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Unraveling the Effects: Broad-spectrum Antibiotics, Gut Microbiota Disruption, and Gastrointestinal Health

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

The modern lifestyle is not complete without antibiotics. By curing and preventing illness, as well as increasing feed efficiency for farm animals, they enhance our quality of life. Antibiotic use does not, however, come without side effects. Despite their importance in treating a variety of bacterial diseases, broad-spectrum antibiotics can have unexpected effects on gut microbiota due to their indiscriminate nature. This review looks at the major effects of broad-spectrum antibiotics on the gut flora and the side effects that may result. Antibiotics cause a disturbance in the delicate equilibrium of gut microbial populations, resulting in a reduction in microbial diversity and an increase in pathogenic organisms. Many gastrointestinal problems, such as dysbiosis, diarrhea, and more serious illnesses like antibiotic-associated colitis, can be brought on by these changes. We investigate the ways in which antibiotics cause microbial imbalances, such as the inhibition of

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helpful bacteria and the encouragement of the expansion of harmful bacteria. We also look at the long-term effects of these changes on gut health and their clinical implications.
This review aims to provide a comprehensive overview of how broad-spectrum antibiotics influence gut health and to inform future research directions in microbiome management and therapeutic interventions.

Keywords: Antibiotic resistance; gut bacteria; microbiome; dysbiosis; diarrhea.

1. INTRODUCTION

Since their discovery, antibiotics have revolutionized the treatment of infectious diseases on a global scale [1]. The normal gut microbiota offers defense against invasive bacteria, which may be potential pathogens, demonstrating the gut microbiota's importance to human health [2].

Within hours of birth, thousands of bacteria, viruses, and some eukaryotes make up the gut microbiota, which colonizes the digestive tract. The last several decades have seen a significant increase in interest in the human microbiota due to numerous studies demonstrating its profound impact on both health and disease [3].

Antibiotics with a broad spectrum of action have the potential to decrease gut microbial diversity, which can result in dysbiosis. This disturbance may have an impact on the gut's helpful and harmful bacterial balance [4,5]. The tremendous advancements in medicine are at risk due to the overuse and misuse of antibiotics, which is now seen as a major public health concern over the past 20 years. Antimicrobial resistance (AR) is an emerging issue that poses a challenge to the efficacious management of infectious illnesses, particularly in affluent nations. Although the overuse of antibiotics was formerly thought to be a problem exclusive to affluent nations, there has been a notable increase in low- and middle-income countries [6].

Furthermore, due to their generally higher rates of serious morbidity and mortality, prolonged hospital stays, high costs for medications, and employee absenteeism, ESKAPE (Enterococcus, S. aureus, K. pneumoniae, A. baumannii, P. aeruginosa, and E. coli) pathogens are a major global source of hospital-acquired resistant infections [6]. One example of a condition directly caused by antibiotic disturbance of the gut microbiota is Clostridium difficile (previously known as Clostridium difficile) infection. A disease can cause anything from little diarrhea to death. When helpful bacteria in the gut are eradicated by antibiotics, C. difficile is allowed to grow [1].

The typical gut microbiota can be impacted by antimicrobial drugs in many ways. Numerous factors determine how much the microbiota has changed as a result of antibiotic use:

i) the agent's spectrum, ii) the dosage and length of therapy, iii) the delivery route, and iv) the agent's pharmacokinetic and pharmacodynamic qualities. For instance, the release of an antibiotic by the salivary glands, bile, or intestinal mucosa may disrupt the natural microbiota at a different location. Some antibiotics can also cause disruptions to the human host's metabolism and vitamin absorption, modify susceptibility to infections, and promote the growth of yeast and/or Clostridium difficile [7].

Antibiotics were recognized as the most potent and life-saving medications to treat infectious infections as soon as they were developed, and they significantly reduced morbidity and death. But humanity quickly discovered that the rise of antimicrobial resistance (AR) was caused by the careless and reckless use, abuse, and overuse of antibiotics. AR is a serious health issue that threatens the advancements of contemporary medicine worldwide [6].

2. THERAPEUTIC OPTIONS

We can particularly target the gut microbiota to improve long-term health since it is very flexible during development. A number of possible treatment approaches have been identified to address disorders associated with gut dysbiosis, including genetically modified phages, dietary therapy, probiotics, prebiotics, FMT, and VNS. These approaches alter the makeup of the gut microbiota whether directly or indirectly. Consequently, they represent a promising therapeutic avenue for addressing medication-induced dysbiosis in young children and perhaps improving chronic illnesses [8].

