EFFECTIVENESS OF CEFTRIAXONE VERSUS COMBINED PHENOXYMETHYLPENICILLIN AND NETILMICIN IN SEVERE PNEUMONIA MANAGEMENT

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ABSTRACT :

The Pharmacokinetic Profile Intravenous ceftriaxone 0.5, 1 or 2g produces mean peak plasma concentrations (Cmax) of 82, 151 and 257 mg/L, respectively, whereas intramuscular ceftriaxone 0.5 or 1g achieves Cmax After 2 to 3 hours of receiving 2g of intravenous ceftriaxone, the plasma concentration typically reaches 38 to 76 mg/L. However, 24 hours later, the average plasma concentration is usually between 12 and 20 mg/L .Repeated once-daily intravenous administration of ceftriaxone 2g results in an 8% increase in mean Cmax, and repeated intramuscular administration of ceftriaxone 1g results in 11% accumulation of the drug. Ceftriaxone attaches to albumin in the blood, and the strength of this attachment weakens as ceftriaxone levels in the blood increase. It's about 95% attached at low concentrations (more than 70 mg/L) and about 58% attached at high concentrations (around 600 mg/L). Ceftriaxone spreads throughout the body, and in healthy individuals, it can occupy a volume ranging from 5.8 to 15.5 litters. Ceftriaxone tends to accumulate in the bile, resulting in average concentrations of about 153 mg/L one hour after receiving a 1g dose and approximately 44 mg/L after three hours. The drug is primarily eliminated unchanged by the kidneys; 45 to 60% of a 0.5 to 3g dose is excreted in the urine of healthy subjects within 48 hours. The excess ceftriaxone is expelled in the bile and feces as non-active substances. The total clearance of ceftriaxone from the bloodstream depends on the dose. It goes up from an average of 0.61 to 1.0 litters per hour after a 0.5g intravenous dose to 1.18 and 1.29 litters per hour after a 2g intravenous dose. The mean elimination half-life (t½) of ceftriaxone in healthy adults is ≈6 to 9 hours, which is considerably longer than that of other **Penicillin V** and **Netilmicin** (0.6 to 4.4 hours). The time it takes for ceftriaxone to reduce by half (t½) remains the same, regardless of how much, how often, or how it's given.

The ceftriaxone drug are effectively in severe pneumonia to the combination of penicillin v and netilmiicin, but the ceftriaxone drug caused some rear conduction.

KEYWORD : Severepneumonia ,Ceftriaxone, Phenoxymethylpenicillin, Netilmicin, Antibiotic therapy,Treatment efficacy,Clinical outcomes, Hospitalization duration, Adverse events, Antibiotic resistance, Empirical therapy, Comparative study, Patient outcomes, Healthcare guidelines ,Infectious disease management.

INTRODUCTION:

Severe pneumonia remains a formidable global health challenge, responsible for significant morbidity and mortality, particularly among vulnerable populations. Prompt and effective antibiotic therapy is the cornerstone of pneumonia management, but the choice of antibiotics has evolved over time, and treatment guidelines have varied. One enduring question in this context is whether Ceftriaxone, a third-generation cephalosporin with a broad spectrum of activity, can match or surpass the effectiveness of the longstanding combination of Benzylpenicillin and Gentamicin in severe pneumonia management.

Historically, the combination of Benzylpenicillin and Gentamicin has been favored for its coverage of both typical and atypical pneumonia pathogens. However, concerns about antimicrobial resistance, the risk of adverse effects, and the desire for simplified treatment regimens have prompted the exploration of alternative antibiotic therapies. Ceftriaxone's broad antibacterial spectrum, including activity against Streptococcus pneumoniae and many Gram-negative bacteria, makes it an appealing candidate for empirical therapy in severe pneumonia.

This study aims to address this critical question by conducting a rigorous comparative analysis of the effectiveness of Ceftriaxone versus the combination of Benzylpenicillin and Gentamicin in the management of severe pneumonia. The study assesses clinical outcomes, treatment response rates, the duration of hospitalization, and the incidence of adverse events to provide insights into the relative merits of these two antibiotic regimens.

In the face of evolving antibiotic resistance patterns and the need for optimized pneumonia treatment strategies, this investigation holds the potential to inform clinical practice and contribute to improved patient care. The findings from this study could influence antibiotic selection and guide clinicians in their efforts to combat severe pneumonia effectively.

