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A Comprehensive Review on Penicillin

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Abstract: *Penicillin, the frst widely used antibiotic, revolutionized medical treatment by offering a potent mechanism against numerous bacterial infections. It remains one of the most clinically signifcant β-lactam antibiotics, effective against many gram-positive cocci, certain gramnegative cocci, and anaerobes. This review discusses penicillin's mechanism of action, pharmacokinetics, clinical applications, resistance patterns, adverse reactions, and the importance of interprofessional collaboration in optimizing therapeutic outcomes. Despite its long history, penicillin continues to play a key role in infection management, though bacterial resistance and allergic responses remain challenges. Understanding its pharmacological profle and clinical nuances helps maximize its effectiveness while minimizing adverse effects and resistance risks..*

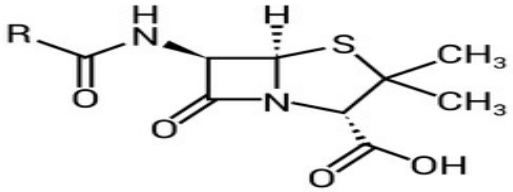
Keywords: Penicillin, β-lactam antibiotics, bacterial resistance, pharmacokinetics, antimicrobial therapy, hypersensitivity

I. INTRODUCTION

Penicillin is among the most widely utilized antibiotics globally and represents a cornerstone in modern medicine. Since its discovery by Alexander Fleming in 1928, penicillin has saved countless lives and remains a primary therapeutic option for various bacterial infections. Belonging to the β-lactam class of antibiotics, penicillin exerts bactericidal activity by targeting bacterial cell wall synthesis. Despite the availability of newer antibiotics, penicillin continues to be used because of its effectiveness, affordability, and broad safety profle. However, the rise of penicillin-resistant bacterial strains necesstrong activity against gram-positive cocci (e.g., Streptococcus pyogenes, Streptococcus pneumoniae), gram-positive rods (e.g., Bacillus anthracis, Listeria monocytogenes), and several anaerobes and gram-negative cocci (Neisseria meningitidis). The drug's clinical utility extends to treating infections such as pneumonia, meningitis, syphilis, actinomycosis, and endocarditis [2].Different forms of penicillin have specifc indications:Penicillin G: Used for severe systemic infections such as anthrax, meningitis, tetanus, actinomycosis, and syphilis.Penicillin V: Preferred for mild-to-moderate infections such as tonsillitis, pharyngitis, and scarlet fever.Benzathine penicillin: Used for long-term prophylaxis in rheumatic fever and for treating syphilis [3].Later generations, such as ampicillin, amoxicillin, carbenicillin, and piperacillin, expanded the antibacterial spectrum to include certain gram-negative organisms like Proteus mirabilis, Escherichia coli, and Pseudomonas aeruginosa [4].

Structure of penicillin [5]