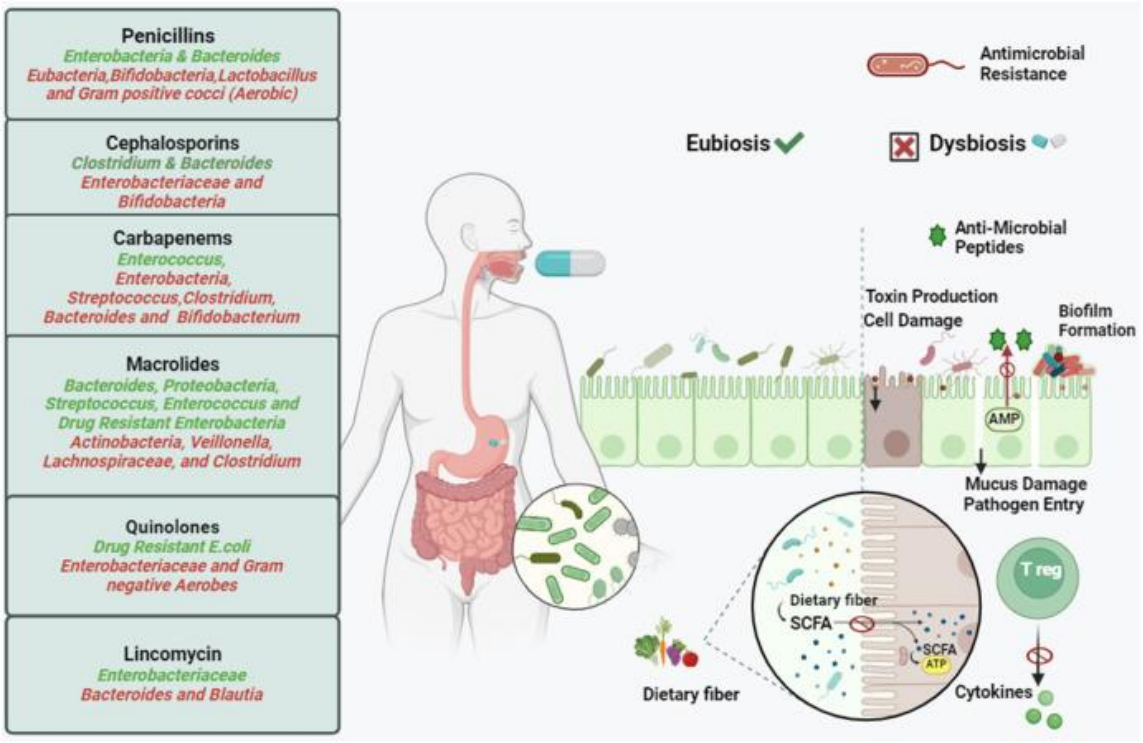

Fig. 1. Action of antibiotics on gut cells and microbiome

Organisms represented using green and red colour indicates their increasing and decreasing concentration in the presence of appropriate antibiotics respectively. Increased Antibiotic Resistance, Toxin production, cell damage, biofilm formation, Mucus damage & pathogen entry, downregulation of cytokine production in T regulatory cells (T_{reg}), Antimicrobial peptides from AMP genes and ATP production from short chain Fatty Acid (SCFA) were down regulated as a result of antibiotic induced gut dysbiosis [3].

3. IMPACT OF ANTIBIOTICS DURING PREGNANCY AND LACTATION

Scientists studied the temporal effects of cefoperazone, when administered during the peripartum period in an interleukin 10 (IL-10)-deficient murine model of colitis, on both the mother's and the offspring's microbiota in order to gain an understanding of the potential impact of antibiotic administration on offspring during pregnancy. Children born to dams exposed to cefoperazone had changed gut microbiota well into adulthood and were more vulnerable to both chemically and spontaneously caused colitis. The microbiota in milk is influenced by the use of antibiotics by mothers during lactation, and this can have an impact on the composition of microorganisms in the infant's gut [1].

4. IMPACT OF ANTIBIOTIC ADMINISTRATION DIRECTLY TO INFANTS ON THE INFANT GUT MICROBIOTA

As one of the primary causes of mortality and morbidity in preterm infants, sepsis is frequently prevented and treated in neonates by the use of antibiotics. The gut microbiota of preterm newborns is distinct, with an increased concentration of pathogens like Clostridiums and a delayed colonization of common bacteria like Bacteroides and Bifidobacteria. The varying composition of microbiota could be caused by a variety of factors, including antibiotic use, medical procedures following delivery, hospital environments, and premature birth [9].

