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Antibiotics as Major Disruptors of Gut Microbiota

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Advances in culture-independent research techniques have led to an increased understanding of the gut microbiota and the role it plays in health and disease. The intestine is populated by a complex microbial community that is organized around a network of metabolic interdependencies. It is now understood that the gut microbiota is vital for normal development and functioning of the human body, especially for the priming and maturation of the adaptive immune system. Antibiotic use can have several negative effects on the gut microbiota, including reduced species diversity, altered metabolic activity, and the selection of antibiotic-resistant organisms, which in turn can lead to antibiotic-associated diarrhea and recurrent *Clostridioides difficile* infections. There is also evidence that early childhood exposure to antibiotics can lead to several gastrointestinal, immunologic, and neurocognitive conditions. The increase in the use of antibiotics in recent years suggests that these problems are likely to become more acute or more prevalent in the future. Continued research into the structure and function of the gut microbiota is required to address this challenge.

Keywords: antibiotic overuse, antibiotic resistance, gut microbiota, microbial diversity, antibiotic-associated diarrhea (AAD), enterotypes

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INTRODUCTION

Scientific advances made in recent decades have led to an increased recognition of the role of the human gut microbiota in health and disease (Ananthakrishnan et al., 2019). Prior to that, little research had been conducted into the non-pathogenic microorganisms that inhabit the gastrointestinal tract (Guarner, 2012). Because most of these microorganisms cannot be cultured, they remained largely unexplored before the advent of molecular techniques. Ample experimental and clinical evidence now shows that gut microorganisms are required for the optimal functioning of the human body (Guarner, 2015).

In 1885, Louis Pasteur hypothesized that animals raised in sterile conditions would not be able to survive (Pasteur, 1885). Bernard S. Wostmann and his team proved Pasteur's hypothesis wrong when they developed methods for breeding animals in germ-free conditions (Wostmann, 1981). However, they discovered that germ-free animals required large quantities of nutrient-rich food, yet

Microbiology Guide to Interpreting Minimum Inhibitory Concentration (MIC)

Historically, most in vitro susceptibility testing was performed by disk diffusion (Kirby-Bauer) method. The size of the growth-free zone determined whether the bacterium was considered to be susceptible, resistant or intermediate to a particular antibiotic.

While used as a guide to select an effective antibiotic, Kirby-Bauer testing could not tell the clinician the exact concentration of antibiotic needed to achieve a therapeutic result. Now, by a quantitative method of susceptibility testing known as the minimum inhibitory concentration (MIC), the precise concentration of antibiotic required to inhibit growth of a pathogen can be determined.

Your IDEXX microbiology results will show the identity of the organism and the appropriate antibiotic sensitivity pattern against each organism. Most antibiograms will include MICs in order to determine the most effective antibiotic that will result in effective treatment.

This guide provides a detailed explanation of the following concepts important in implementing the MIC:

- The MIC number is the lowest concentration (in µg/ml) of an antibiotic that inhibits the growth of a given strain of bacteria. (See the "What Is an MIC?" section.)
- An MIC number for one antibiotic CANNOT be compared to the MIC number for another antibiotic. (See the "How Are MICs Used?" section.)
- The choice of antibiotic should be based on the MIC number, the site of infection and an antibiotic's breakpoint. Consider safety, ease of use and cost when determining the optimum antibiotic.

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REGULAR ARTICLE

ANTIBIOTICS PRODUCING BACTERIA ISOLATED FROM FARMLANDS

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ABSTRACT

The need for new antibiotics has been highlighted recently with the increasing pace of emergence of drug resistance pathogens. Emerging strains of bacteria resistant to most advanced antibiotics have become issues of very important public health concern. Modification of existing antibiotics with the addition of side chains or other chemical group and genomics based drug targeting have been the preferred method of drug development at the corporate level in recent years. In this regard, soil samples were collected from farmlands located in Ibadan in Oyo state, Ago – Iwoye, and Ikenne in Ogun state, Nigeria. Two putative *Streptomyces* strains and *Bacillus* strains isolated from the 16 selected farmland soils were characterized and assessed for antibiotic production and activity against a wide range of bacteria including *Klebsiella pneumonia*, *Serratia marcesns*, *Proteus vulgaris*, *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus*, and *Enterococcus faecalis*.
The extracts of the putative obtained from *Streptomyces somaliensis*, *Streptomyces anulatus*, *Bacillus megaterium*, and *Bacillus subtilis* showed activities against minimum of 3 and maximum of the 4 of the 7 tested bacteria. Inhibition zones were found to range between 2.0 – 25.0 mm diameters at a concentration of 1ml. The minimum inhibitory concentration (MICs) of the crude extracts against the tested organisms ranged from 50% and above.
Bacillus megaterium, and *Streptomyces somaliensis* were found to inhibit all the pathogenic bacteria, while *S. anulatus* was unable to inhibit *Proteus vulgaris* and *Staphylococcus aureus*, and *B. Subtilis* was unable to inhibit *Enterococcus faecalis*.

