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The Issue of Drug Resistance and the Danger of Disposing of Drug Waste

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Review Article

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Abstract:

The frequency of infectious illness deaths has increased public awareness of the risks associated with it and advanced worldwide research on antibiotics. Conversely, greater demand and usage of antibiotics is the cause of elevated antibiotic levels in natural ecosystems. Natural selection and adaptation resulted in gene changes that gave rise to antibiotic resistance in bacterial populations. The proliferation of antibiotic resistance genes in ecosystems led to the creation of antibiotic-resistant bacteria, which in turn led to the widespread rise of several antibiotic-resistant illnesses. The mechanisms that lead to cross-resistance to many medications (multidrug resistance), which is comparable to what is frequently observed in patients, have been uncovered. More recently, it has been shown that downstream genes, which are closely related to cell-cycle checkpoints, also seem to have a direct role in defining a patient's susceptibility to cytotoxic medications by controlling the cell's reaction to the damage caused by the drug. This review article examines a number of findings pertaining to the movement, persistence, and destiny of antibiotics as well as genes that cause antibiotic resistance in natural settings.

Key Words: Drug resistance; Antibiotic resistance; Environment; Contamination.

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INTRODUCTION:

During the era of emerging science, technical advancements led to the emergence of infectious illnesses. As a result, the rate of death and illness rose dramatically on a global scale. The scientific community held up the battle against these illnesses by closely analyzing their molecular processes, their host-pathogen interactions, and their epidemiology in order to identify precise, efficient antimicrobial measures for host survival and safety. Generally speaking, drugs are thought of being alien materials or agents with specific medicinal properties. Even in conjunction with cancer treatments, antifungal or anti-parasitic drugs, etc., they are effective against bacterial infections. The discovery of the use of antibiotics is the largest medical innovation that has affected human survival [1-3]. Antimicrobial resistance is therefore not a novel idea. Antimicrobial resistance was identified prior to the advent of antibiotics. By the 1950s, the scientific community was well aware of the problem of antibiotic resistance. Interestingly, methicillin was first used in a clinical setting in 1959. It was not until two years later that the first case of methicillin-resistant Staphylococcus aureus was found by scientists [4]. In the early years of the twenty-first century, resistance to Gonococci, MDRP-positive P. aeruginosa, and quinolone-resistant E. coli increased due to the increased usage of carbapenem, quinolones, and third-generation cephems. In this discipline, extensively drug-resistant (XDR) and multidrug-resistant (MDR) TB is a relatively new problem. Based on data from 2013, it is estimated that 5 percent of tuberculosis (TB) infections worldwide are MDR-TB cases, meaning the bacteria is resistant to at least two of the most effective first-line anti-TB drugs, isoniazid and rifampicin [5].

Numerous reasons of drug resistance are widely known, including those brought on by giving the medication insufficiently or on schedule, changing pharmacokinetics, or limiting the drug's ability to enter the tumor. A tumor's partial necrosis or inadequate vascularization may be the reason of its limited penetration. Another possibility is that the tumor was localized in hard-to-reach places (sanctuary sites) where there is a tissue-blood barrier (blood-brain, blood-testis, placenta, etc.). Many pathways of cellular drug resistance have been identified thanks to the development of cancer cell lines that are in vitro-selected resistant by exposure to increasing amounts of anticancer drugs. Drug concentrations can be increased while the cell clones are being cultured, allowing for the analysis and identification of genetic and/or biochemical changes [6, 7]. There may be some influence on the occurrence, persistence, and mobility of resistance genes in natural environments due to the potential for long-term, cumulative antibiotic inputs and, consequently, their potential effects on the acquisition and maintenance of antibiotic resistance mechanisms in bacteria. A multitude of reviews, investigations, and opinion pieces have surfaced to discuss the potential connection between the usage of antibiotics and the development of antibiotic resistance [8, 9]. Inevitably this is quite concerning because human exposure to drugs differs significantly from that which is acquired in vitro. It is unclear if the patient's medication resistance at the cellular level is caused by the in vitro results, if at all.