Classification Of Penicillin



Penicillin

$C_{16}H_{18}N_2O_4S$

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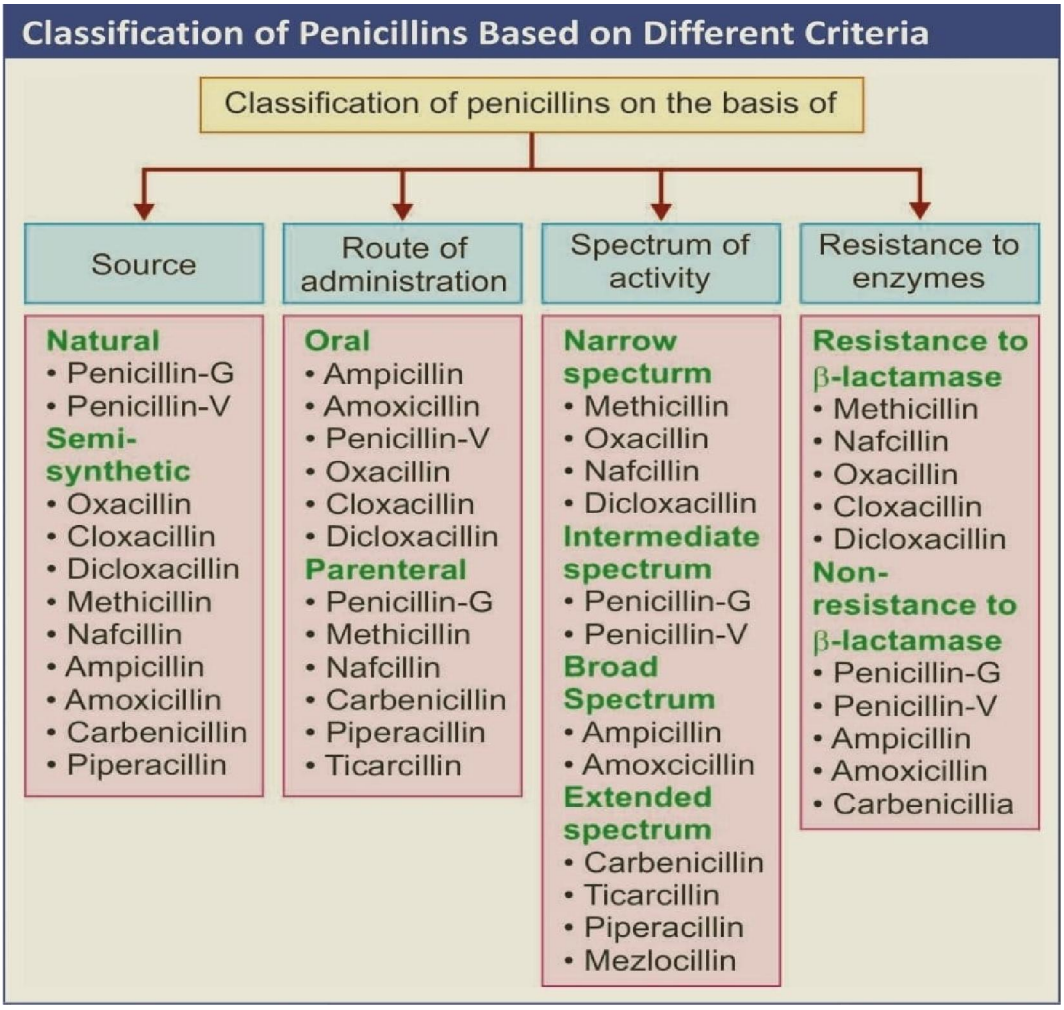

Table : 1 Classification of penicilline[6]

Natural penicillin:

The natural or "first generation" penicillins are bactericidal antibiotics naturally derived from the mold, Penicillium chrysogenum. Their basic structure includes a thiazolidine ring connected to a beta-lactam ring with a variable side chain. Penicillins bind to bacterial proteins and inhibit synthesis of the bacterial cell wall, causing cell lysis particularly in rapidly growing organisms[7]Penicillin G, benzylpenicillin, was originally produced from a natural penicillium fungus. The fungus strain used in the production of penicillin G today has been developed through genetic manipulation to increase the yield from the production process. Of the other natural penicillins, F, K, N, X, O, U1 and U6, none are in clinical use today.[8]

Semi synthetic penicillin:

Semi-synthetic penicillins are modified penicillin derivatives designed to improve absorption and minimize side effects. These antibiotics are derived from natural penicillin and undergo chemical modifications to enhance their efficacy. By altering their structure, scientists aim to create more effective antibiotics while reducing unwanted reactions, making semi-synthetic penicillins a crucial development in the field of antibacterial treatments.Semisynthetic penicillins have been prepared by chemical modification of the p-amino group of p-aminobenzylpenicillin. Semisynthetic penicillins can be grouped into three classes on the basis of their antibacterial spectra. Thus, penicillins

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have a spectrum of activity essentially similar to that of penicillin V and are active primarily against gram-positive cocci, and are often referred to as narrow-spectrum penicillins. These compounds have been described as "acid-stable penicillins" because of their similarity to penicillin V, but this term is no longer favored because it has become obvious that acid stability is a property shared by many other penicillins with very different biological activities.[9]

Oral route of administration:

A few antibacterial agents have excellent bioavailability after oral administration. For example, the fluoroquinolones, metronidazole, tetracycline, minocycline, doxycycline, linezolid, and trimethoprim-sulfamethoxazole are wellabsorbed drugs, for which PO and IV doses are similar. Because absorption and distribution is taking place while a drug is being absorbed after oral administration, peak plasma levels can be delayed and usually are not as high as those achieved by IV infusion.With oral administration, the bioavailability of penicillin G, which is destroyed by gastric acid, is low (< 30%). Penicillin V is more acid-stable and its bioavailability is better (60%–70%) compared to penicillin G. The relative oral bioavailability of amoxicillin (74%–92%) is greater than that of penicillin V. Only 30% to 55% of an oral ampicillin dose is absorbed[10].

Parental route of administration:

Penicillin G potassium or sodium salts can be given intravenously or intramuscularly. Except for the different content of electrolytes, the sodium and potassium salts are therapeutically equivalent.Visually inspect parenteral products for particulate matter and discoloration prior to administration whenever solution and container permit[11].

Mechanism of Action:-

Bacterial cell walls contain peptidoglycan, a crucial structural component that protects cells from osmotic lysis. Penicillin inhibits cell wall synthesis by binding to penicillin-binding proteins (PBPs) such as DD-transpeptidase, preventing the cross-linking of peptidoglycan chains. The βlactam ring of penicillin irreversibly acylates these enzymes, leading to cell wall instability and bacterial death [12].As the bacterial wall weakens, osmotic pressure causes cell lysis. Additionally, penicillin promotes the activation of autolytic enzymes (autolysins and hydrolases), further degrading the peptidoglycan layer [13]. The co-administration of β-lactamase inhibitors (e.g., clavulanic acid) prevents enzymatic degradation of penicillin by β-lactamase-producing bacteria, thereby extending its spectrum and effectiveness [14].

Contraindications :

Contraindications include a previous history of severe allergic reactions to penicillin or its derivatives. It is also contraindicated for patients with a previous history of Stevens-Johnson syndrome after the administration of penicillin or any of its derivatives. Furthermore, it acts antagonistically with tetracyclines and increases the mortality risk by 2.6 times when used to treat pneumococcal meningitis as compared to penicillin alone. However, penicillins are relatively safe during pregnancy and lactation.[15]

Almost all antibacterial agents have been implicated in Clostridium difficile–associated diarrhea (CDAD), including penicillin, with severity ranging from mild diarrhea to fatal colitis. Antibacterial agents alter the normal flora of the colon leading to overgrowth of C difficile. This strain produces toxins A and B that are major contributors to the development of CDAD. During infections caused by hypertoxin-producing strains of C difficile, morbidity and mortality rates increase since these infections are often resistant to antimicrobial treatments and may require colectomy. Systemic antibiotic treatment should be administered if CDAD is suspected or confirmed. Protein supplementation, fluid and electrolyte management, antibiotic treatment, and surgical evaluation are employed based on clinical need.[16]

Pharmacokinetics:-Absorption

Penicillin V is stable in gastric acid and can be administered orally, whereas Penicillin G is acid-labile and given parenterally. Benzathine penicillin G exhibits slow absorption, providing prolonged plasma levels for up to four weeks [8].Distribution Penicillin distributes widely into body tissues, with high concentrations in the kidneys. Protein binding ranges between 60–80%. Penetration into cerebrospinal fuid (CSF) is limited under normal conditions but increases during meningitis [17].

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Metabolism and ExcretionPenicillin undergoes minimal hepatic metabolism and is primarily excreted unchanged by the kidneys via tubular secretion, which is inhibited by probenecid. The half-life is approximately 30 minutes to 2 hours, necessitating frequent dosing in severe infections [18].

Administration and Dosage Forms:-

Penicillin G is available for intravenous (IV) or intramuscular (IM) use, typically administered in divided doses every 4–6 hours. Benzathine penicillin G provides long-acting coverage for prophylaxis and latent infections. Oral formulations of Penicillin V (250–500 mg every 6–8 hours) are preferred for mild infections [19].Special Populations:Pregnancy: Category B; safe for use with adjusted dosing during pregnancy due to increased elimination.Renal impairment: Dose adjustments are necessary to prevent accumulation and toxicity.Pediatrics: Dosage depends on body weight or surface area.Elderly: Dose modifcation may be required due to reduced renal clearance [20].