Keywords: Antibiotics, *Bacillus*, Bacteria, Soil, *Streptomyces*

INTRODUCTION

The term soil refers to the outer loose material of the earth crust (**Certini and Ugolini, 2013**). Living portion of the soil body includes small animals and microorganisms such as fungi and bacteria, but it is generally considered that it's microorganisms that play the important role in soil (**Arifuzzaman *et al.*, 2010**). Actinomycetic bacteria are best known for their ability to produce antibiotics and the *Streptomyces* are the dominant group (**Pidot *et al.*, 2014**). The genus *Streptomyces* is responsible for the formation of more than 60% of known antibiotics (**Gad et al., 2015; Rashad et al., 2015**). Another important species of bacteria known to produce antibiotics is the *Bacillus* spp. Antibiotics are low molecular-weight (non-protein) molecules produced as secondary metabolites, its production is mainly by microorganisms that live in the soil (**Jamil et al., 2007**).
Resistance by pathogenic bacteria has become a major health concern, many Gram positive bacteria and Gram negative opportunistic pathogens were becoming resistant to virtually every clinically available drugs (**Redgrave *et al.*, 2014**). The use of antimicrobial drugs for prophylactic or therapeutic purposes in human and veterinary or for agricultural purposes, have provided the selective pressure favouring the survival and spread of resistant organisms. Selective pressure favouring the survival and spread of vancomycin-resistant enterococci (VRE) was the consequence of the use of antibiotics in food and agricultural practices. Vancomycin-resistance is often associated with multiple-drug resistance (**Chang *et al.*, 2015**).
Another cause of great concern is the Gram-negative antibiotic-resistant opportunistic pathogens. These bacteria, like *Pseudomonas aeruginosa*, are common environmental organisms, which act as opportunistic pathogens in clinical cases where the defense system for patient is compromised (**Sanjar *et al.*, 2016**). For instance, over 80 % of cystic fibrosis (CF) patients become chronically infected with *P. aeruginosa*. In addition, other intrinsically antibiotic resistant organisms such as *Burkholderia cepacia* and *Stenotrophomonas maltophilia* are emerging as opportunistic pathogens (**Chung *et al.*, 2013**). The appearance of multi resistant pathogenic strains have caused a therapeutic problem of enormous proportions (**Barsby *et al.*, 2001**). For instance, they cause substantial morbidity and mortality especially among the elderly and immunocompromised patients. With increasing misuses of antibiotics, the serious problems of antibiotic resistance are developing at an alarming rate. Thus, new therapeutic drugs and approaches are needed to improve the management of these diseases and overcome these problems (**Taylor *et al.*, 2002**).
Hence, intensive search for new antibiotics has become imperative worldwide especially from natural sources such as soil which is known as the greatest source of antibiotics. New microbial metabolites are permanently needed due not only to the increase in resistant pathogens, but also to the evolution of novel diseases and toxicity of currently used compounds (**Parugao *et al.*, 2008**).
This study aims at exploring the antibiotics production potentials of some indigenous soil bacteria isolated from farmlands in some selected locations in Oyo and Ogun state, South Western part of Nigeria. The objectives include: (i) to isolate antibiotic producing bacteria from farmland (ii) to characterize to species level the isolated bacteria (iii) to determine and estimate the antimicrobial efficiency of each of the antibiotics produced by the bacteria.

MATERIALS AND METHOD

Study area

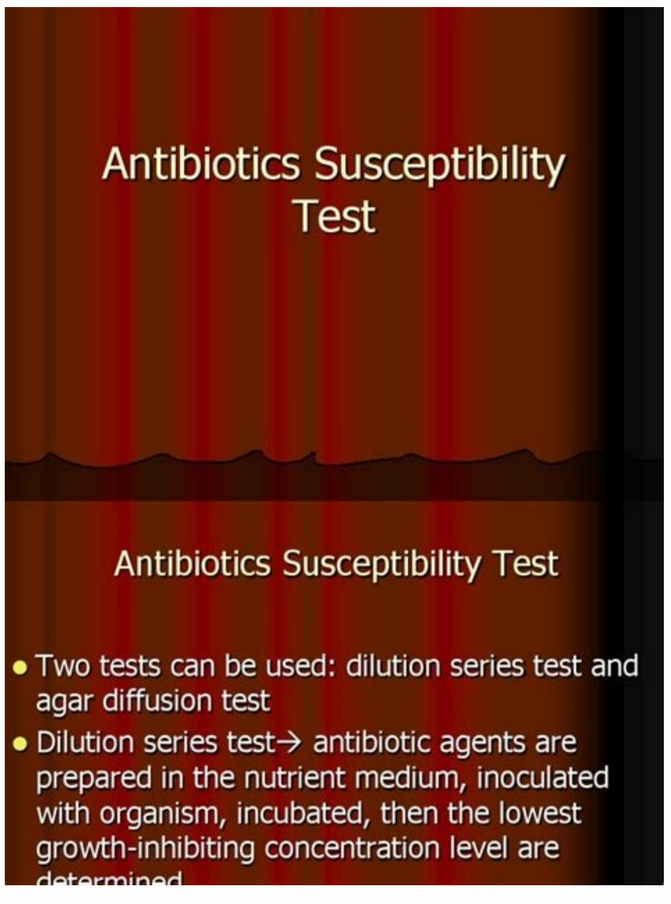
The soil samples were collected from farmlands located in Ibadan, Ago – Iwoye, and Ikenne. Seven samples were collected from individual farmlands in Ibadan which is the capital of Oyo state, while five samples were collected from government farmland located in Ago – Iwoye, and four other samples were collected from IITA research station located in Ikenne, both located in Ogun state.

Media used

The media used were nutrient agar, potato starch casein agar, starch casein agar, and Mac Conkey agar. They were prepared according to the manufacturer's instruction. The media were left to cool to about 45°c after sterilization before being poured aseptically into the Petri dish.
Serial dilution of soil samples: The soil samples were labeled according to the area of collection. Then 1g was weighed from each soil samples for serial dilution where the 10^{-1} to 10^{-4} dilutions were plated.

Plating of the samples

The diluted soil samples were inoculated onto the appropriate agar medium using the streaking method, and they were labeled accordingly. Nutrient agar was used for isolating bacteria, while potato starch casein agar was used for isolating actinomycetes. After inoculation, the plates were incubated at 37°C over night for bacteria, and while in the case of actinomycetes incubation lasted for 4 days at a temperature of 30°C before morphological changes can be seen.



