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Beta lactam antibiotics examples

Have you ever wondered how certain antibiotics work wonders against bacterial infections? One key player in this field is beta-lactam, a class of antibiotics that has transformed modern medicine. From penicillin to cephalosporins, beta-lactams are essential in treating various infections and saving countless lives.In this article, you'll explore the fascinating world of beta-lactam antibiotics, including their mechanism of action and common examples. You'll discover why these drugs are so effective at disrupting bacterial cell walls and how they continue to evolve in response to antibiotic resistance. Are you ready to dive into the science behind these life-saving medications? Understanding beta-lactams not only broadens your knowledge but also highlights their critical role in healthcare today.Beta-lactam antibiotics play a crucial role in treating bacterial infections. They target the bacterial cell wall, leading to cell lysis and death. Here are some key examples of beta-lactam antibiotics:Penicillin: Developed in the 1920s, penicillin is one of the first and most widely used antibiotics. It's effective against gram-positive bacteria like Staphylococcus and Streptococcus.Amoxicillin: A derivative of penicillin, amoxicillin offers a broader spectrum of activity. It treats respiratory tract infections and urinary tract infections effectively.Cephalosporins: This group includes several generations with varying effectiveness against bacteria:First generation (e.g., Cephalexin): Effective against gram-positive bacteria.Second generation (e.g., Cefuroxime): Broader coverage including some gram-negative bacteria.Third generation (e.g., Ceftriaxone): Even wider spectrum, often used for severe infections.Carbapenems: These powerful agents combat multi-drug resistant bacteria. Examples include imipenem and meropenem; they're reserved for serious infections due to their potency.Monobactams: Aztreonam serves as an example here; it specifically targets gram-negative bacteria without affecting gram-positive ones.These antibiotics remain vital in healthcare due to their effectiveness against various bacterial pathogens while adapting to emerging resistance patterns.Understanding these examples enhances your knowledge of beta-lactam antibiotics' significance in modern medicine.Beta-lactam antibiotics primarily function by disrupting bacterial cell wall synthesis. This disruption ultimately leads to cell lysis and death, making it an effective treatment option for various bacterial infections.Inhibition of cell wall synthesis is a key action of beta-lactams. These antibiotics target penicillin-binding proteins (PBPs), which play a crucial role in assembling and maintaining the bacterial cell wall. When beta-lactams bind to PBPs, they inhibit their activity, preventing the cross-linking of peptidoglycan layers. As a result, the structural integrity of the bacteria weakens. The bacteria can't withstand osmotic pressure and eventually burst.The spectrum of activity varies among different beta-lactam antibiotics. For example:Penicillin effectively targets gram-positive bacteria like Streptococcus pneumoniae.Amoxicillin offers broader coverage against both gram-positive and some gram-negative organisms such as Escherichia coli.Cephalosporins, categorized into generations, extend their range from first-generation (like cefazolin) targeting mainly gram-positive bacteria to third-generation agents (like ceftriaxone) that are effective against more resistant strains.Carbapenems, such as meropenem, have broad-spectrum activity against multi-drug resistant pathogens.Monobactams, specifically aztreonam, are useful for treating infections caused by gram-negative bacteria while sparing most gram-positive organisms.Understanding these mechanisms helps you appreciate how beta-lactam antibiotics combat bacterial infections effectively.Beta-lactam antibiotics comprise several classes, each with distinct characteristics and applications. Understanding these types enhances your knowledge of their use in treating infections.Penicillins are among the earliest discovered antibiotics. They target primarily gram-positive bacteria. Common examples include:Penicillin G: Used for serious bacterial infections such as pneumonia.Amoxicillin: A broad-spectrum