Furthermore, as healthcare systems strive to provide efficient and evidence-based care, the results of this study may contribute to the development of updated treatment guidelines, ultimately benefiting patients and reducing the burden of severe pneumonia on public health.

Severe pneumonia continues to pose a substantial clinical challenge, both in terms of patient outcomes and healthcare resources. In the midst of evolving healthcare landscapes, antimicrobial resistance concerns, and the ongoing pursuit of optimal treatment strategies, the question of which antibiotics are most effective for managing severe pneumonia remains a topic of paramount importance.

Traditionally, the combination of Benzylpenicillin and Gentamicin has been a cornerstone of severe pneumonia treatment, offering broad coverage against a range of pathogens. However, the shifting landscape of antibiotic resistance, coupled with the desire for streamlined treatment approaches, prompts a re-evaluation of this standard of care. In this context, Ceftriaxone, a third-generation cephalosporin known for its wide spectrum of antibacterial activity, emerges as a compelling candidate for empirical therapy in severe pneumonia cases.

This study seeks to address the contemporary need for evidence-based antibiotic choices in the management of severe pneumonia. It conducts a rigorous comparative analysis of Ceftriaxone versus the combination of Benzylpenicillin and Gentamicin, assessing key clinical parameters such as treatment response rates, duration of hospitalization, and the incidence of adverse events. These critical outcomes will help elucidate whether Ceftriaxone can stand as a viable alternative to the time-honored combination therapy.

In a healthcare landscape characterized by the relentless emergence of resistant pathogens, treatment optimization is essential. This investigation is poised to provide valuable insights that can guide clinicians in their quest to effectively combat severe pneumonia. Moreover, as healthcare systems strive for evidence-based practices to enhance patient care and resource utilization, the findings from this study have the potential to shape updated treatment guidelines and alleviate the burden of severe pneumonia on healthcare systems and public health.

In a world where infectious diseases continue to challenge our healthcare infrastructure, the quest for superior treatment strategies remains unceasing. This study represents a timely and critical endeavor to advance understanding of severe pneumonia management and refine our approaches to this life-threatening condition.

SEVERE PNEUMONIA :

Pneumonia is an inflammation of the air sacs in the lungs(alveoli) and the girding towel. It frequently leads to a unforeseen high fever, the feeling that you're veritably bad, a cough and briefness of breath. Because pneumonia is generally caused by bacteria, it can generally be treated effectively with antibiotics.

Vaccinations that can help infection by certain origins are also available. People who are else in good health generally recover within a many weeks. But pneumonia should n't be taken too smoothly It can take one or occasionally indeed several months until you're back to full strength.

Pneumonia may occasionally lead to life- hanging complications, especially if you have formerly been weakened by another illness. Pneumonia can also be dangerous in babies and in aged age.

Severe pneumonia is a critical and potentially life-threatening respiratory condition characterized by the acute inflammation and infection of the lungs. It often leads to the impairment of oxygen exchange in the body, causing severe breathing difficulties.

This condition can be caused by various pathogens, including bacteria, viruses, or fungi, and it typically presents with symptoms such as high fever, rapid breathing, chest pain, and a productive cough. Prompt medical intervention, usually involving antibiotics and supportive care, is crucial in managing severe pneumonia to prevent complications and ensure a successful recovery.

PNEUMONIA CAN BE RISKY FOR BOTH BABIES AND OLDER PEOPLE :

Pneumonia can be dangerous for individuals of all ages, but the severity and risks vary depending on age and overall health.

IN BABIES :

1. **Babies, especially those under 2 years old, are vulnerable to pneumonia because their immune systems are not fully developed.**
2. Common causes include viruses, bacteria, or other germs.
3. Pneumonia in infants can lead to symptoms such as fast or difficult breathing, fever, cough, and poor feeding.
4. Severe cases may result in hospitalization, dehydration, and complications like respiratory distress syndrome.

IN OLDER AGE:

1. Pneumonia is a significant concern for older adults, especially those over 65, due to weakened immune systems and age-related health issues.
2. Seniors with chronic diseases like diabetes, COPD, or heart disease are at higher risk.
3. Pneumonia in older adults can lead to severe respiratory distress, confusion, high fever, and even sepsis.
4. Hospitalization is common, and pneumonia can be life-threatening for the elderly, particularly if they have underlying health problems.