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1. Abraham, E. P., and E. Chain. 1940. An enzyme from bacteria able to destroy penicillin. Rev. Infect. Dis. 10:677-678. [PubMed] [Google Scholar]2. Alekshun, M. N., and S. B. Levy. 2007. Molecular mechanisms of antibacterial multidrug resistance. Cell 128:1037-1050. [PubMed] [Google Scholar]3. Allen, H. K., J. Donato, H. H. Wang, K. A. Cloud-Hansen, J. E. Davies, and J. Handelsman. 2010. Call of the wild: antibiotic resistance genes in natural environments. Nat. Rev. Microbiol. 8:251-259. [PubMed] [Google Scholar]4. Allen, H. K., L. A. Moe, J. Rodbumrer, A. Gaarder, and J. Handelsman. 2009. Functional metagenomics reveals diverse beta-lactamases in a remote Alaskan soil. ISME J. 3:243-251. [PubMed] [Google Scholar]5. Allou, N., E. Cambau, L. Massias, F. Chau, and B. Fantin. 2009. Impact of low-level resistance to fluoroquinolones due to qnrA1 and qnrS1 genes or a gyrA mutation on ciprofloxacin bactericidal activity in a murine model of Escherichia coli urinary tract infection. Antimicrob. Agents Chemother. 53:4292-4297. [PMC free article] [PubMed] [Google Scholar]6. American Academy of Microbiology. 2009. Antibiotic resistance: an ecological perspective on an old problem. Based on a colloquium held in the Fondation Mérieux Conference Center in Annecy, France, 12 to 14 October 2008. ASM Press, Washington, DC.7. American Academy of Microbiology. 2005. Vaccine development: current status and future needs. Based on a colloquium held in Washington, DC, 4 to 6 March 2005. ASM Press, Washington, DC.8. Aminov, R. I. 2009. The role of antibiotics and antibiotic resistance in nature. Environ. Microbiol. 11:2970-2988. [PubMed] [Google Scholar]9. Aminov, R. I., and R. I. Mackie. 2007. Evolution and ecology of antibiotic resistance genes. FEMS Microbiol. Lett. 271:147-161. [PubMed] [Google Scholar]10. Andersson, D. I. 2006. The biological cost of mutational antibiotic resistance: any practical conclusions? Curr. Opin. Microbiol. 9:461-465. [PubMed] [Google Scholar]11. Balaban, N., T. Goldkorn, R. T. Nhan, L. B. Dang, S. Scott, R. M. Ridgley, A. Rasooly, S. C. Wright, J. W. Larrick, R. Rasooly, and J. R. Carlson. 1998. Autoinducer of virulence as a target for vaccine and therapy against Staphylococcus aureus. Science 280:438. [PubMed] [Google Scholar]12. Baltz, R. H. 2006. Marcel Faber Roundtable: is our antibiotic pipeline unproductive because of starvation, constipation or lack of inspiration? J. Ind. Microbiol. Biotechnol. 33:507-513. [PubMed] [Google Scholar]13. Baquero, F., J. L. Martinez, and R. Canton. 2008. Antibiotics and antibiotic resistance in water environments. Curr. Opin. Biotechnol. 19:260-265. [PubMed] [Google Scholar]14. Barbe, V., D. Vallenet, N. Fonknechten, A. Kreimeyer, S. Oztas, L. Labarre, S. Cruveiller, C. Robert, S. Duprat, P. Wincker, L. N. Ornston, J. Weissenbach, P. Marlière, G. N. Cohen, and C. Médigue. 2004. Unique features revealed by the genome sequence of Acinetobacter sp. ADP1, a versatile and naturally transformation competent bacterium. Nucleic Acids Res. 32:5766-5779. [PMC free article] [PubMed] [Google Scholar]15. Barlow, M., and B. G. Hall. 2002. Phylogenetic analysis shows that the OXA beta-lactamase genes have been on plasmids for millions of years. J. Mol. Evol. 55:314-321. [PubMed] [Google Scholar]16. Bartoloni, A., L. Pallecchi, H. Rodriguez, C. Fernandez, A. Mantella, F. Bartalesi, M. Strohmeyer, C. Kristiansson, E. Gotuzzo, F. Paradisi, and G. M. Rossolini. 2009. Antibiotic resistance in a very remote Amazonas community. Int. J. Antimicrob. Agents 33:125-129. [PubMed] [Google Scholar]17. Baysarowich, J., K. Koteva, D. W. Hughes, L. Ejim, E. Griffiths, K. Zhang, M. Junop, and G. D. Wright. 2008. Rifamycin antibiotic resistance by ADP-ribosylation: structure and diversity of Arr. Proc. Natl. Acad. Sci. U. S. A. 105:4886-4891. [PMC free article] [PubMed] [Google Scholar]18. Benveniste, R., and J. Davies. 1973. Aminoglycoside antibiotic-inactivating enzymes in actinomycetes similar to those present in clinical isolates of antibiotic-resistant bacteria. Proc. Natl. Acad. Sci. U. S. A. 70:2276-2280. [PMC free article] [PubMed] [Google Scholar]19. Bergstrom, C. T., M. Lo, and M. Lipsitch. 2004. Ecological theory suggests that antimicrobial cycling will not reduce antimicrobial resistance in hospitals. Proc. Natl. Acad. Sci. U. S. A. 101:13285-13290. [PMC free article] [PubMed] [Google Scholar]20. Boucher, H. W., G. H. Talbot, J. S. Bradley, J. E. Edwards, D. Gilbert, L. B. Rice, M. Scheld, B. Spellberg, and J. Bartlett. 2009. Bad bugs, no drugs: no ESKAPE! An update from the Infectious Diseases Society of America. Clin. Infect. Dis. 48:1-12. [PubMed] [Google Scholar]21. Boucher, Y., M. Labbate, J. E. Koenig, and H. W. Stokes. 2007. Integrons: mobilizable platforms that promote genetic diversity in bacteria. Trends Microbiol. 15:301-309. [PubMed] [Google Scholar]22. Bouvier, M., M. Ducos-Galand, C. Loot, D. Bikard, and D. Mazel. 2009. Structural features of single-stranded integron cassette attC sites and their role in strand selection. PLoS Genet. 5:e1000632. [PMC free article] [PubMed] [Google Scholar]23. Brazas, M. D., and R. E. Hancock. 2005. Using microarray gene signatures to elucidate mechanisms of antibiotic action and resistance. Drug Discov. Today 10:1245-1252. [PubMed] [Google Scholar]24. Brisson-Noël, A., M. Arthur, and P. Courvalin. 1988. Evidence for natural gene transfer from gram-positive cocci to Escherichia coli. J. Bacteriol. 170:1739-1745. [PMC free article] [PubMed] [Google Scholar]25. Brochet, M., E. Couvé, M. Zouine, C. Poyart, and P. Glaser. 