Adverse Effects

Penicillin is generally safe but may cause adverse effects in susceptible individuals.6.1. Hypersensitivity ReactionsThe most signifcant adverse effect is hypersensitivity, which can manifest as rash, urticaria, angioedema, bronchospasm, or anaphylaxis. Immediate reactions occur within minutes, while delayed reactions may appear days or weeks after therapy initiation [21].6.2. Gastrointestinal and Hematologic EffectsCommon side effects include nausea, vomiting, diarrhea, and stomatitis. Pseudomembranous colitis may occur due to disruption of intestinal fora. High doses can induce Coombs-positive hemolytic anemia or neutropenia [22].6.3. Neurological and Renal EffectsLarge IV doses may cause

neurotoxicity (seizures, myoclonus, coma) or renal injury due to interstitial nephritis. Electrolyte disturbances such as hyperkalemia can occur with Penicillin G potassium formulations [23]. Adverse drug reactions associated with the penicillins include diarrhoea, hypersensitivity, nausea, rash, neurotoxicity, urticaria, and superinfection (including candidiasis) in ≥ 1% of people. Infrequent adverse effects (0.1–1% of people) include fever, vomiting, erythema, dermatitis, angioedema, seizures (especially in those with epilepsy), and pseudomembranous colitis.Penicillin may induce serum sickness or a serum sickness-like reaction in some individuals. Serum sickness is a type III hypersensitivity reaction that occurs one to three weeks following exposure to drugs including penicillin. It is not a true drug allergy, because allergies are type I hypersensitivity reactions, but repeated exposure to the offending agent can result in an anaphylactic reaction. Allergy will occur in 1–10% of people, presenting as a skin rash following exposure. IgE-mediated anaphylaxis will occur in approximately 0.01% of patients.[24]

Drug Interactions:-

Penicillin should not be combined with bacteriostatic agents like sulfonamides or erythromycin due to antagonistic effects [25]. Probenecid prolongs penicillin plasma levels by inhibiting renal excretion, while nonsteroidal anti-infammatory drugs (NSAIDs) such as aspirin may also increase half-life [26].

Penicillin can reduce the effectiveness of oral contraceptive and increase the bleeding risk when used with oral anticoagulant like warfarin.[27] Drugs like aspirin and indomethacin may conpete with penicillin for excretion, potentially increasing penicillin levels. Live vaccine,such as the live cholera vaccine and live typhoid vaccine should not be given with penicillin[28] .

Penicillin allergy:

For the treatment of different kinds of bacterial infections. These medications are commonly used to treat ear infections, strep throat, sinus infections, and to prevent dental infections.Common symptoms of an allergic reaction include skin redness, itching, rash or swelling. These symptoms can be caused by other conditions. Some symptoms, like nausea, vomiting or diarrhea, are common with antibiotics. They are often mistaken for an allergy.When a penicillin allergy is reported, the health care professional will substitute different antibiotics and often uses more expensive, less effective antibiotics. Penicillins are the safest and most effective antibiotics for many infections.Avoiding penicillin antibiotics is associated with higher health care costs, increased risk for antibiotic resistance, and less effective antibiotic therapy.Allergy testing removes the allergy in over 90% of individuals with a

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penicillin allergy. Since penicillin allergy does not always persist for a lifetime, many patients with severe histories of penicillin allergy are able to restart the medication safely if instructed to do so by a health care professional.Roughly 80% of all patients with a severe allergy to penicillin lose their sensitivity after 10 years. Identifying a patient as indeed not allergic to a medication will permit better options for treatment, targeted therapy, and decrease the length of stays in the hospital along with the costs of the medicines.[29]

Penicillin allergy test:

With a skin test, the allergist or nurse puts a small amount of the suspect penicillin in your skin with a tiny needle. A positive reaction to a test causes a discolored, itchy, raised bump.

