bacteria encoded with antibiotic-resistant genes (Madigan et al. 2019).
The figure displays the World Health Organization priority pathogens that are in need of new antibiotics due to antibiotic resistance (Barancheshme et al. 2018).

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Antibiotic resistance</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PRIORITy 1: CRITICAL</strong></td>
<td></td>
</tr>
<tr>
<td>Acinetobacter baumannii</td>
<td>Carbapenem</td>
</tr>
<tr>
<td>Pseudomonas aeruginosa</td>
<td>Carbapenem</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td>Carbapenem, ESBL(^a)-producing</td>
</tr>
<tr>
<td><strong>PRIORITy 2: HIGH</strong></td>
<td></td>
</tr>
<tr>
<td>Enterococcus faecium</td>
<td>Vancomycin</td>
</tr>
<tr>
<td>Staphylococcus aureus</td>
<td>Methicillin, vancomycin-intermediate, and resistant</td>
</tr>
<tr>
<td>Helicobacter pylori</td>
<td>Clarithromycin</td>
</tr>
<tr>
<td>Campylobacter spp.</td>
<td>Fluoroquinolone</td>
</tr>
<tr>
<td>Salmonellae</td>
<td>Fluoroquinolone</td>
</tr>
<tr>
<td>Neisseria gonorrhoeae</td>
<td>Cephalosporin, fluoroquinolone</td>
</tr>
<tr>
<td><strong>PRIORITy 3: MEDIUM</strong></td>
<td></td>
</tr>
<tr>
<td>Streptococcus pneumoniae</td>
<td>Penicillin-non-susceptible</td>
</tr>
<tr>
<td>Haemophilus influenzae</td>
<td>Ampicillin</td>
</tr>
<tr>
<td>Shigella spp.</td>
<td>Fluoroquinolone</td>
</tr>
</tbody>
</table>

\(^a\)Extended Spectrum Beta-Lactamases. The ESBL enzyme breaks down and destroys most antibiotics causing them to be inactive, which is why they are not effective against infections caused by these types of bacteria.
Why is antibiotic resistance a problem?

1. Antibiotic resistant bacteria can cause illnesses that were once easily treatable with antibiotics to become untreatable, leading to dangerous infections. In some cases, the antibiotic-resistant infections can lead to serious disability or even death (CDC 2017).
2. Antibiotic-resistant bacteria are often more difficult to kill and more expensive to treat (CDC 2017).
3. Antibiotic resistant bacteria can be found nearly everywhere antibiotics are disposed of (Madigan et al. 2019).
4. According to a O’Neill 2014, unless countermeasures are taken the number of fatalities worldwide from antibiotic resistance will reach 10 million a year by 2050, which would exceed cancer as the current leading cause of death (Azuma et al. 2019, p. 1).
5. Total economic losses caused by antibiotic resistance would exceed 100 trillion dollars in terms of global gross domestic production (Azuma et al. 2019, p. 1).
Summary: Antibiotic resistance is getting in our water systems and has risks of increased pathogenicity, infection, hospitalization, and mortality.

<table>
<thead>
<tr>
<th>AR hotspot reservoirs</th>
<th>[1] AR in drinking water sources</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medical facilities</td>
<td>Surface water</td>
</tr>
<tr>
<td>Funeral parlors</td>
<td></td>
</tr>
<tr>
<td>On-site sanitation systems e.g. septic tanks</td>
<td>Groundwater system</td>
</tr>
<tr>
<td>Aquaculture</td>
<td>Adsorption on soil matrix</td>
</tr>
<tr>
<td>Cemeteries/ gravesites</td>
<td>Infiltration</td>
</tr>
<tr>
<td>Households</td>
<td>Recharge</td>
</tr>
<tr>
<td>Stormwater</td>
<td>AR in soil matrix</td>
</tr>
</tbody>
</table>

- Wastewaters
- Leachate
- Sediments
- Biowastes

AR: antibiotic resistance

<table>
<thead>
<tr>
<th>Water treatment</th>
<th>[4] AR in drinking water</th>
</tr>
</thead>
<tbody>
<tr>
<td>Conventional water treatment</td>
<td>- Residual AR</td>
</tr>
<tr>
<td>Advanced water treatment</td>
<td>- AR from biofilms in reticulation systems</td>
</tr>
</tbody>
</table>

- Ingestion

Risks/impacts:
1. Development of antimicrobial resistance
2. Increased virulence & pathogenicity
3. Increase microbial infections
4. Morbidity
5. Mortality

Figure: Sanganyado et al. 2019, p. 1
How is antibiotic resistance accumulating in our water system?