2008. A naturally occurring gene amplification leading to sulfonamide and trimethoprim resistance in Streptococcus agalactiae. J. Bacteriol. 190:672-680. [PMC free article] [PubMed] [Google Scholar]26. Brötze-Oesterhelt, H., and N. A. Brunner. 2008. How many modes of action should an antibiotic have? Curr. Opin. Pharmacol. 8:564-573. [PubMed] [Google Scholar]27. Bryskier, A. (ed.). 2005. Antimicrobial agents: antibacterials and antifungals. ASM Press, Washington, DC.28. Bush, K., and G. A. Jacoby. 2010. Updated functional classification of β-lactamases. Antimicrob. Agents Chemother. 54:969-976. [PMC free article] [PubMed] [Google Scholar]29. Bushman, F. 2002. Lateral DNA transfer. Cold Spring Harbor Laboratory Press, Cold Spring Harbor, NY.30. Canton, R. 2009. Antibiotic resistance genes from the environment: a perspective through newly identified antibiotic resistance mechanisms in the clinical setting. Clin. Microbiol. Infect. 15(Suppl. 1):20-25. [PubMed] [Google Scholar]31. Carlsson, G., S. Orn, and D. G. J. Larsson. 2009. Effluent from bulk drug production is toxic to aquatic vertebrates. Environ. Toxicol. Chem. 28:2656-2662. [PubMed] [Google Scholar]32. Cases, I., and V. de Lorenzo. 2005. Promoters in the environment: transcriptional regulation in its natural context. Nat. Rev. Microbiol. 3:105-118. [PubMed] [Google Scholar]33. Chater, K. F., and C. Bruton. 1985. Resistance, regulatory and production genes for the antibiotic methylenomycin are clustered. EMBO J. 4:229-241. [PMC free article] [PubMed] [Google Scholar]34. Chee-Sanford, J. C., R. I. Mackie, S. Koike, I. G. Krapac, Y.-F. Lin, A. C. Yannarell, S. Maxwell, and R. I. Aminov. 2009. Fate and transport of antibiotic residues and antibiotic resistance genes following land application of manure waste. J. Environ. Qual. 38:1086-1106. [PubMed] [Google Scholar]35. Couce, A., and J. Blazquez. 2009. Side effects of antibiotics on genetic variability. FEMS Microbiol. Rev. 33:531-538. [PubMed] [Google Scholar]36. Dantas, G., M. O. A. Sommer, R. D. Oluwasegun, and G. M. Church. 2008. Bacteria subsisting on antibiotics. Science 320:100-103. [PubMed] [Google Scholar]37. Da Re, S., F. Garnier, E. Guerin, S. Campoy, F. Denis, and M. C. Ploy. 2009. The SOS response promotes qnrB quinolone-resistance determinant expression. EMBO Rep. 10:929-933. [PMC free article] [PubMed] [Google Scholar]38. Datta, N., and V. M. Hughes. 1983. Plasmids of the same Inc groups in enterobacteria before and after the medical use of antibiotics. Nature 306:616-617. [PubMed] [Google Scholar]39. Davies, J. 1995. Vicious circles: looking back on resistance plasmids. Genetics 139:1465-1468. [PMC free article] [PubMed] [Google Scholar]40. Davies, J. 1990. What are antibiotics? Archaic functions for modern activities. Mol. Microbiol. 4:1227-1232. [PubMed] [Google Scholar]41. Davies, J., G. B. Spiegelman, and G. Yim. 2006. The world of subinhibitory antibiotic concentrations. Curr. Opin. Microbiol. 9:1-9. [PubMed] [Google Scholar]42. D'Costa, V. M., E. Griffiths, and G. D. Wright. 2007. Expanding the soil antibiotic resistome: exploring environmental diversity. Curr. Opin. Microbiol. 10:481-489. [PubMed] [Google Scholar]43. D'Costa, V. M., K. M. McGrann, D. W. Hughes, and G. D. Wright. 2006. Sampling the antibiotic resistome. Science 311:374-377. [PubMed] [Google Scholar]44. DeLeo, F. R., and H. F. Chambers. 2009. Reemergence of antibiotic-resistant Staphylococcus aureus in the genomics era. J. Clin. Invest. 119:2464-2474. [PMC free article] [PubMed] [Google Scholar]45. Demain, A. L., and S. Sanchez. 2009. Microbial drug discovery: 80 years of progress. J. Antibiot. (Tokyo) 62:5-16. [PMC free article] [PubMed] [Google Scholar]46. Depardieu, F., I. Podglajen, R. Leclercq, E. Collatz, and P. Courvalin. 2007. Modes and modulations of antibiotic resistance gene expression. Clin. Microbiol. Rev. 20:79-114. [PMC free article] [PubMed] [Google Scholar]47. DeVincent, S. J., and C. Viola. 2006. Deliberations of an advisory committee regarding priorities, sources, and methods for collecting animal antimicrobial use data in the United States. Prev. Vet. Med. 73:133-151. [PubMed] [Google Scholar]48. Dionisio, F., I. Matic, M. Radman, O. R. Rodrigues, and F. Taddei. 2002. Plasmids spread very fast in heterogeneous bacterial communities. Genetics 162:1525. [PMC free article] [PubMed] [Google Scholar]49. Doyle, M. P. 2006. Antimicrobial resistance: implications for the food system. Compr. Rev. Food Sci. Food Saf. 5:71-137. [Google Scholar]50. Enright, M. C., D. A. Robinson, G. Randle, E. J. Feil, H. Grundmann, and B. G. Spratt. 2002. The evolutionary history of methicillin-resistant Staphylococcus aureus (MRSA). Proc. Natl. Acad. Sci. U. S. A. 99:7687-7692. [PMC free article] [PubMed] [Google Scholar]51. Fajardo, A., N. Martinez-Martin, M. Mercadillo, J. C. Galan, B. Ghysels, S. Matthijs, P. Cornelis, L. Wiehlmann, B. Tummler, F. Baquero, and J. L. Martinez. 2008. The neglected intrinsic resistome of bacterial pathogens. PloS One 3:e1619. [PMC free article] [PubMed] [Google Scholar]52. Feil, E. J., M. C. Maiden, M. Achtman, and B. G. Spratt. 1999. The relative contributions of recombination and mutation to the divergence of clones of Neisseria meningitidis. Mol. Biol. Evol. 16:1496-1502. [PubMed] [Google Scholar]53. Fenton, J. J., H. H. Harsch, and D. Klein. 1973. Production of volatile nitrogenous compounds from the degradation of streptomycin by Pseudomonas maltophilia. J. Bacteriol. 116:1267-1272. [PMC free article] [PubMed] [Google Scholar]54. Fick, J., H. Soderstrom, R. H. Lindberg, C. Phan, M. Tysklind, and D. G. J. Larsson. 