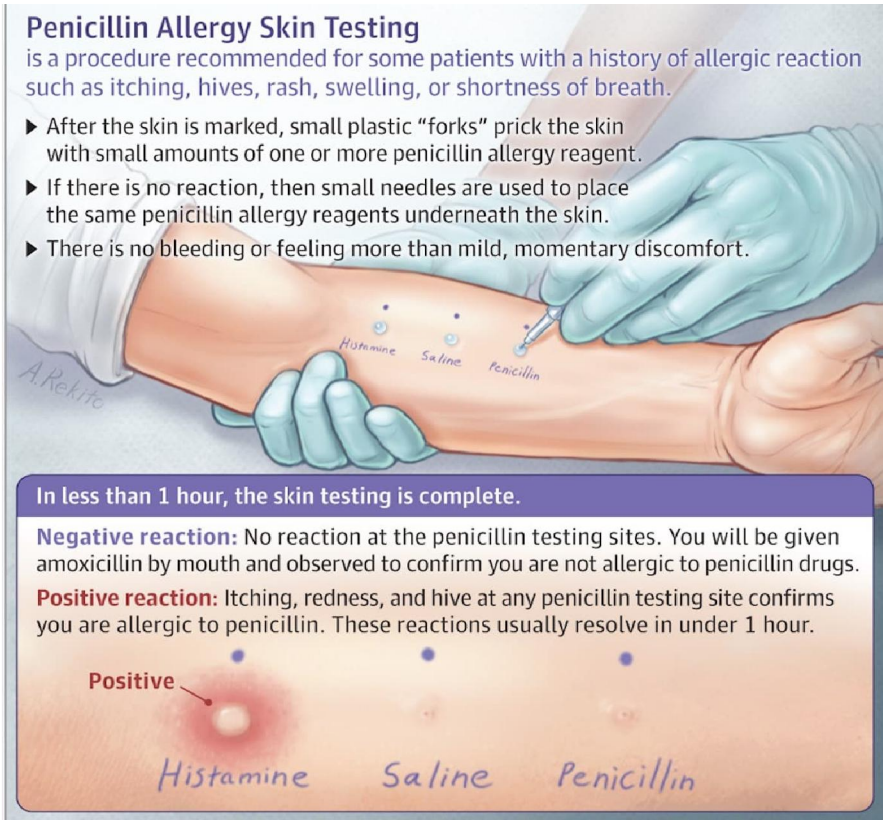

Fig : Penicillin Allergy Skin Testing.[30]

A positive result means the likelihood of penicillin allergy is high. A negative test result usually means you're not at high risk of an allergy to penicillin. But a negative result is more difficult to understand because some kinds of medicine reactions cannot be detected with skin tests.[30]

Spectrum of activity:

The natural penicillins are primarily effective against aerobic, gram-positive organisms such as streptococci, enterococci, and some staphylococci that do not produce beta lactamase. Newer synthetic penicillins such as the aminopenicillins and extended spectrum penicillins have increased this spectrum to include activity against some gram-negative organisms such as H influenza, N gonorrhoeae, and E coli that have not developed resistance. The addition of beta lactamase inhibitors to some.[31]

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Bacterial Resistance:-

The rise in penicillin-resistant organisms poses a major clinical challenge. Resistance mechanisms include β-lactamase production, altered PBPs, and reduced membrane permeability in gram-negative bacteria [32]. Extended-spectrum β-lactamases (ESBLs) and methicillinresistant Staphylococcus aureus (MRSA) exemplify signifcant resistance threats. Combination therapies with β-lactamase inhibitors (e.g., piperacillin-tazobactam) and antibiotic stewardship programs help mitigate resistance [33].Staphylococcal Penicillinase Staphylococci are the only common gram-positive pathogens Where β-lactamases have caused major resistance problems.Penicillinases occurred in only about 5% of Staphylococcus.Aureus isolates when benzylpenicillin was introduced but hav Since spread, by means of plasmid transfer and strain selection to 80 to 90% of isolates, both of S. aureus and of the coagulase-[34]

Monitoring and Toxicity:-

Routine therapeutic monitoring is not required for most patients; however, in long-term therapy, renal, hepatic, and hematologic function should be assessed. Overdose symptoms include neurotoxicity and electrolyte imbalance, managed by discontinuation and supportive care [35]. Generally, no monitoring is required for patients on penicillin. However, one study suggested therapeutic drug monitoring during the treatment of endocarditis caused by enterocci to determine penicillin exposure and dosing. This vigilance will decrease the chances of antibiotic resistance while improving the therapeutic impact.[36] Prolonged administration of penicillin requires monitoring hematologic, renal, and hepatic function.