In the first four days of life, the gut microbiota of 26 infants receiving the broad-spectrum antibiotic cefalexin showed less variety than that of the control group of infants not receiving antibiotics. This information was obtained from a study on the effects of this medication. In addition, the antibiotic prevented the growth of certain bacterial species, including bifidobacteria, and caused an uncommon colonization of Enterococcus during the first week of treatment. Additionally, compared to the control infants who

did not receive antibiotics, a higher Enterobacteriaceae population was seen one month after antibiotic therapy. Antibiotics alter the dominant members of the bacterial population, which may have a significant impact on the developing baby's immune system, metabolism, and growth. The use of antibiotics in infancy and children has been linked to changes in the microbial makeup and metabolic processes, an increased risk of developing allergies and asthma in later life, and obesity [1].

5. IMPACT ON ADULTS

Studies on antibiotic-treated healthy people with cefprozil, ciprofloxacin, and amoxicillin revealed that the microbial composition remained altered for up to 12 weeks following treatment termination, with the emergence of antibiotic-resistant bacteria and partial restoration. Distinctions depending on antibiotic types, such as bacteriostatic or bactericidal, also have an impact on gut flora. The growth of Gram-negative bacteria and increased lipopolysaccharide synthesis genes have been linked to bacteriostatic medications. Conversely, cidal drugs were associated with a rise in Gram-positive bacteria and an overexpression of genes involved in endospore production. Even when antibiotics are taken systemically, they still have an impact on the stomach. Antibiotics used in dental procedures have the potential to increase the amount of resistant strains taken orally, raise the lowest inhibitory dose, and eradicate non-pathogenic strains, all of which might result in systemic infections and inflammation [3].

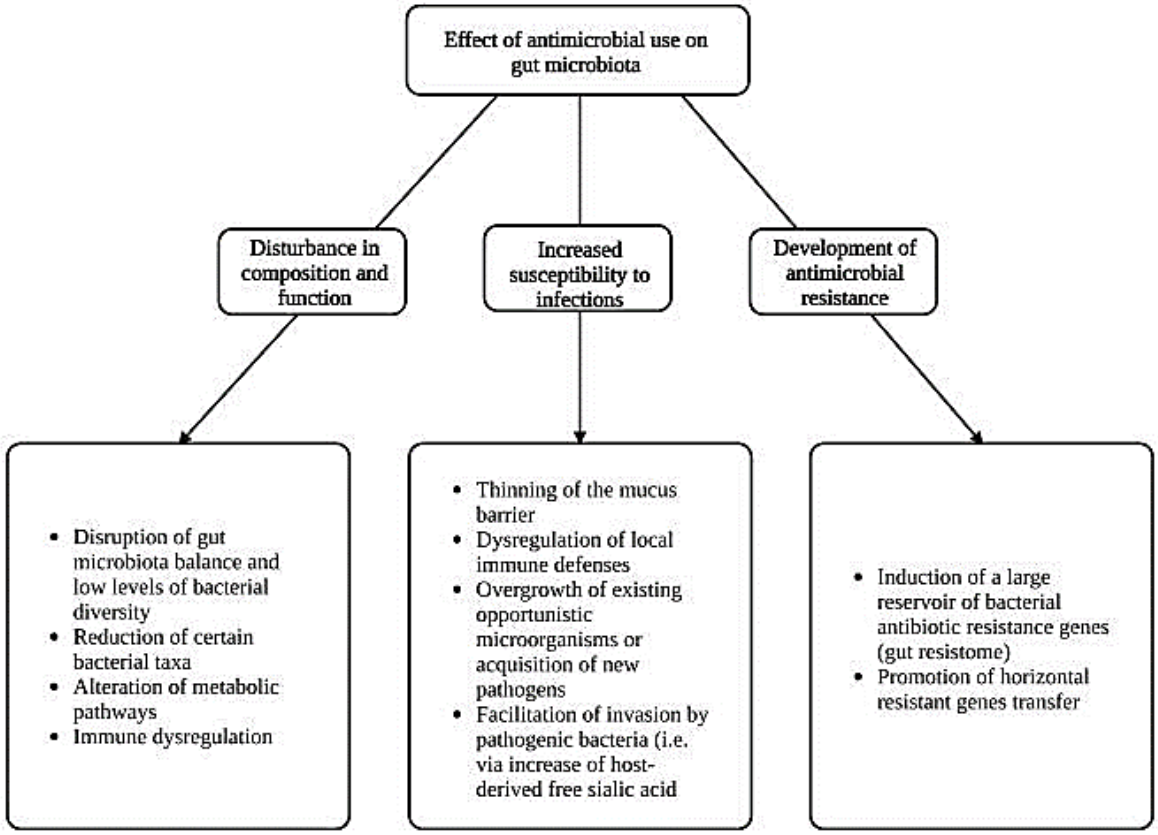

Fig. 2. Effect of antimicrobial use on gut microbiota [10]