2009. Contamination of surface, ground, and drinking water from pharmaceutical production. Environ. Toxicol. Chem. 28:2522-2527. [PubMed] [Google Scholar]55. Finland, M. 1979. Emergence of antibiotic resistance in hospitals, 1935-1975. Rev. Infect. Dis. 1:4-22. [PubMed] [Google Scholar]56. Finlay, B. B., and R. E. Hancock. 2004. Can innate immunity be enhanced to treat microbial infections? Nat. Rev. Microbiol. 2:497-504. [PubMed] [Google Scholar]57. Forsman, M., B. Häggström, L. Lindgren, and B. Jaurin. 1990. Molecular analysis of β-lactamases from four species of Streptomyces: comparison of amino acid sequences with those of other β-lactamases. Microbiology 136:589-598. [PubMed] [Google Scholar]58. Funnell, B. E., and G. J. Phillips (ed.). 2004. Plasmid biology. ASM Press, Washington, DC.59. Gale, E. F., E. Cundliffe, P. E. Reynolds, M. H. Richmond, and M. J. Waring (ed.). 1981. The molecular basis of antibiotic action, 2nd ed. John Wiley, Chichester, United Kingdom.60. Gillings, M., Y. Boucher, M. Labbate, A. Holmes, S. S. Krishnan, M. Holley, and H. W. Stokes. 2008. The evolution of class 1 integrons and the rise of antibiotic resistance. J. Bacteriol. 190:5095-5100. [PMC free article] [PubMed] [Google Scholar]61. Gillings, M. R., M. P. Holley, and H. W. Stokes. 2009. Evidence for dynamic exchange of qac gene cassettes between class 1 integrons and other integrons in freshwater biofilms. FEMS Microbiol. Lett. 296:282-288. [PubMed] [Google Scholar]62. Gillings, M. R., S. Krishnan, P. J. Worden, and S. A. Hardwick. 2008. Recovery of diverse genes for class 1 integron-integrases from environmental DNA samples. FEMS Microbiol. Lett. 287:56-62. [PubMed] [Google Scholar]63. Gniadkowski, M. 2008. Evolution of extended-spectrum beta-lactamases by mutation. Clin. Microbiol. Infect. 14(Suppl. 1):11-32. [PubMed] [Google Scholar]64. Gomez, M. J., and A. A. Neyfakh. 2006. Genes involved in intrinsic antibiotic resistance of Acinetobacter baylyi. Antimicrob. Agents Chemother. 50:3562-3567. [PMC free article] [PubMed] [Google Scholar]65. Gottlieb, D. 1976. The production and role of antibiotics in soil. J. Antibiot. (Tokyo) 29:987-1000. [PubMed] [Google Scholar]66. Guerin, E., G. Cambray, S. Da Re, D. Mazel, and M. C. Ploy. 2010. The SOS response controls antibiotic resistance by regulating the integrase of integrons. Med. Sci. (Paris) 1:28-30. [PubMed] [Google Scholar]67. Guerin, E., G. Cambray, N. Sanchez-Alberola, S. Campoy, I. Erill, S. Da Re, B. Gonzalez-Zorn, J. Barbé, M. C. Ploy, and D. Mazel. 2009. The SOS response controls integron recombination. Science 324:1034. [PubMed] [Google Scholar]68. Guilfoile, P. G., and C. R. Hutchinson. 1991. A bacterial analog of the mdr gene of mammalian tumor cells is present in Streptomyces peucetius, the producer of daunorubicin and doxorubicin. Proc. Natl. Acad. Sci. U. S. A. 88:8553-8557. [PMC free article] [PubMed] [Google Scholar]69. Hacker, J., and J. B. Kaper. 2000. Pathogenicity islands and the evolution of microbes. Annu. Rev. Microbiol. 54:641-679. [PubMed] [Google Scholar]70. Hakenbeck, R. 1998. Mosaic genes and their role in penicillin-resistant Streptococcus pneumoniae. Electrophoresis 19:597-601. [PubMed] [Google Scholar]71. Hawkey, P. M., and A. M. Jones. 2009. The changing epidemiology of resistance. J. Antimicrob. Chemother. 64(Suppl. 1):i3-i10. [PubMed] [Google Scholar]72. Helinski, D. R. 2004. Introduction to plasmids: a selective view of their history, p. 1-21. In B. E. Funnell and G. J. Phillips (ed.), Plasmid biology. ASM Press, Washington, DC.73. Hodgkin, D. C. 1949. The X-ray analysis of the structure of penicillin. Adv. Sci. 6:85-89. [PubMed] [Google Scholar]74. Holmes, A. J., M. R. Gillings, B. S. Nield, B. C. Mabbutt, K. M. Nevalainen, and H. W. Stokes. 2003. The gene cassette metagenome is a basic resource for bacterial genome evolution. Environ. Microbiol. 5:383-394. [PubMed] [Google Scholar]75. Hopwood, D. A. 2007. How do antibiotic-producing bacteria ensure their self-resistance before antibiotic biosynthesis incapacitates them? Mol. Microbiol. 63:937-940. [PubMed] [Google Scholar]76. Horrevorts, A. M., J. Borst, R. J. T. Puyk, R. D. Ridder, G. Dzoljic-Danilovic, J. E. Degener, K. F. Kerrebijn, and M. F. Michel. 1990. Ecology of Pseudomonas aeruginosa in patients with cystic fibrosis. J. Med. Microbiol. 31:119-124. [PubMed] [Google Scholar]77. Jacobs, C., L.-J. Huang, E. Bartowsky, S. Normark, and J. T. Park. 1994. Bacterial cell wall recycling provides cytosolic muropeptides as effectors for β-lactamase induction. EMBO J. 13:4684-4694. [PMC free article] [PubMed] [Google Scholar]78. Jacoby, G. A. 2009. AmpC β-lactamases. Clin. Microbiol. Rev. 22:161-182. [PMC free article] [PubMed] [Google Scholar]79. Kashmiri, S. V. S., and R. D. Hotchkiss. 1975. Evidence of tandem duplication of genes in a merodiploid region of pneumococcal mutants resistant to sulfonamide. Genetics 81:21. [PMC free article] [PubMed] [Google Scholar]80. Kelly, C. P., and J. T. LaMont. 2008. Clostridium difficile--more difficult than ever. N. Engl. J. Med. 359:1932-1940. [PubMed] [Google Scholar]81. Kohanski, M. A., D. J. Dwyer, B. Hayete, C. A. Lawrence, and J. J. Collins. 2007. A common mechanism of cellular death induced by bactericidal antibiotics. Cell 130:797-810. [PubMed] [Google Scholar]82. Levy, S. B., and B. Marshall. 2004. Antibacterial resistance worldwide: causes, challenges and responses. Nat. Med. 10(Suppl.):S122-S129. [PubMed] [Google Scholar]83. Liebert, C. A., R. M. Hall, and A. O. Summers. 