Toxicity :Overdose Signs and Symptoms

Penicillin is a drug with limited toxicity. Compared to other drugs, relatively high doses of penicillin can be administered by clinicians without causing harm to the patients. Estimates show that 5 g/kg body weight IV can cause convulsions in a patient. At the site of sensitive areas such as the anterior chamber of the eye or the subarachnoid space, penicillin exhibits local toxicity as a result of high-dose injections. Pure preparations of penicillin are reportedly harmless to the lungs and veins.[37] Other reports indicate the topical use of penicillin prevents coagulation of dental cavities.

Overdose Management Neurotoxicity from penicillin mandates the withdrawal of the offending penicillin. Given that penicillins may inhibit GABA transmission, IV benzodiazepines and EEG monitoring may also be instituted in refractory cases.[38]

Interprofessional Collaboration:-

Optimal use of penicillin requires coordination between physicians, pharmacists, nurses, and microbiologists. Pharmacists play a critical role in dosing guidance and patient education. Nurses monitor for allergic reactions and ensure adherence. Interprofessional collaboration enhances antimicrobial stewardship, minimizes resistance, and improves patient outcomes [39].

Therapeutic uses of penicillin:

Penicillin is one of the most widely used broad-spectrum antibiotics in the world and is indicated in a myriad of clinical applications. Penicillin is effective against infections caused by gram-positive cocci, gram-positive rods, most anaerobes, and gram-negative cocci. Penicillin is a mainstay for the management and treatment of several infections from the class of drugs known as β-lactam antibiotics.

Notably, some bacterial species developed resistance to penicillin, including enterococci. Thus, because of resistance, penicillin is only used on susceptible organisms. Infections from enterococci are now treated with penicillin, streptomycin, or gentamicin. Certain gram-negative rods are also resistant to penicillin because penicillin poorly traverses the porin channel.[39]

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II. CONCLUSION

Penicillin remains a cornerstone antibiotic despite nearly a century since its discovery. Its effectiveness, safety, and affordability make it indispensable in managing bacterial infections. However, growing bacterial resistance necessitates rational prescribing and vigilant surveillance. Continued research into resistance mechanisms, development of novel β-lactamase inhibitors, and coordinated interprofessional strategies are essential for preserving penicillin's clinical utility.