To answer, we will look at disposal methods at 3 levels:

- Small scale: Human disposal
- Medium Scale: Hospital disposal
- Large Scale: Factory disposal
Small Scale: Human Disposal

→ Over prescription of antibiotics has led to an increase in improper and uneducated human disposal, which is harmful to our environment and our water systems.

→ “Every month, 135 million people use prescription medicines with a total of 4 billion prescriptions given out each year” (Wu et al., 2009 p.26).

→ It is not only flushing down the pharmaceuticals in the toilet or sink that has led to pharmaceutical presence in our water system. There is presence of pharmaceuticals from human waste (urine and fecal matter) that poses threats to our environment (Wu et al., 2009 p.5).
Human Disposal

After using the pharmaceutical, metabolism takes place, from here it will be excreted to the sewer as urine or feces. This process will begin by going through a water treatment before making its way into the sewer (The environmental side effects of medication, Boxall).

-Wastewater could be collected and treated and then reused or discharged into a water source; otherwise, it may enter the water sources and carry all the unknown and biologically active pollutants directly or indirectly over to the human body (Health risks associated with pharmaceuticals in wastewater, Koopaei).
For many antibiotics, urine and feces from users can contain considerable amounts of active residues (Antibiotics in the environment, Larsson).

In high-income countries with well-developed sewage infrastructure, discharge to the environment is reduced, but microbial communities within the treatment plants can be exposed to µg/L concentrations of selected antibiotics (Antibiotics in the environment, Larsson).

Much of the antibiotics accumulate in sludge that may be spread on farmland with the intent to recycle nutrients (Antibiotics in the environment, Larsson).

In surface waters receiving municipal waste-water, concentrations of antibiotics rarely exceed 1 µg/L, but are more regularly in the low ng/L range (Antibiotics in the environment, Larsson).
“Environmental monitoring has identified a number of pharmaceuticals, present in some environments at levels high enough to harm aquatic organisms” (Wu et al., 2009 p.10).

Let’s remember: Sick patients still need access to life-saving medicines but the environment needs to be protected from unnecessary harm (Wu et al., 2009 p.26).
Medium Scale: Hospital Disposal

- Hospitals are a major source of antibiotics released into the environment (Diwan et al. 2013, p. 1).
- The development of antibiotic resistance results from exposure of bacteria to antibiotics in the environment, particularly the aquatic environment (Diwan et al. 2013, p. 1).
- Significant quantities of antibiotics in unchanged form or as active metabolites enter into the aquatic environment through hospital wastewater (Diwan et al. 2013, p. 1).
Hospital Wastewater

- Bacteria resistant to antibiotics have been discovered at high levels in hospital sewage effluent (Azuma et al. 2019, p. 2).
- Wastewater from hospitals is possibly the main source of pathogenic and antibiotic-resistant organisms and as well as the antibiotic resistant genes that are released into the environment (Barancheshme et al. 2018).
- This is a result of continuous use of pharmaceutical compounds in hospitals (Azuma et al. 2019, p. 2).
Hospital Wastewater  ➔  Accumulation ARGs

- Antibiotic resistance genes (ARGs) have been identified in microbial communities of hospitals due to the wide consumption of human antibiotics in the environments of hospitals (Barancheshme et al. 2018).

- These genes include: $tet(M)$, $tet(O)$, $tet(S)$, $tet(Q)$, $tet(W)$, and $mec(A)$

- Three studies showed that the antibiotic family Fluoroquinolones, and the ARGs $bla_{TEM}$, $qnr(S)$, $erm(B)$, $sul(1)$ and $tet(W)$ were detected at the highest concentration in hospital wastewater (Barancheshme et al. 2018).

- Another study showed that hydrophobic antibiotics, like tetracycline or ciprofloxacin, were detected in all sludge samples of the hospital and fluoroquinolones were consistently found in hospital effluents (Baquero et al. 2008).
Summary: The graph shows higher resistance of E. coli in hospital effluent relative to levels at a sewage treatment plant. It measures CRE, carbapenem-resistant enterobacteriaceae and ESBL, extended-spectrum β-lactamase. CRE is a family of highly resistant bacteria that includes E. coli. ESBL are enzymes that confer resistance to many antibiotics.
Regulating Medication Waste in Hospital Settings