1999. Transposon Tn21, flagship of the floating genome. Microbiol. Mol. Biol. Rev. 63:507-522. [PMC free article] [PubMed] [Google Scholar]83a. Linton, A. H. 1977. Antibiotic resistance: the present situation reviewed. Vet. Rec. 100:354-360. [PubMed] [Google Scholar]84. Lipp, E. K., A. Huq, and R. R. Colwell. 2002. Effects of global climate on infectious disease: the cholera model. Clin. Microbiol. Rev. 15:757-770. [PMC free article] [PubMed] [Google Scholar]85. Liu, B., and M. Pop. 2009. ARDB—Antibiotic Resistance Genes Database. Nucleic Acids Res. 37:D443-D447. [PMC free article] [PubMed] [Google Scholar]86. Livermore, D. M., R. Canton, M. Gniadkowski, P. Nordmann, G. M. Rossolini, G. Arlet, J. Ayala, T. M. Coque, I. Kern-Zdanowicz, F. Luzzaro, L. Poirel, and N. Woodford. 2007. CTX-M: changing the face of ESBLs in Europe. J. Antimicrob. Chemother. 59:165-174. [PubMed] [Google Scholar]87. Lomovskaya, O., H. I. Zgurskaya, M. Totrov, and W. J. Watkins. 2007. Waltzing transporters and 'the dance macabre' between humans and bacteria. Nat. Rev. Drug Discov. 6:56-65. [PubMed] [Google Scholar]88. Long, K. S., J. Poehlsgaard, C. Kehrenberg, S. Schwartz, and B. Vester. 2006. The Cfr rRNA methyltransferase confers resistance to phenicols, lincosamides, oxazolidinones, pleuromutilins, and streptogramin A antibiotics. Antimicrob. Agents Chemother. 50:2500-2505. [PMC free article] [PubMed] [Google Scholar]89. Marshall, B. M., D. J. Ochieng, and S. B. Levy. 2009. Commensals: unappreciated reservoir of antibiotic resistance. Microbe 4:231-238. [Google Scholar]90. Martinez, J. L. 2009. The role of natural environments in the evolution of resistance traits in pathogenic bacteria. Proc. Biol. Sci. 276:2521-2530. [PMC free article] [PubMed] [Google Scholar]91. Martinez, J. L., F. Baquero, and D. Andersson. 2007. Predicting antibiotic resistance. Nat. Rev. Microbiol. 5:958-965. [PubMed] [Google Scholar]92. Masterton, R. G. 2005. Antibiotic cycling: more than it might seem? J. Antimicrob. Chemother. 55:1-5. [PubMed] [Google Scholar]93. Mazel, D. 2006. Integrons: agents of bacterial evolution. Nat. Rev. Microbiol. 4:608-620. [PubMed] [Google Scholar]94. Mendez, C., and J. Salas. 2001. The role of ABC transporters in antibiotic-producing organisms: drug secretion and resistance mechanisms. Res. Microbiol. 152:341-350. [PubMed] [Google Scholar]95. Moura, A., I. Henriques, K. Smalla, and A. Correia. 2010. Wastewater bacterial communities bring together broad-host range plasmids, integrons and a wide diversity of uncharacterized gene cassettes. Res. Microbiol. 161:58-66. [PubMed] [Google Scholar]96. Mwangi, M. M., S. W. Wu, Y. Zhou, K. Sieradzki, H. de Lencastre, P. Richardson, D. Bruce, E. Rubin, E. Myers, E. D. Siggia, and A. Tomasz. 2007. Tracking the in vivo evolution of multidrug resistance in Staphylococcus aureus by whole-genome sequencing. Proc. Natl. Acad. Sci. U. S. A. 104:9451-9456. [PMC free article] [PubMed] [Google Scholar]97. Nandi, S., J. J. Maurer, C. Hofacre, and A. O. Summers. 2004. Gram-positive bacteria are a major reservoir of class 1 antibiotic resistance integrons in poultry litter. Proc. Natl. Acad. Sci. U. S. A. 101:7118-7122. [PMC free article] [PubMed] [Google Scholar]98. Nikolaou, K. C., and T. Montagnon. 2008. Molecules that changed the world. Wiley VCH, Weinheim, Germany.99. Nordmann, P., and L. Poirel. 2005. Emergence of plasmid-mediated resistance to quinolones in Enterobacteriaceae. J. Antimicrob. Chemother. 56:463-469. [PubMed] [Google Scholar]100. Norman, A., L. H. Hansen, and S. J. Sorensen. 2009. Conjugative plasmids: vessels of the communal gene pool. Philos. Trans. R. Soc. Lond. B. Biol. Sci. 364:2275-2289. [PMC free article] [PubMed] [Google Scholar]101. Novick, R. P., and E. Geisinger. 2008. Quorum sensing in staphylococci. Annu. Rev. Genet. 42:541-564. [PubMed] [Google Scholar]102. Ogawara, H., N. Kawamura, T. Kudo, K.-I. Suzuki, and T. Nakase. 1999. Distribution of β-lactamases in actinomycetes. Antimicrob. Agents Chemother. 43:3014-3017. [PMC free article] [PubMed] [Google Scholar]103. Pallecchi, L., A. Bartoloni, F. Paradisi, and G. M. Rossolini. 2008. Antibiotic resistance in the absence of antimicrobial use: mechanisms and implications. Expert Rev. Anti Infect. Ther. 6:725-732. [PubMed] [Google Scholar]104. Pallecchi, L., C. Lucchetti, A. Bartoloni, F. Bartalesi, A. Mantella, H. Gamboa, A. Carattoli, F. Paradisi, and G. M. Rossolini. 2007. Population structure and resistance genes in antibiotic-resistant bacteria from a remote community with minimal antibiotic exposure. Antimicrob. Agents Chemother. 51:1179-1184. [PMC free article] [PubMed] [Google Scholar]105. Pallecchi, L., E. Riccobono, A. Mantella, F. Bartalesi, S. Sennati, H. Gamboa, E. Gotuzzo, A. Bartoloni, and G. M. Rossolini. 2009. High prevalence of qnr genes in commensal enterobacteria from healthy children in Peru and Bolivia. Antimicrob. Agents Chemother. 53:2632-2635. [PMC free article] [PubMed] [Google Scholar]106. Payne, D. J., M. N. Gwynn, D. J. Holmes, and D. L. Pompliano. 2007. Drugs for bad bugs: confronting the challenges of antibacterial discovery. Nat. Rev. Drug Discov. 6:29-40. [PubMed] [Google Scholar]107. Peleg, A. Y., H. Seifert, and D. L. Paterson. 2008. Acinetobacter baumannii: emergence of a successful pathogen. Clin. Microbiol. Rev. 21:538-582. [PMC free article] [PubMed] [Google Scholar]108. Perez, F., A. M. Hujer, K. M. Hujer, B. K. Decker, P. N. Rather, and R. A. Bonomo. 2007. Global challenge of multidrug-resistant Acinetobacter baumannii. Antimicrob. Agents Chemother. 