Mechanism of drug resistance:

The genetic characterization of antibiotic-resistant bacterial strains has led to the discovery of several molecular routes of resistance. Antibiotic resistance can be attributed to five main mechanisms: enzymatic activity, which directly inactivates or destroys the antibiotic; Antibiotic-targeting bacterial protein modifications, decreased membrane permeability to antibiotics, activation of efflux pumps that discharge drugs, and activation of resistant bacterial metabolic pathways are all examples of antibiotic-resistant bacterial modifications. Since bacteria are able to degrade or alter antibiotics, they are resistant to their effects. Drug inactivation by hydrolysis is a significant mechanism of antibiotic resistance. The transfer of chemical groups can also render antibiotics inactive. Bacterial enzymes add chemical groups to the antibiotic's vulnerable locations on the molecule as a consequence of steric hindrance, which stops the antibiotic from binding to its target protein. Not only may a large variety of different chemical groups be transferred, but also the enzymes that comprise the vast and diverse family of antibiotic-resistant enzymes, including acyl, phosphate, nucleotidyl, and ribitoyl groups.

Drug resistance can also develop throughout the course of treating non-infectious human illnesses. Drug resistance in cancer cells may also be seen. Efflux pumps function in cancer cells not only to lower antimicrobial resistance but also to prevent the accumulation of chemotherapeutic drugs within these cells. Efflux pump proteins belonging to the ABC superfamily, including as P-glycoprotein (P-gp), Multidrug resistance Protein 1, Breast Cancer Resistance Protein, and Lung Resistance-Related Protein, are commonly involved in this. The capacity of the glutathione S-transferase enzyme to catalyze the conjugation of glutathione to a xenobiotic molecule by creating a thio ether link may also cause anticancer drugs to become inert. The therapeutic targets of treatment-resistant cancer cells may also shift. Strogen is not necessary for the growth of breast cancer-resistant tumor cells that lack strogen receptors, in contrast to normal cells. Endocrine treatment resistance results from this. Because cancer cells have different lipid compositions and high cholesterol content, they are less permeable to chemotherapy drugs via their membranes than normal cells [3, 10].

Antibiotics into the environment:

A variety of methods, such as the drug production process, the disposal of unneeded medication and container debris, and the usage and application of drug-containing waste material, can release antibiotics used in animal husbandry into the environment [11, 12]. Other possible routes of antibiotic residue entrance into the environment include the excretion of waste products by grazing animals, the air dispersal of feed and manure dust containing antibiotics, and the unintentional release of products from spills or discharges. There are several possible sources of drug residues in the environment outside animal husbandry, and it is difficult to determine how much each source contributes. A lot of antibiotics are not fully absorbed in the stomach, which causes the parent drug and its breakdown products to be excreted [13–15]. According to Elmund et al. (1971), up to 75% of the antibiotics given to animals in feedlots may be released into the environment.

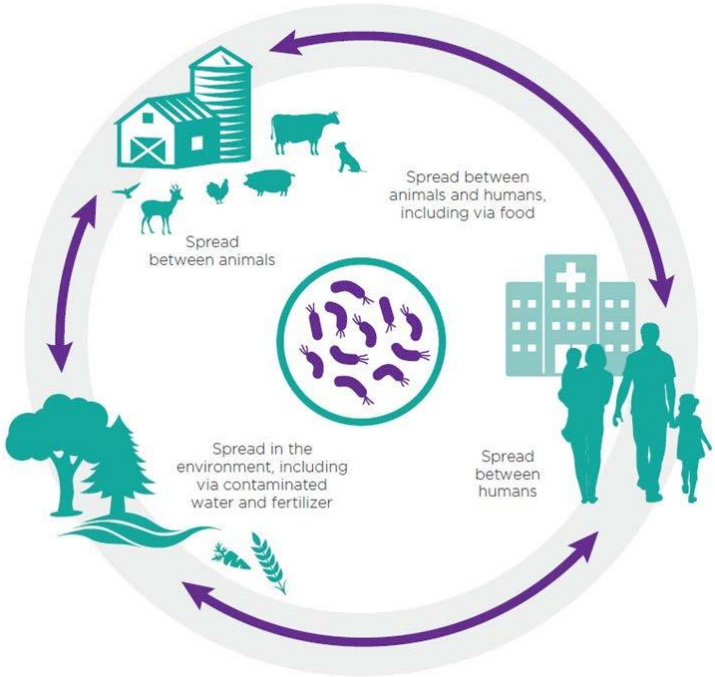

Figure 1. Pharmaceutical Disposal and Antibiotic Resistance

Antibiotic degradation mechanisms:

Hydrolysis can be a significant mechanism for antibiotic degradation since antibiotics from livestock operations are typically released into the environment through water (effluent). Antibiotics belonging to the beta-lactam, macrolide, and sulfonamide families seem to be the most vulnerable to hydrolysis [16]. It is anticipated that these half-life will extend to temperatures that are more climate-relevant. According to Doi and Stoskopf (2000), oxytetracycline's half-life in deionized water was 0.26 days at comparatively high temperatures (43°C), while it was comparatively stable at low temperatures (4°C). Under somewhat acidic and basic conditions, beta-lactams hydrolyze quickly [17]. Another abiotic activity that may alter antibiotics released into the environment is photolysis. Antibiotics in soil can photodegrade at the surface of liquid manure as well as at the soil-atmosphere contact. The photodegradation conditions in soils might differ greatly from those in aqueous solutions, and the rates of transformation in soils can also change markedly from those in water [18]. The harmful effects of antibiotics on the local bacteria have also been shown to be inherent to the biodegradation process. It was discovered that activated sludge in waste water treatment was inhibited by a variety of antibiotic concentrations [19].

Drug waste disposal:

The influence of the effluents from hospitals, industries, and urban settlements discharged as sewage into the aquatic ecosystem causes selection; thereby promotes the acquisition and dissemination of resistance genes. The improper disposal of unused, stored, or expired pharmaceuticals ends up in landfills, water supplies and drains that lead to contamination promotes the selection and development of resistance among inhabibting microbiota [20, 21]. Due to the growing population and their increased need for clean drinking water, the river is being overfished in terms of both quantity and quality. Its contamination is mostly from point and non-point sources, including home sewage, industrial waste, idol immersion, animal swimming, and agricultural runoffs. The area is inundated with untreated and inadequately treated sewage [22]. Understanding the resistance profile of occupant bacteria that may contribute to infections in human hosts seems crucial, given the potential threat to human health posed by the preservation of the resistance gene pool and the bacteria's ability to spread across various groups in the urban aquatic environment.

Overcoming drug resistance:

Numerous studies have been conducted in an effort to reverse P-glycoprotein-mediated MDR. There are numerous compounds known to have the ability to change drug resistance. They fall into several chemical classes, such as hormones, immunesuppressives, beta-blockers, and anti-arrhythmics. Almost all reversal agents are substrates of P-glycoprotein and compete with the cytotoxic drug for extrusion from the cell, despite the fact that the process of MDR reversal might be complicated. Sadly, it was discovered that verapamil, the first of these medicines to be investigated, was very cardiotoxic.
at dosages that allow patients to have the plasma concentrations required to reverse medication resistance in culture. More recently, cyclosporin-A and its analogs, such as PSC-833, which has no immunosuppressive, cardiac, or renal effects, were created and are being studied in clinical settings.

Certain reverters, such cyclosporin A and verapamil, especially its analog PSC-833, significantly affect the anticancer drug's pharmacokinetics. This may be due to a decrease in clearance and an increase in plasma concentration of 40%–60% over time, which increases the drug's toxicity. Because of MRP overexpression, reversers that are effective in vitro at reversing P-glycoprotein-mediated MDR appear to be much less active in reversing MDR. Research is being done on other drugs that seem to impede the drug efflux more effectively because MRP is overexpressed rather than MDR-1 [23]. However, a wide phylogenetic range of bacteria, including those that are indigenous to soil and water habitats, appear to be involved in the acquisition of antibiotic resistances. Using antibiotic-producing bacteria to acquire resistance genes is not a common mechanism of resistance acquisition seen in a wide variety of bacteria, according to phylogenetic analyses of the genes involved in erythromycin and tetracycline resistances. These analyses also show how these genes have evolved over time. Even though the origin and function of these genes are still unknown, resistance genes have been preserved in bacteria since before the advent of current antibiotics.

CONCLUSION:

Drug resistance is one of the major problems facing modern science. Research is still ongoing to determine the expected biochemical and molecular mechanisms of resistance complexity, which have detrimental impacts on life. Understanding the dynamics of pathogen fitness cost and tolerance has led to new opportunities for a broader biological interest in the clinical field. The reversibility procedure is slowed significantly by the intrinsic approaches. Although the precise processes behind the acquisition and maintenance of antibiotic resistance genes in natural settings are still poorly understood, lateral gene transfer events are being supported by a growing body of research. The application of bioinformatics techniques enables precision medicine by altering the development and administration of therapeutic medications to treat infectious and non-infectious disorders, including malignancies.

Competing interest: None.