Prevention through vaccination (such as the pneumonia and influenza vaccines), good hygiene, and avoiding exposure to sick individuals is crucial for both babies and older adults. Timely medical care is essential if symptoms of pneumonia arise, as prompt treatment can greatly improve outcomes in people of all ages.

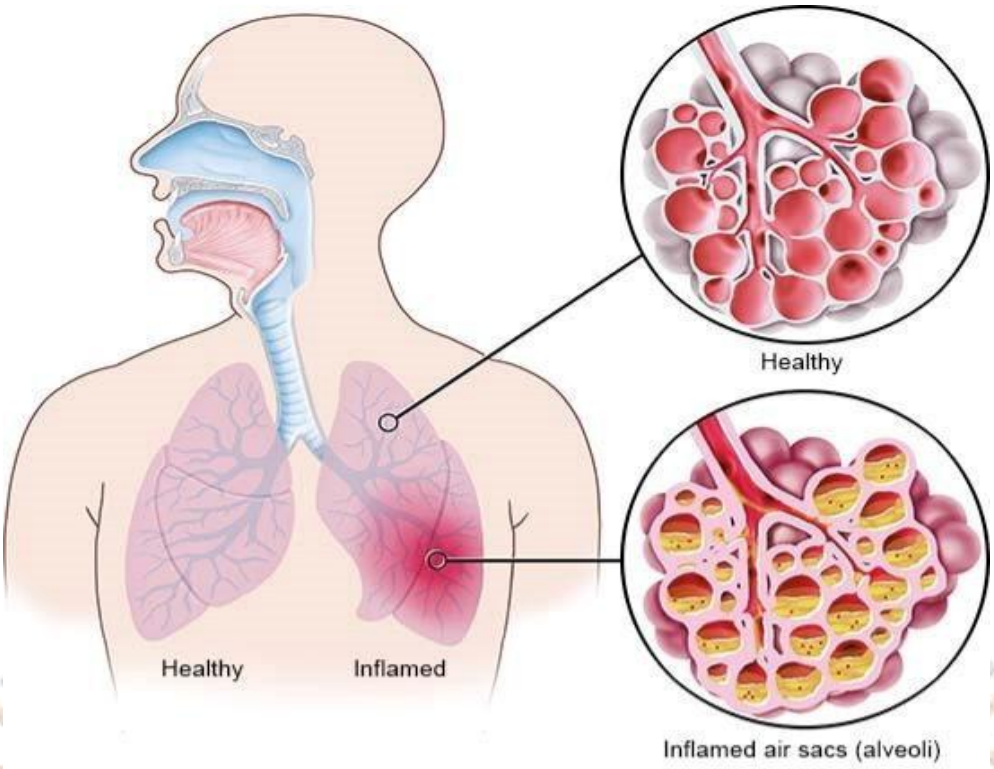


Fig-01(Pneumonia)

TREATING PNEUMONIA IN OLDER ADULTS :

Managing community-acquired pneumonia (CAP) in older adults is crucial, as they are at higher risk for complications. Here's an overview of key considerations:

1) **Diagnosis**: Promptly diagnose CAP through clinical assessment, chest X-rays, and laboratory tests.
2) **Antibiotics:** Initiate empiric antibiotics based on severity, comorbidities, and local resistance patterns. Common choices include amoxicillin, amoxicillin/clavulanate, or Fluor quinolones.
3) **Severity Assessment:** Assess severity using tools like the CURB-65 or CRB-65 score to determine the need for hospitalization.
4) **Hospitalization:** Consider hospitalization for severe cases, such as those with respiratory distress, confusion, or significant comorbidities.
5) **Oxygen Therapy:** Administer supplemental oxygen when needed to maintain adequate oxygen saturation levels.
6) **Fluid Management:** Ensure appropriate fluid balance, avoiding over-hydration in most cases.
7) **Vaccinations:** Encourage vaccinations against influenza and pneumococcus to prevent future episodes.
8) **Supportive Care:** Provide supportive care, including pain management, fever control, and chest physiotherapy.
9) **Monitor For Complications:** Regularly assess for complications like sepsis, respiratory failure, and pleural effusion.
10) **Discharge Planning:** Develop a plan for transitioning patients to outpatient care, including oral antibiotics and follow-up.
11) **Follow-up:** Schedule follow-up appointments to monitor recovery and adjust treatment as necessary.