- In hospitals, pharmaceutical waste is generally discarded down the drain or landfilled, except chemotherapy agents, which are often sent to a regulated medical waste incinerator (E. Pines 2008, p. 8).
- These practices were developed at a time when knowledge was not available about the potential adverse effects of introducing waste pharmaceuticals into the environment (E. Pines 2008, p. 8).
- The two largest sources of pharmaceuticals entering the sewer system are believed to be from hospitals and households (E. Pines 2008, p. 44).
- Wastewater treatment plants are designed to remove conventional pollutants but not low concentrations of pharmaceuticals as they are chemical specific. Drugs added to landfill will eventually percolate into groundwater (E. Pines 2008, p. 44).
- Per the EPA (United States Environmental Protection Agency) it’s expected that approximately 5% of pharmaceuticals are being addressed by the Universal Waste Rule which means the other 95% is not regulated/considered as waste including antibiotics (E. Pines 2008, p. 37).
Hospitals: The bottom line

- Continuous use of pharmaceuticals and antibiotics in hospitals has lead to resistant bacteria arising in hospitals.
- These resistant bacteria can end up in water systems through hospital effluent from hand washing and toilet or human waste (urine and fecal)

![Image of bacteria and pill]
Large Scale: Factory Disposal

- Bacterial resistance in pharmaceutical manufacturing wastewaters may result from high concentrations of chemical oxygen demand, antibiotics, and micro-organisms (Linxuan Li, 2018).

- Research shows an increase in multiple microbials antibiotic resistance in the discharge of pharmaceutical wastewater in the receiving waters, which may exert health risk to human beings through different routes (Linxuan Li, 2018).
Large Scale: Factory Disposal (Testing Treated Water)

In one study; A1, A2, A3, A4, and A5 are all different processes in the treatment of water before it returns to the “return water” Samples were taken from each of the treatment areas and tested for antibacterial genes, and resistant bacteria itself.
Results

Of the bacteria tested in the different treatment zones, the resulting graph shows the percentage of bacteria found in these zones that were resistant to tetracycline and sulfonamide antibiotics, which were the most highly produced antibiotics in the industrial plant.

Fig. 3 The log concentration of bacteria (tetracycline and sulfonamide resistant) in the samples

(Linxuan Li, 2018)
Summary

In summary, antibiotic resistant bacteria can accumulate in our water system due to improper:

- Human disposal
- Hospital disposal
- Factory disposal

Education and regulation of pharmaceutical waste can aid in awareness of improper disposal of medications, thus reducing antibacterial resistance.
Importance of proper disposal of medications

- Antibiotic resistance has been an increasing threat among the environment and humans. With wastes from hospitals, residential, and agricultural areas the dissemination of antibiotics in drinking waters is intensifying the resistance of antibiotic bacteria, antibiotic genes, and antibiotic residues (Le et al. 2018, p 507).

- There are a number of research projects to find the most efficient way to remove these resistant microbial factors but one of the main questions that arises is how to ascertain the spread of the resistance before it enters the water system.

- Proper disposal of medications, including but not limiting to antibiotics, is crucial to help avoid the upsurge of antibiotic resistance in the water system.
What can be done to help fix this resistance problem?

1. Preliminary disinfection of hospital wastewater before its discharge into the sewage system or rivers can prohibit the spread ARGs into the environment (Brancheshme et al., 2018).

2. Dispose of medications properly:
   - Drug take back events
   - Give unused medications to local pharmacies
   - Household trash*
     - It’s important to follow the simple steps outlined for disposing of medications in the trash
   - Use Medication Disposal Bags

(FDA 2019)
What’s Next?

Further research addressing the issue of antibiotic resistance could look into:

- Investigating low-cost water treatment methods on antibiotic resistance to reduce human disease through drinking water (Sanganyado et al. 2019, p. 10).
- Establishing a direct epidemiological link between antibiotic resistance in drinking water and human health (Sanganyado et al. 2019, p. 10).
- There is little data to contribute to improper small scale human disposal of pharmaceuticals because research is still in its infancy, however, there are methods set in place by the EPA to monitor potential risks on human disposal and human use of pharmaceuticals (Wu et al., 2009 p. 45).
- More research could be done to look at the effectiveness of treating antibiotic resistant bacteria with UV light (Conner-Kerr et al. 1998).
Conclusion

Antibiotic resistance is on the rise stemming from various factors including the overuse of prescriptions, improper disposal of pharmaceuticals, as well as water systems with filters that aren’t able to combat the majority of antibiotics in the water.

Regulating proper disposal of pharmaceuticals in hospital settings and large factories is critical to the environment as the evolution of microbes is being pushed to resistance giving rise to multi-drug resistant strains.

Research is currently being done to better prevent antibiotic resistant bacteria and the proliferation of antibiotic genes.

You Can Make a Difference to Help Keep our Water Clean & Free from Antibiotics