51:3471-3484. [PMC free article] [PubMed] [Google Scholar]109. Petkovic, H., J. Cullum, D. Hranueli, I. S. Hunter, N. Peric-Concha, J. Pigac, A. Thamchaipenet, D. Vujaklija, and P. F. Long. 2006. Genetics of Streptomyces rimosus, the oxytetracycline producer. Microbiol. Mol. Biol. Rev. 70:704-728. [PMC free article] [PubMed] [Google Scholar]110. Piddock, L. J. 2006. Clinically relevant chromosomally encoded multidrug resistance efflux pumps in bacteria. Clin. Microbiol. Rev. 19:382-402. [PMC free article] [PubMed] [Google Scholar]111. Piddock, L. J. 2006. Multidrug-resistance efflux pumps—not just for resistance. Nat. Rev. Microbiol. 4:629-636. [PubMed] [Google Scholar]112. Poirel, L., T. Naas, and P. Nordmann. 2010. Diversity, epidemiology, and genetics of class D β-lactamases. Antimicrob. Agents Chemother. 54:24-38. [PMC free article] [PubMed] [Google Scholar]113. Poole, K. 2005. Efflux-mediated antimicrobial resistance. J. Antimicrob. Chemother. 56:20-51. [PubMed] [Google Scholar]114. Projan, S. J. 2003. Why is big pharma getting out of antibacterial drug discovery? Curr. Opin. Microbiol. 6:427-430. [PubMed] [Google Scholar]115. Qin, J., R. Li, J. Raes, M. Arumugam, K. S. Burgdorf, C. Manichanh, T. Nielsen, N. Pons, F. Levenez, T. Yamada, D. R. Mende, J. Li, J. Xu, S. Li, D. Li, J. Cao, B. Wang, H. Liang, H. Zheng, Y. Xie, J. Tap, P. Lepage, M. Bertalan, J.-M. Batto, T. Hansen, D. L. Paslier, A. Linneberg, H. B. Nielsen, E. Pelletier, P. Renault, T. Sicheritz-Ponten, K. Turner, H. Zhu, C. Yu, S. Li, M. Jian, Y. Zhou, Y. Li, X. Zhang, S. Li, N. Qin, H. Yang, J. Wang, S. Brunak, J. Doré, F. Guarner, K. Kristiansen, O. Pedersen, J. Parkhill, J. Weissenbach, M. Consortium, P. Bork, S. D. Ehrlich, and J. Wang. 2010. A human gut microbial gene catalogue established by metagenomic sequencing. Nature 464:59-65. [PMC free article] [PubMed] [Google Scholar]116. Queenan, A. M., and K. Bush. 2007. Carbapenemases: the versatile β-lactamases. Clin. Microbiol. Rev. 20:440-458. [PMC free article] [PubMed] [Google Scholar]117. Reading, C., and M. Cole. 1977. Clavulanic acid: a beta-lactamase-inhibiting beta-lactam from Streptomyces clavuligerus. Antimicrob. Agents Chemother. 11:852-857. [PMC free article] [PubMed] [Google Scholar]118. Recchia, G. D., and R. M. Hall. 1995. Gene cassettes: a new class of mobile element. Microbiology 141:3015-3027. [PubMed] [Google Scholar]119. Riesenfeld, C. S., R. M. Goodman, and J. Handelsman. 2004. Uncultured soil bacteria are a reservoir of new antibiotic resistance genes. Environ. Microbiol. 6:981-989. [PubMed] [Google Scholar]120. Roberts, M. C. 2008. Update on macrolide-lincosamide-streptogramin, ketolide, and oxazolidinone resistance genes. FEMS Microbiol. Lett. 282:147-159. [PubMed] [Google Scholar]121. Robicsek, A., G. A. Jacoby, and D. C. Hooper. 2006. The worldwide emergence of plasmid-mediated quinolone resistance. Lancet Infect. Dis. 6:629-640. [PubMed] [Google Scholar]122. Ryan, F. 1992. The forgotten plague: how the battle against tuberculosis was won—and lost. Little, Brown and Company, Boston, MA.123. Schluter, A., L. Krause, R. Szczepanowski, A. Goesmann, and A. Puhler. 2008. Genetic diversity and composition of a plasmid metagenome from a wastewater treatment plant. J. Biotechnol. 136:65-76. [PubMed] [Google Scholar]124. Shah, N. S., A. Wright, G. H. Bai, L. Barrera, F. Boulahbal, N. Martin-Casabona, F. Drobniewski, C. Gilpin, M. Havelkova, R. Lepe, R. Lumb, B. Metchock, F. Portaels, M. F. Rodrigues, S. Rusch-Gerdes, A. V. Deun, V. Vincent, K. Laserson, C. Wells, and J. P. Cegielski. 2007. Worldwide emergence of extensively drug-resistant tuberculosis. Emerg. Infect. Dis. 13:380-387. [PMC free article] [PubMed] [Google Scholar]125. Sheehan, J., and K. R. Henery-Logan. 1959. The total synthesis of penicillin V. J. Am. Chem. Soc. 81:3089-3094. [Google Scholar]126. Shoemaker, N. B., H. Vlamakis, K. Hayes, and A. A. Salyers. 2001. Evidence for extensive resistance gene transfer among Bacteroides spp. and among Bacteroides and other genera in the human colon. Appl. Environ. Microbiol. 67:561-568. [PMC free article] [PubMed] [Google Scholar]127. Skurray, R. A., and N. Firth. 1997. Molecular evolution of multiply-antibiotic-resistant staphylococci, p. 167-191. In D. J. Chadwick (ed.), Antibiotic resistance: origins, evolution, selection and spread. Wiley, Chichester, United Kingdom.128. Sommer, M. O. A., G. Dantas, and G. M. Church. 2009. Functional characterization of the antibiotic resistance reservoir in the human microflora. Science 325:1128-1131. [PMC free article] [PubMed] [Google Scholar]129. Sorensen, S. J., M. Bailey, L. H. Hansen, N. Kroer, and S. Wuertz. 2005. Studying plasmid horizontal transfer in situ: a critical review. Nat. Rev. Microbiol. 3:700-710. [PubMed] [Google Scholar]130. Sotgiu, G., G. Ferrara, A. Matteelli, M. D. Richardson, R. Centis, S. Ruesch-Gerdes, O. Toungoussova, J.-P. Zellweger, A. Spanevello, D. Cirillo, C. Lange, and G. B. Migliori. 2009. Epidemiology and clinical management of XDR-TB: a systematic review by TBNET. Eur. Respir. J. 33:871-881. [PubMed] [Google Scholar]131. Springman, A. C., D. W. Lacher, G. Wu, N. Milton, T. S. Whittam, H. D. Davies, and S. D. Manning. 2009. Selection, recombination, and virulence gene diversity among group B streptococcal genotypes. J. Bacteriol. 191:5419-5427. [PMC free article] [PubMed] [Google Scholar]132. Stokes, H. W., and R. M. Hall. 1989. A novel family of potentially mobile DNA elements encoding site-specific gene-integration functions: integrons. Mol. Microbiol. 3:1669-1683. [PubMed] [Google Scholar]133. Strahilevitz, J., G. A. Jacoby, D. C. Hooper, and A. Robicsek. 