6. CONTROL MEASURES

The main line of defense against MDRO transmission in hospitals is hand hygiene, which is followed by environmental cleaning, contact precautions, and, in certain cases, topical decolonization procedures (e.g., MRSA). Rationalizing the use of antibiotics by putting into practice efficient antimicrobial stewardship techniques is an important strategy to prevent severe alterations in the gut flora.

Choice of antibiotics- The kind and range of antibiotics that are used determine how quickly resistance develops. For instance, an increased risk of MDRO colonization has been linked to the needless and extended use of anti-anaerobic antibiotics.

Dose- Still, as antimicrobial neglecting can also result in resistance, correct dosage is essential [10].

He use of recently developed substances, such as beta-lactamase enzymes and charcoal-based substances, that absorb the remaining portion of an antibiotic excreted fecally or biliarily before it reaches the colon, is another intriguing strategy for preserving gut microbiota. This protects the gut microbiota without changing antibiotic serum levels [10].

Fecal microbiota transplantation (FMT) is the process of directly altering the recipient's gut microbial composition and conferring a health benefit by administering a donor's solution of fecal matter into the recipient's intestinal tract. FMT has proven to be effective in treating recurring infections caused by Clostridium difficile. It may also have therapeutic promise for other problems like obesity, metabolic syndrome, inflammatory bowel disease, and functional gastrointestinal disorders, according to some early indications [11].

7. PROBIOTICS AND PREBIOTICS IN SYMBIOSIS FOR GUT HARMONY

Probiotics are live microorganisms, mostly yeast and bacteria, that provide health benefits when consumed in appropriate amounts. Probiotics influence the intestinal microbiota and support the upkeep of a balanced and healthy gut environment through a number of mechanisms [3]. Probiotics, sometimes referred to as the "good bacteria," are live microorganisms that, when taken in sufficient quantities, have health advantages. Among the most well-known probiotics are Lactobacillus and Bifidobacterium species, which are found naturally in human digestive systems. The delicate equilibrium of the gut microbiota is preserved in large part by these beneficial bacteria. Prebiotics are non-digestible fibers that feed good bacteria in the stomach, enhancing the effects of probiotics. Prebiotics give these microbes the nourishment they require to survive and multiply, while probiotics add good bacteria. Several fruits, vegetables, and whole grains include prebiotics such as inulin, fructooligosaccharides (FOS), and galactosaccharides (GOS) [12].

Fecal bulk, which is a key indicator of intestinal health, is largely influenced by microbial mass. Eating dietary fibers lowers the incidence of colorectal cancer (CRC), if only partially because of the diluting and excretion of toxins through fecal bulk, which is facilitated by the presence of water-holding fibers and fermentative bacteria [13].

Monitoring and Follow-Up: During and after antibiotic treatment, routine monitoring of the makeup of the gut microbiota and gastrointestinal health can aid in the early detection and management of any negative effects. To better assist gut repair, follow-up evaluations might inform dietary recommendations and treatment modifications.

8. CONCLUSION

Antibiotics have the potential to have long-lasting negative effects on patients, affecting the gut microbiota's diversity, composition, and altered activities. Because of its state at the time of therapy, the gut microbiota's activity affects how well various clinical medicines work. Nevertheless, our limited understanding of antibiotic activity spectrum, gut microbial resistance mechanisms to different antibiotics, and the degree of harm that certain antibiotics produce limits treatments to lessen these damages to the gut microbiota. Drug-microbiome interactions are discovered to be bidirectional, even if non-antibiotics such probiotics contribute to antibiotic resistance that is facilitated by the microbiome. Antibiotics have the potential to alter the gut microbiome, and bacteria can also alter the medications' chemical makeup and cause antibiotic resistance. We are now hopeful that precision medicine, resistance gene therapy, and system biology techniques may enable us to take advantage of the host-microbe interaction to develop safe and efficient treatment plans.

DISCLAIMER (ARTIFICIAL INTELLIGENCE)

Author(s) hereby declare that NO generative AI technologies such as Large Language Models (ChatGPT, COPILOT, etc) and text-to-image generators have been used during writing or editing of manuscripts.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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