antibiotic effective against both gram-positive and some gram-negative bacteria; often prescribed for ear infections.Ampicillin: Similar to amoxicillin but can be given intravenously for severe infections.These medications work by inhibiting cell wall synthesis, leading to bacterial death.Cephalosporins are categorized into generations based on their spectrum of activity. Each generation has a broader range of effectiveness against various bacteria. Examples include:First Generation (Cefazolin): Effective against gram-positive bacteria; commonly used before surgery to prevent infection.Second Generation (Cefuroxime): Targets both gram-positive and some gram-negative organisms; useful for respiratory tract infections.Third Generation (Ceftriaxone): Broad-spectrum antibiotic effective against more resistant strains, often used in hospital settings.Fourth Generation (Cefepime): Provides enhanced activity against pseudomonas aeruginosa and other difficult-to-treat pathogens.These antibiotics disrupt the bacterial cell wall similarly to penicillins but vary in their resistance profiles.Carbapenems are powerful beta-lactams recommended for multi-drug resistant infections. They maintain efficacy against a wide range of pathogens. Key examples include:Meropenem: Often used for severe or high-risk bacterial infections due to its broad coverage including some resistant strains.Imipenem/Cilastatin: Combines imipenem with cilastatin to prevent rapid breakdown by kidney enzymes, extending its action.These agents are crucial in critical care settings where drug-resistant bacteria pose significant risks.Monobactams represent a unique class specifically targeting gram-negative bacteria. The primary example is:Aztreonam: Effective only against aerobic gram-negative organisms like Pseudomonas aeruginosa while sparing most anaerobic flora.This selectivity makes it an excellent choice when treating patients allergic to penicillin, as it presents minimal cross-reactivity with other beta-lactams.Understanding these types equips you with valuable insights into how beta-lactam antibiotics function effectively within clinical contexts.Beta-lactam antibiotics play a crucial role in treating various bacterial infections. Their effectiveness and broad spectrum of activity make them essential tools in modern medicine.Penicillin is widely used for treating streptococcal infections. Amoxicillin, another common beta-lactam, targets respiratory tract infections like pneumonia. Cephalosporins serve diverse purposes; first-generation options treat skin and soft tissue infections while third-generation agents address more resistant strains. Carbapenems, such as meropenem, are reserved for severe cases involving multi-drug-resistant organisms. Monobactams like aztreonam specifically target gram-negative bacteria, making them suitable alternatives for patients with penicillin allergies.Bacterial resistance to beta-lactam antibiotics poses significant challenges. Many bacteria produce beta-lactamase enzymes that deactivate these drugs. This issue leads to treatment failures and necessitates the development of new agents to combat resistant strains. Increased use of carbapenems highlights growing resistance among pathogens, emphasizing the need for careful antibiotic stewardship. Continuous monitoring of resistance patterns helps inform effective treatment strategies and preserve the efficacy of existing antibiotics. Sign Up Now &Daily Live Classes3000+ TestsStudy Material & PDFQuizzes With Detailed Analytics+ More BenefitsGet Free Access Now As a library, NLM provides access to scientific literature. Inclusion in an NLM database does not imply endorsement of, or agreement with, the contents by NLM or the National Institutes of Health. Learn more: PMC Disclaimer | PMC Copyright Notice β-Lactams are the most widely used class of antibiotics. Since the discovery of benzylpenicillin in the 1920s, thousands of new penicillin derivatives and related β-lactam classes of cephalosporins, cephamycins, monobactams, and carbapenems have been discovered. Each new class of β-lactam has been developed either to increase the spectrum of activity to include additional bacterial species or to address specific resistance mechanisms that have arisen in the targeted bacterial population. Resistance to β-lactams is primarily because of bacterially produced