2009. Plasmid-mediated quinolone resistance: a multifaceted threat. Clin. Microbiol. Rev. 22:664-689. [PMC free article] [PubMed] [Google Scholar]134. Strohl, W. R. 1997. Biotechnology of antibiotics, 2nd ed. Marcel Dekker, Inc., New York, NY.135. Swann, M. 1969. Report of the joint committee on the use of antibiotics in animal husbandry and veterinary medicine. Her Majesty's Stationery Office, London, United Kingdom.136. Szczepanowski, R., B. Linke, I. Krahn, K.-H. Gartemann, T. Gützkow, W. Eichler, A. Pühler, and A. Schlüter. 2009. Detection of 140 clinically relevant antibiotic-resistance genes in the plasmid metagenome of wastewater treatment plant bacteria showing reduced susceptibility to selected antibiotics. Microbiology 155:2306-2319. [PubMed] [Google Scholar]137. Tamae, C., A. Liu, K. Kim, D. Sitz, J. Hong, E. Becket, A. Bui, P. Solaimani, K. P. Tran, H. Yang, and J. H. Miller. 2008. Determination of antibiotic hypersensitivity among 4,000 single-gene-knockout mutants of Escherichia coli. J. Bacteriol. 190:5981-5988. [PMC free article] [PubMed] [Google Scholar]138. Thomson, C. J., and S. G. Amyes. 1992. TRC-1: emergence of a clavulanic acid-resistant TEM beta-lactamase in a clinical strain. FEMS Microbiol. Lett. 70:113-117. [PubMed] [Google Scholar]139. Toleman, M. A., P. M. Bennett, and T. R. Walsh. 2006. ISCR elements: novel gene-capturing systems of the 21st century? Microbiol. Mol. Biol. Rev. 70:296-316. [PMC free article] [PubMed] [Google Scholar]140. Tuomanen, E., S. Lindquist, S. Sande, M. Galleni, K. Light, D. Gage, and S. Normark. 1991. Coordinate regulation of beta-lactamase induction and peptidoglycan composition by the amp operon. Science 251:201-204. [PubMed] [Google Scholar]141. Vallino, J. J. 2003. Modeling microbial consortiums as distributed metabolic networks. Biol. Bull. 204:174. [PubMed] [Google Scholar]142. Vazquez, D., T. Staehelin, M. L. Celma, E. Battaner, R. Fernandez-Munoz, and R. E. Munro. 1969. Inhibitors as tools in elucidating ribosome function, p. 100-125. In T. Bucher and H. Sies (ed.), Inhibitors as tools in cell research. Springer-Verlag, Heidelberg, Germany.143. Velayati, A. A., M. R. Masjedi, P. Farnia, P. Tabarsi, J. Ghanavi, A. H. ZiaZarifi, and S. E. Hoffner. 2009. Emergence of new forms of totally drug-resistant tuberculosis bacilli: super extensively drug-resistant tuberculosis or totally drug-resistant strains in Iran. Chest 136:420-425. [PubMed] [Google Scholar]144. Ventura, M., C. Canchaya, A. Tauch, G. Chandra, G. F. Fitzgerald, K. F. Chater, and D. van Sinderen. 2007. Genomics of Actinobacteria: tracing the evolutionary history of an ancient phylum. Microbiol. Mol. Biol. Rev. 71:495-548. [PMC free article] [PubMed] [Google Scholar]145. Vernaz, N., K. Hill, S. Leggeat, D. Nathwani, G. Philips, P. Bonnabry, and P. Davey. 2009. Temporal effects of antibiotic use and Clostridium difficile infections. J. Antimicrob. Chemother. 63:1272-1275. [PubMed] [Google Scholar]146. Waksman, S. A. 1973. History of the word 'antibiotic.' J. Hist. Med. Allied Sci. 28:284-286. [PubMed] [Google Scholar]147. Walsh, C. 2003. Antibiotics: actions, origins, resistance. ASM Press, Washington, DC.148. Walsh, T. R. 2006. Combinatorial genetic evolution of multiresistance. Curr. Opin. Microbiol. 9:476-482. [PubMed] [Google Scholar]149. White, D. G., M. N. Alekshun, and P. F. McDermott (ed.). 2005. Frontiers in antimicrobial resistance: a tribute to Stuart B. Levy. ASM Press, Washington, DC.150. Wright, G. D. 2007. The antibiotic resistome: the nexus of chemical and genetic diversity. Nat. Rev. Microbiol. 5:175-186. [PubMed] [Google Scholar]150a. Wright, G. D., and M. Morar. The genomic enzymology of antibiotic resistance. Annu. Rev. Genet., in press. [PubMed]151. Yassin, A., and A. S. Mankin. 2007. Potential new antibiotic sites in the ribosome revealed by deleterious mutations in RNA of the large ribosomal subunit. J. Biol. Chem. 282:24329-24342. [PubMed] [Google Scholar]152. Yeh, P. J., M. J. Hegreness, A. P. Aiden, and R. Kishony. 2009. Drug interactions and the evolution of antibiotic resistance. Nat. Rev. Microbiol. 7:460-466. [PMC free article] [PubMed] [Google Scholar]Page 2Modes of action and resistance mechanisms of commonly used antibioticsAntibiotic classExample(s)Target Mode(s) of resistanceβ-LactamsPenicillins (ampicillin), cephalosporins (cephamycin), penems (meropenem), monobactams (aztreonam)Peptidoglycan biosynthesisHydrolysis, efflux, altered targetAminoglycosidesGentamicin, streptomycin, spectinomycinTranslationPhosphorylation, acetylation, nucleotidylation, efflux, altered targetGlycopeptidesVancomycin, teicoplaninPeptidoglycan biosynthesisReprogramming peptidoglycan biosynthesisTetracyclinesMinocycline, tigecyclineTranslationMonooxygenation, efflux, altered targetMacrolidesErythromycin, azithromicinTranslationHydrolysis, glycosylation, phosphorylation, efflux, altered targetLincosamidesClindamycinTranslationNucleotidylation, efflux, altered targetStreptograminsSynercidTranslationC-O lyase (type B streptogramins), acetylation (type A streptogramins), efflux, altered targetOxazolidinonesLinezolidTranslationEfflux, altered targetPhenicolsChloramphenicolTranslationAcetylation, efflux, altered targetQuinolonesCiprofloxacinDNA replicationAcetylation, efflux, altered targetPyrimidinesTrimethoprimC1 metabolismEfflux, altered targetSulfonamidesSulfamethoxazoleC1 metabolismEfflux, altered targetRifamycinsRifampinTranscriptionADP-ribosylation, efflux, altered targetLipopeptidesDaptomycinCell membraneAltered targetCationic peptidesColistinCell membraneAltered target, efflux

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