REFERENCES

1. Friedland IR, McCracken GH. Management of infections caused by antibiotic-resistant Streptococcus pneumoniae. N Engl J Med. 1994;331(6):377–82.
2. Herman DJ, Gerding DN. Antimicrobial resistance among enterococci. Antimicrob Agents Chemother. 1991;35(1):1–4.
3. Kache PA, Person MK, Seeman SM, McQuiston JR, McCollum J, Traxler RM. Rat-Bite Fever in the United States: An Analysis Using Multiple National Data Sources, 2001–2015. Open Forum Infect Dis. 2020;7(6):ofaa197.
4. Perry CM, Markham A. Piperacillin/tazobactam: an updated review of its use in the treatment of bacterial infections. Drugs. 1999;57(5):805–43.
5. https://share.google/images/HCnrxtx0yD7g2W5u4 assest on 21 nov 2025
6. / X https://share.google/2iRyAAQK2m5zmSo17 J on X: "Antibiotic Penicillin Classification"assest on 22 nov 2025
7. Elissa Lane Miller CNM, PhD the penicillin a review and update 2002,426-434.
https://share.google/zuXzh1xff5NsJE7TR assest on 22 nov 2025
G.N.Rolinson,R.Sutherland Semisynthetic penicilliins Science Direct 10 april 2008
https://share.google/zDxhYctLm8mQZ5q1o assest on 21 nov 2025
https://share.google/AZshF0sNEbaofO1Z3 drug summary assest on 20 nov 2025
12. Spratt BG, Cromie KD. Penicillin-binding proteins of gram-negative bacteria. Rev Infect Dis. 1988;10(4):699–711.
13. Harcourt BH, Anderson RD, Wu HM, et al. Population-Based Surveillance of Neisseria meningitidis Antimicrobial Resistance in the United States. Open Forum Infect Dis. 2015;2(3):ofv117.
14. Perry CM, Markham A. Ibid.
15.Levison ME, Levison JH. Pharmacokinetics and pharmacodynamics of antibacterial agents. Infect Dis Clin North Am. 2009 Dec;23(4):791-815, vii
16. Smits WK, Lyras D, Lacy DB, Wilcox MH, Kuijper EJ. Clostridium difficile infection. Nat Rev Dis Primers. 2016 Apr 07;2:16020. [PMC free article]
17.McCo. llum J, Traxler RM. Penicillin pharmacokinetics. Clin Pharmacol Rev. 2020;14(3):211–24.
18. Probenecid interactions. J Antimicrob Chemother. 2019;74(9):2501–9
19. CDC. Penicillin treatment guidelines. 2023.
20. ACOG. Group B Streptococcus prophylaxis recommendations. 2021.
21. Herman DJ. Hypersensitivity reactions to penicillin. Ann Allergy. 2018;120(4):335–42.
22. Perry CM. Adverse effects of penicillin. Clin Drug Investig. 2017;37(5):421–33.
23. Harcourt BH. Neurological toxicity of β-lactam antibiotics. CNS Drugs. 2016;30(2):95–105.
24. https://en.wikipedia.org/wiki/Side_effects_of_penicillin assest on 20 nov 2025
25. Spratt BG. Drug antagonism with bacteriostatic agents. Rev Infect Dis. 1988;10(4):705–8.
26. McCracken GH. Drug interactions of penicillin. Clin Pharm. 2015;22(1):13–21.
27. Annas Moussa , Pawet Radkowski ,Antibiotic drug interaction in the intensive care unit ;Aliterature review 2024, 13(6),503
28. https://share.google/Ri4Oo9QI75PmSG9BP drug summary assest on 21 nov 2025
29.https://share.google/HLEH1rKI7oYPgrGjU evaluation for a penicilline allergy mayo clinic health system assest on 21 nov 2025
30.Carey Goldberg think you're allergic to penicilline maybe not ,specialist say,and that's worth knowing 2019

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Impact Factor: 8.2

31. Elissa Lane Miller CNM,PhD The penicillins A review and update 2002 ;426-434
32. CDC. Contraindications for β-lactam antibiotics. 2023.
33. Friedland IR. Mechanisms of β-lactam resistance. J Infect Dis. 1994;169(3):567–75.
34. Perry CM, Markham A. Resistance trends in β-lactam antibiotics. Drugs. 2020;80(5):489–512.
35.. Gerriets V, Yip DW. Penicillin toxicity and monitoring. StatPearls [Internet]. 2024.22. Jagdale DM. Interprofessional collaboration in antibiotic stewardship. Pratibhatai Pawar Coll Pharm Rev. 2025;1(1):1–8
36.Öbrink-Hansen K, Wiggers H, Bibby BM, Hardlei TF, Jensen K, Kragh Thomsen M, Brock B, Petersen E. Penicillin G Treatment in Infective Endocarditis Patients - Does Standard Dosing Result in Therapeutic Plasma Concentrations? Basic Clin Pharmacol Toxicol. 2017 Feb;120(2):179-186.
37.STEWART GT. TOXICITY OF THE PENICILLINS. Postgrad Med J. 1964 Dec;40(Suppl):SUPPL:160-9.
38.Grill MF, Maganti RK. Neurotoxic effects associated with antibiotic use: management considerations. Br J Clin Pharmacol. 2011 Sep;72(3):381-93.
39.Derek W. Yip; Valerie Gerriets, Penicilline national liabrary of medicine 2004