REFERENCES

1. Ligon BL (2004) Penicillin: its discovery and early development. Paper presented at the seminars in pediatric infectious diseases
2. Dougherty TJ, Pucci MJ (2011) Antibiotic discovery and development. Springer Science & Business Media, New York
3. Rafi, I. k. and Hoque, M. (2023). Short notes on molecular mechanisms behind antimicrobial drug resistance. GSC Biological and Pharmaceutical Sciences, 24(03), 001–009. DOI: https://doi.org/10.30574/gscbps.2023.24.3.0353
4. Jevons, M.P.,1961. Celbenin– Resistant Staphylococci.BritishMedicalJournal1,124
5. Klopper M, Warren RM, Hayes C, van Pittius NCG, Streicher EM, Müller B (2013) Emergence and spread of extensively and totally drug-resistant tuberculosis, South Africa. Emerg Infect Dis 19:449–455. doi:10.3201/EID1903.120246
6. van Kalken CK, Giaccone G, van der Valk P. Multidrug resistance gene (P-glycoprotein) expression in the human fetus. Am J Pathol 1992;141:1063-1072.
7. Hoque, M et al., (2023). A Mini Review on Cancer Epigenetics. Middle East Res J. Med. Sci, 3(2): 28-38. DOI: 10.36348/merjms.2023.v03i02.002
8. Kümmerer, K. 2004. Resistance in the environment. J. Antimicrob. Chem. 54:311–320.
9. Hoque, M et al., Connection between chronic kidney disease and non-alcoholic fatty liver disease: A brief notes to know. Int. J. in Pharm. Sci., 2023, Vol 1, Issue 11, 410-415. DOI: 10.5281/zenodo.10188636
10. Robbins, N., Caplan, T., Cowen, L.E., 2017. Molecular evolution of antifungal drug resistance. Annual Review of Microbiology 71 (1).
11. Buchberger, W.W. 2007. Novel analytical procedures for screening of drug residues in water, waste water, sediment and sludge. Anal. Chim. Acta 593:129–139
12. Utah Department of Health. 2007. Medication disposal summary report. Available at http://health.utah.gov/prescription/pdf/NewHampshire_Disposal_technical.pdf
13. Boxall, A.B.A., L.A. Fogg, P.A. Blackwell, P. Kay, E.J. Pemberton, and A. Croxford. 2004. Veterinary medicines in the environment. Rev. Environ. Contam. Toxicol. 180:1–91.
14. Elmund, G.K., S.M. Morrison, D.W. Grant, and M.P. Nevins. 1971. Role of excreted chlortetracycline in modifying the decomposition process in feedlot waste. Bull. Environ. Contam. Toxicol. 6:129–135.
15. Rafi, I. K et al., (2023). The Impact of Banana Consumption on Bangladeshi Rickshaw Pullers' Assessing Cholesterol, Liver and Blood Pressure Functions. Middle East Res J Biological Sci, 3(2): 24-28. DOI: 10.36348/merjbs.2023.v03i02.001
16. Huang, C.-H., J.E. Renew, K.L. Smeby, K. Pinkston, and D.L. Sediak. Assessment of potential antibiotic contaminants in water and preliminary occurrence analysis.p. 46–57. In Proc. of the 2nd Int. Conf. on Pharmaceuticals and Endocrine Disrupting Chemicals in Water, Minneapolis, MN. October 2001. Natl. Groundwater Assoc., Westerville, OH.
17. Hou, J.P., and J.W. Poole. 1969. Kinetics and mechanism of degradation of ampicillin in solution. J. Pharm. Sci. 58:447–454.
18. Balmer, M.E., K.-U. Goss, and R.P. Schwarzenbach. 2000. Photolytic transformation of organic pollutants on soil surfaces–An experimental approach. Environ. Sci. Technol. 34:1240–1245
19. Gartiser, S., E. Urich, R. Alexy, and K. Kümmerer. 2007. Anaerobic inhibition and biodegradation of antibiotics in ISO test schemes. Chemosphere 66:1839–1848.
20. Rodgers K., McLellan I., Peshkur T., Williams R., Tonner R., Hursthouse A.S. Can the legacy of industrial pollution influence antimicrobial resistance in estuarine sediments. Environ. Chem. Lett. 2019;17(2):595–607
21. Kraemer S.A., Ramachandran A., Perron G.G. Antibiotic pollution in the environment: from microbial ecology to public policy. Microorganisms. 2019;7(6):180. doi: 10.3390/microorganisms7060180.
22. Sharma D., Kansal A. Water quality analysis of River Yamuna using water quality index in the national capital territory, India (2000–2009) App. Water Sci. 2011;1(3–4):147–157. doi: 10.1007/s13201-011-0011-4
23. Broxterman HJ, Giaccone G, Lankelma J. MRP and other drug transport-related resistance to natural product agents. Curr Opin Oncol 1995;7:532-540.