β-lactamase enzymes that hydrolyze the β-lactam ring, thereby inactivating the drug. The newest effort to circumvent resistance is the development of novel broad-spectrum β-lactamase inhibitors that work against many problematic β-lactamases, including cephalosporinases and serine-based carbapenemases, which severely limit therapeutic options. This work provides a comprehensive overview of β-lactam antibiotics that are currently in use, as well as a look ahead to several new compounds that are in the development pipeline. The most widely used antibiotics are the β-lactams (e.g., penicillin). Efforts to develop broad-spectrum inhibitors of bacterially produced β-lactamase enzymes may curb resistance to this important class of antibiotics. When Alexander Fleming was searching for an antistaphylococcal bacteriophage in his laboratory in the 1920s, he deliberately left plates out on the bench to capture airborne agents that might also serve to kill staphylococci (Fleming 1929). His success was greater than he must have hoped for. His initial publication on benzylpenicillin described a substance that was unstable in aqueous solution but that might serve as an antiseptic or as a selective agent for isolation of Gram-negative bacteria that were present in mixed cultures of staphylococci and streptococci. As the potential utility of penicillin G as a parenteral therapeutic agent became more obvious, Fleming, Abraham, Florey, and a consortium of scientists from England and the United States were able to optimize the isolation and identification of benzylpenicillin to assist in the treatment of Allied soldiers in World War II (Macfarlane 1979). These activities set the stage for the launch of the most successful class of antibiotics in history. β-Lactam antibiotics are currently the most used class of antibacterial agents in the infectious disease armamentarium. As shown in Figure 1, β-lactams account for 65% of all prescriptions for injectable antibiotics in the United States. Of the β-lactams, cephalosporins comprise nearly half of the prescriptions (Table 1). The β-lactams are well tolerated, efficacious, and widely prescribed. Their major toxicity is related to an allergic response in a small percentage of patients who react to related side chain determinants; notably, these reactions are most common with penicillins and cephalosporins with minimal reactivity caused by monobactams (Saxon et al. 1984; Moss et al. 1991). The bactericidal mechanism of killing by β-lactams is perceived to be a major advantage in the treatment of serious infections. When these agents were threatened by the rapid emergence of β-lactamases, β-lactamase-stable agents were developed, as well as potent β-lactamase inhibitors (BLIs). In this introductory description of the β-lactams, the most commonly available β-lactams and BLIs will be presented, with a brief summary of their general characteristics. Occasional agents have been included for their historical or scientific importance. Note that resistance mechanisms will be discussed in detail in other articles in this collection. Proportion of prescriptions in the United States for injectable antibiotics by class for years 2004–2014. The percentage of standard units for each injectable antibiotic prescribed in the United States from 2004 to 2014 is shown as follows: β-lactams, 65.24%; glycopeptides, 9%; fluoroquinolones, 8%; macrolides/ketolides, 6%; aminoglycosides, 5%; polymyxins, 1%; trimethoprim/sulfamethoxazole, 0.5%; tetracyclines (excluding tigecycline), 0.4%; all other antibiotics (including daptomycin, linezolid, and tigecycline), 4.21%. (Data from the IMS MDART Quarterly Database on file at AstraZeneca.) Usage of parenteral β-lactams by class from 2004–2104 in the United States Class of β-lactam Percentage of prescriptionsa Narrow spectrum penicillins 3.12 Broad spectrum penicillinsb 36.54 Cephalosporins 47.49 Monobactams 1.66 Carbapenems 11.20 β-Lactam antibiotics are bactericidal agents that interrupt bacterial cell-wall formation as a result of covalent binding to essential penicillin-binding proteins (PBPs), enzymes that are involved in the terminal steps of peptidoglycan cross-linking in both Gram-negative and Gram-positive bacteria. Every bacterial species has its own distinctive set of PBPs that can range from three to eight enzymes per species (Georgopapadakou