12) **Prevention:** Educate patients about infection prevention, including hand hygiene and respiratory etiquette.

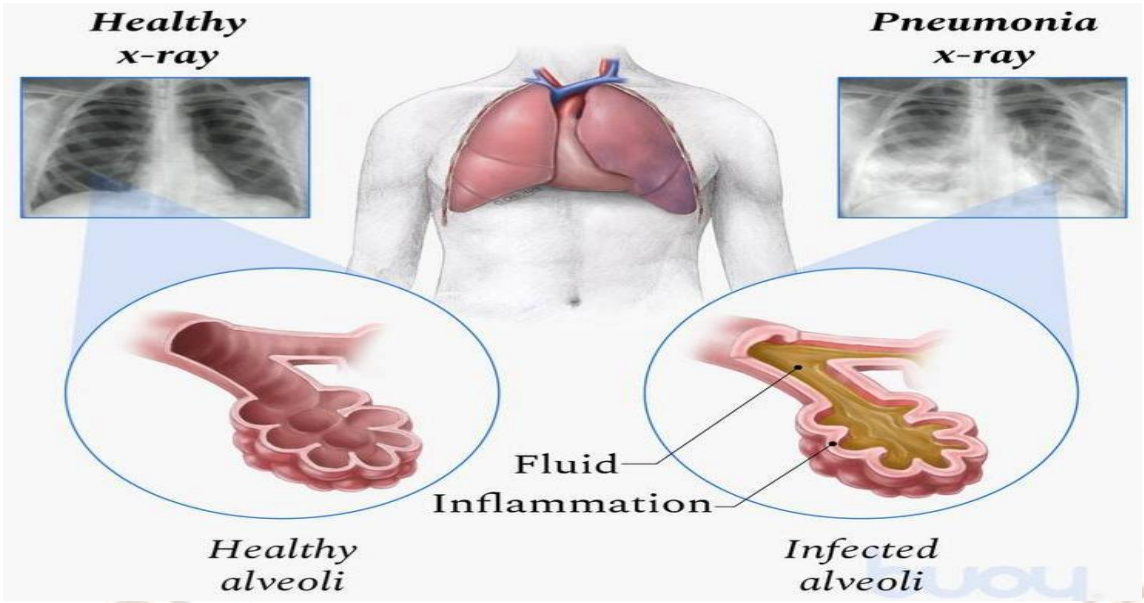
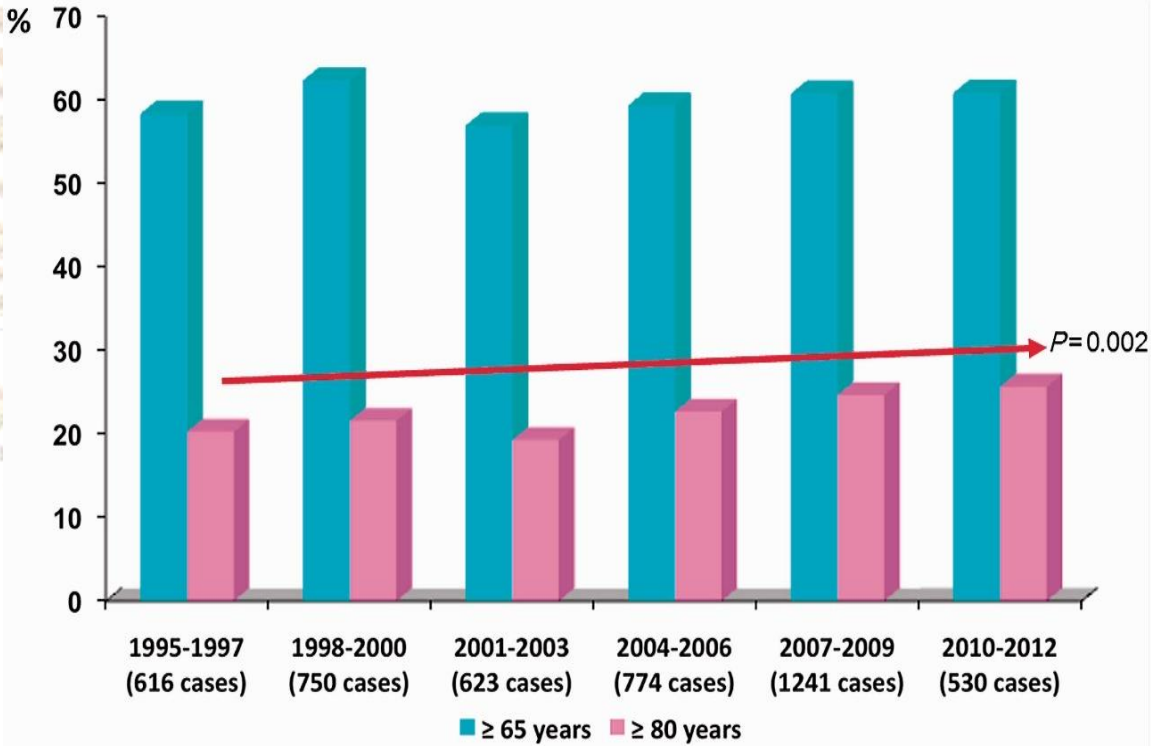