and Liu 1980). The inhibition of bacterial peptidoglycan transpeptidation by penicillin was described mechanistically in a classical paper by Tipper and Strominger (1965), who noted a structural similarity of penicillin G to the terminal d-Ala-d-Ala dipeptide of the nascent peptidoglycan in the dividing bacterial cell. This mechanism is now known to involve binding of penicillin, or another β-lactam, to an active site serine found in all functional PBPs (Georgopapadakou et al. 1977). The resulting inactive acyl enzyme may then slowly hydrolyze the antibiotic to form a microbiologically inactive entity (Frère and Joris 1985). In addition to these functionalities, recent work has shown the binding of selected β-lactams, such as ceftaroline, to an allosteric site in PBP2a from Staphylococcus aureus, resulting in an increased sensitization of the organism to the antibiotic (Otero et al. 2013; Gonzales et al. 2015). PBPs may be divided into classes according to molecular mass (Goffin and Ghuysen 1998; Massova and Mobashery 1998), with low-molecular-mass PBPs serving mainly as monofunctional d-Ala-d-Ala carboxypeptidases. High-molecular-mass PBPs have been divided into two subclasses, one of which (class A) includes bifunctional enzymes with both a transpeptidase and a transglycosylase domain, and the second of which (class B) encompasses d-Ala-d-Ala-dependent transpeptidases. At least one PBP is deemed to be essential in each species, with a unique specificity for β-lactam binding that varies among each species and each β-lactam class (Curtis et al. 1979; Georgopapadakou and Liu 1980). In Gram-negative bacteria, essential PBPs include the high-molecular-weight PBPs 1a and 1b that are involved in cell lysis, PBP2, the inhibition of which results in a cessation of cell division and the formation of spherical cells, and PBP3 for which inhibition arrests cell division, resulting in filamentation. Cell death may occur as a result of inhibiting one or more of these PBPs (Spratt 1977, 1983). The roles of PBPs in Gram-positive bacteria and Mycobacterium tuberculosis are discussed in detail in Fisher and Mobashery (2016). Penicillin G (benzylpenicillin) was the first β-lactam to be used clinically, most frequently to treat streptococcal infections for which it had high potency (Rammelkamp and Keefer 1943; Hirsh and Dowling 1946). Another naturally occurring penicillin, penicillin V (phenoxymethylpenicillin), in an oral formulation is still used therapeutically and prophylactically for mild to moderate infections caused by susceptible Streptococcus spp., including use in pediatric patients (Pottegard et al. 2015). However, the selection of penicillin-resistant penicillinase-producing staphylococci in patients treated with penicillin G led to decreased use of this agent, and prompted the search for more penicillins with greater stability to the staphylococcal β-lactamases (Kirby 1944, 1945; Medeiros 1984). A list of historically important and clinically useful penicillins is provided in Table 2. Among the penicillinase-stable penicillins of clinical significance are methicillin, oxacillin, cloxacillin, and nafcillin, with the latter suggested as the β-lactam of choice for skin infections, catheter infections, and bacteremia caused by methicillin-susceptible S. aureus (Bamberger and Boyd 2005). All were used primarily for staphylococcal infections until the emergence of methicillin-resistant S. aureus (MRSA) in 1979–1980 (Hemmer et al. 1979; Saroglou et al. 1980). Penicillins of current and historical utility Penicillins with improved activity against Gram-negative pathogens included the orally bioavailable ampicillin and amoxicillin, both of which were introduced in the 1970s. These agents were initially used for the treatment of infections caused by Enterobacteriaceae and did not effectively inhibit the growth of Pseudomonas aeruginosa, which became more of a concern during the late 1970s. Carbenicillin was the first antipseudomonal penicillin to be introduced, but lacked stability to β-lactamase hydrolysis and was less potent than piperacillin or ticarcillin, later antipseudomonal penicillins. These latter drugs were considered to be potent broad-spectrum penicillins that included penicillin-susceptible staphylococci, enteric bacteria, anaerobes, and P. aeruginosa in their spectrum of activity. They were used