Fig-02 (Pneumonia In Older Adults)

It's essential to tailor the management to each patient's individual needs and consider their age, comorbidities, and overall health. Consulting with a healthcare professional is crucial for the best outcomes.

Fig-03 (The Community-Acquired Pneumonia In Older Adults)



SYMPTOMS OF PNEUMONIA :

Severe pneumonia can cause a range of symptoms, which may include:

1) **High fever**

2) Rapid, Shallow Breathing

3) Rapid Pulse

4) Muscle Pain

5) Weakness

6) Severe cough, often with mucus or phlegm

7) Low Energy And Extreme Tiredness

8) Shortness Of Breath

9) Produces Green, Yellow, Or Bloody Mucus

10) Chest pain, Especially When Breathing Or Coughing

11) Confusion Or Changes In Mental Awareness

12) Bluish Lips Or Nails, Indicating A Lack Of Oxygen

13) Fatigue And Weakness

14) Bluish Color To Lips And Fingernails

15) Nausea And Vomiting & Diarrhea

16) Sweating And Chills

17) Lower than normal body temperature (in adults older than age 65 and people with weak immune systems)

CAUSES OF PNEUMONIA :

Pneumonia can be caused by various factors, with infections being the most common cause. Here are some of the primary causes of pneumonia:

1) **Bacterial Infections:** Bacteria such as Streptococcus pneumoniae, Haemophilus influenza, and Staphylococcus aureus can infect the lungs and lead to pneumonia.

2) **Viral Infections:** Viruses like the influenza virus (flu), respiratory syncytial virus (RSV), and the common cold viruses can cause viral pneumonia.

3) **Fungal Infections:** Fungi, such as Pneumocystis jirovecii (common in people with weakened immune systems) and certain types of molds, can lead to fungal pneumonia.

4) **Aspiration:** Inhaling food, liquids, or other irritants into the lungs can cause aspiration pneumonia.
5) **Chemical Irritants:** Breathing in chemical irritants, like toxic fumes or chemicals, can lead to chemical pneumonia.

6) **Parasitic Infections:** Although less common, parasites like Pneumocystis carinii can cause pneumonia, especially in people with compromised immune systems.

7) **Hospital-Acquired (Nosocomial) Pneumonia:** Some people can develop pneumonia during or after a hospital stay, often due to antibiotic-resistant bacteria.

8) **Community-Acquired Pneumonia (CAP):** This refers to pneumonia contracted outside of healthcare settings and is typically caused by common bacteria or viruses.

9) **Ventilator-Associated Pneumonia (VAP):** Patients on ventilators in hospitals are at risk of developing pneumonia due to the presence of a breathing tube.

10) **Immune System Weakening:** Weakened immune systems, caused by conditions like HIV/AIDS, cancer, or certain medications, make individuals more susceptible to pneumonia.

11) **Age:** Young children and the elderly are more vulnerable to pneumonia.

12) **Viruses, Including COVID-19 :** Some of the viruses that cause colds and the flu can cause pneumonia. Contagions are the most common cause of pneumonia in children youngish than 5 times. Viral pneumonia is usually mild. But in some cases it can come veritably serious. Coronavirus 2019(COVID-19) may beget pneumonia, which can come severe.

13) **Mycoplasma Pneumonia.** This type has kindly different symptoms and physical signs and is appertained to as atypical pneumonia. It's caused by the bacterium Mycoplasma pneumoniae. It generally causes a mild, wide pneumonia that affects all age groups.