extensively to treat serious nosocomial infections, especially when combined with a β-lactamase inhibitor (see below). Two parenteral penicillins with unusual chemical structures, mecillinam and temocillin (Table 2), were introduced to treat infections caused by enteric bacteria before the global emergence of extended-spectrum β-lactamases (ESBLs) in the late 1980s. Mecillinam (also known as amdinocillin), with a 6-β-amidino side chain, is a narrow-spectrum β-lactam that binds exclusively to PBP2 in enteric bacteria (Curtis et al. 1979). Because of this specificity, it shows synergy in vitro in combination with other β-lactams that bind to PBPs 1a/1b and/or PBP3 in Gram-negative bacteria (Hanberger et al. 1991), thus decreasing the possibility that a point mutation in a single PBP would lead to resistance (Hickman et al. 2014). Temocillin, the 6-α-methoxypenicillin analog of ticarcillin, had greater stability than ticarcillin to hydrolysis by serine β-lactamases, but lost antibacterial activity against Gram-positive bacteria, anaerobic Gram-negative pathogens, and some enteric bacteria that included the important pathogens Enterobacter spp. and Serratia marcescens (Martinez-Beltran et al. 1985). Mecillinam and temocillin are currently enjoying a resurgence in interest owing to their stability to many ESBLs (Livermore et al. 2006; Rodriguez-Villalobos et al. 2006), often resulting in greater than 90% susceptibility when tested against many contemporary ESBL-producing Enterobacteriaceae (Giske 2015; Zykov et al. 2016). Because increasing numbers of β-lactamases have compromised the use of penicillins as single agents (Bush 2013), there is currently limited therapeutic use of the penicillins as monotherapy. Ampicillin, amoxicillin, piperacillin, and ticarcillin have continued to be useful, primarily as a result of their combination with an appropriate β-lactamase inhibitor (see below). However, even ampicillin, amoxicillin, penicillin G, and penicillin V are still active as monotherapy against Group A streptococci, and Treponema pallidum, two of the few bacterial species that do not produce β-lactamases (Schaar et al. 2014). During the 1950s, the discovery of the naturally occurring penicillinase-stable cephalosporin C opened a new pathway to the development of hundreds of novel cephalosporins (Newton and Abraham 1956; Abraham 1987) to treat infections caused by the major penicillinase-producing pathogen of medical interest at that time, S. aureus. Dozens of cephalosporins were introduced into clinical practice (Abraham 1987), either as parenteral or oral agents. The molecules exhibited antibacterial activity with MICs often ≤4 μg/mL against not only staphylococci, but also Streptococcus pneumoniae and non-β-lactamase-producing enteric bacteria. The parenteral agents were generally eightfold more potent than the oral agents that were used in some cases to replace oral penicillins in penicillin-allergic patients. The early cephalosporins, for example, those in the cephalosporin I subclass (Bryskier et al. 1994) introduced before 1980, were labile to hydrolysis by many β-lactamases that emerged following their introduction into clinical practice, so that only a few of the early molecules remain in use (see Table 3), primarily to treat mild to moderate skin infections caused by methicillin-susceptible S. aureus (MSSA) (Giordano et al. 2006). Cefazolin with high biliary concentrations is still used for surgical prophylaxis and for treatment of abdominal infections (Sudo et al. 2014) and is effective as empiric therapy in 80% of Japanese children with their first upper urinary tract infection (Abe et al. 2016). Cephalosporins of current clinical utility or of historical interest When the TEM-1 penicillinase began to appear on transmissible plasmids in Neisseria gonorrhoeae (Ashford et al. 1976) and Haemophilus influenzae (Gunn et al. 1974; Khan et al. 1974), it was quickly recognized that the penicillins and cephalosporins in medical use were becoming ineffective, not only in treating those TEM-1-producing organisms, but also for the enteric bacteria and P. aeruginosa that could all acquire this enzyme. Another surge of synthetic activity in the pharmaceutical industry provided both oral and parenteral cephalosporins with stability to this common enzyme. These agents tended to have decreased potency against the staphylococci, but gained antibacterial activity against Gram-negative pathogens. Cefuroxime, dosed parenterally or orally as the axetil ester, was the only member of the cephalosporin II class (Bryskier et al. 1994) with both oral and systemic dosage forms, but its stability to β-lactamase hydrolysis was diminished compared to later oral cephalosporins (Jacoby and Carreras 1990). As seen with cefuroxime, acceptable oral bioavailability of cefpodoxime required esterification through addition of a proxetil group to attain sufficient absorption for efficacy (Bryskier and Belfiglio 1999). Of the oral agents approved after 1983 in Table 3, cefdinir was generally more stable to hydrolysis, not only to the original TEM enzyme, but also to the AmpC cephalosporinases that are produced at a basal level in many enteric bacteria and P. aeruginosa (Payne and Amyes 1993; Labia and Morand 1994). Among the parenteral agents introduced in the 1980s were the cephamycin cefoxitin, and cephalosporins in the cephalosporin III and cephalosporin IV subclasses (Bryskier et al. 1994), which continue to serve as important antibiotics for the treatment of serious infections caused by Gram-negative pathogens. The novel oxacephem moxalactam, or latamoxef, which had similar antimicrobial activity to the cephalosporin III/IV subclasses, has exquisite stability to hydrolysis by β-lactamases (Sato et al. 2015), but was not a highly successful antibiotic owing, in part, to a relatively high frequency of bleeding in patients treated with this drug (Brown et al. 1986). The cephamycin cefoxitin is notable for its characteristic 7-methoxy side chain that confers stability to the TEM-type β-lactamases, including ESBLs. It has useful antibacterial activity against MSSA and enteric bacteria that do not produce high levels of AmpC cephalosporinases (Jacoby and Han 1996). Cefotaxime, cefoperazone, ceftriaxone, and ceftazidime, designated as subclass cephalosporin III, and cefepime in the cephalosporin IV subclass, are also known as expanded-spectrum cephalosporins with increased hydrolytic stability to the common penicillinases, SHV-1 and TEM-1 β-lactamase (Martinez-Martinez et al. 1996). These agents have diminished activity against staphylococci and enterococci compared to earlier cephalosporins, but have more potent activity against Gram-negative organisms. Cefepime tends to have lower MICs against enteric bacteria than the other expanded-spectrum cephalosporins, attributed to greater penetration through the OmpF outer-membrane porin protein (Nikaido et al. 1990; Bellido et al. 1991). Cefotaxime and ceftriaxone are often used to treat susceptible streptococcal infections; all can be used to treat serious infections caused by enteric bacteria if the organisms test susceptible. Notably, ceftazidime and cefepime have maintained their observed activity against P. aeruginosa, with recent susceptibility rates exceeding 80% (Sader et al. 2015). A liability of the expanded-spectrum cephalosporins, however, began to emerge only a few years after the introduction of cefotaxime, when the ESBLs were identified with the ability to hydrolyze all of the β-lactams, with the exception of the carbapenems. These enzymes, in addition to both serine and metallo-carbapenemases, have severely compromised the activity of almost all penicillins and cephalosporins, necessitating the development of combination therapy with other β-lactams, β-lactamase inhibitors, or antibiotics from other classes. Ceftolozane, recently approved in combination with tazobactam for the treatment of complicated urinary tract infections and complicated intraabdominal infections, shows potent antipseudomonal activity, and includes activity against enteric bacteria that produce some ESBLs (Zhanel et al. 2014), particularly CTX-M-producing isolates (Estabrook et al. 2014). Another recent addition to the cephalosporin family is the siderophore-substituted cephalosporin S-649266 with a catechol in the 3-position, thus allowing the molecule to enter the cells via an iron transport mechanism (Kohira et al. 2015). In addition to increased penetrability, the cephalosporin is stable to hydrolysis by many carbapenemases, resulting in activity against many β-lactam-resistant enteric bacteria (Kohira et al. 2015). In the mid-1990s, reports began to emerge describing cephalosporins with MICs