TYPES OF PNEUMONIA : There are several types of pneumonia, including:

1) **Community-Acquired Pneumonia (CAP):** This is the most common type and occurs outside of healthcare settings. It can be caused by various bacteria, viruses, or other microorganisms.

2) **Hospital-Acquired Pneumonia (HAP):** This develops during a hospital stay, often in patients on ventilators or with weakened immune systems. It can be caused by drug-resistant bacteria.

3) **Aspiration Pneumonia:** Occurs when foreign materials, such as food or vomit, are inhaled into the lungs, leading to infection.

4) **Atypical Pneumonia:** Caused by atypical bacteria like Mycoplasma or Chlamydia. Symptoms may be milder than typical bacterial pneumonia.

5) **Viral Pneumonia:** Caused by viruses like influenza (the flu) or COVID-19. It's generally less severe than bacterial pneumonia but can be serious.

6) **Fungal Pneumonia:** Caused by fungal infections like histoplasmosis or cryptococcosis, often seen in people with weakened immune systems.

7) **Chemical Pneumonia:** Can occur when toxic chemicals are inhaled, damaging the lungs and leading to inflammation.

8) **Walking Pneumonia:** A milder form of pneumonia often caused by Mycoplasma pneumoniae, characterized by mild symptoms that allow patients to continue daily activities.

9) **Double Pneumonia:** When both lungs are affected by pneumonia simultaneously, it's referred to as double pneumonia, which can be more severe.

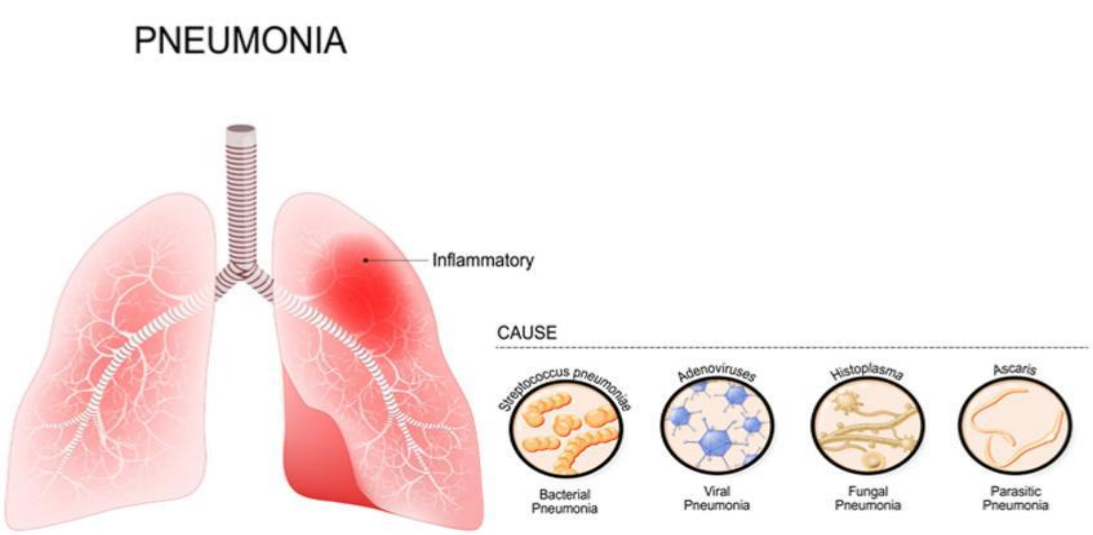


Fig-04 (Types Of Pneumonia)

HOW IS PNEUMONIA DIAGNOSED :

The Opinion is generally made grounded on your recent health history(similar as surgery, a cold wave, or trip exposures) and the extent of the illness. Grounded on these factors, your healthcare provider may diagnose pneumonia simply on a thorough history and physical test. The following tests may be used to confirm the diagnosis .

1. **Chest X-ray. This Test Takes :**

Filmland of internal apkins, bones, and organs, including the lungs.

2. **Blood Tests :** This test may be used to see whether infection is present and if infection has spread to the bloodstream(blood societies). Arterial blood gas testing checks the quantum of oxygen in your bloodstream.

Fig-05 (Blood Tests)

3. Sputum Culture :

This test is done on the material that's coughed up from the lungs and into the mouth. It's often used to see if there's an infection in the lungs.

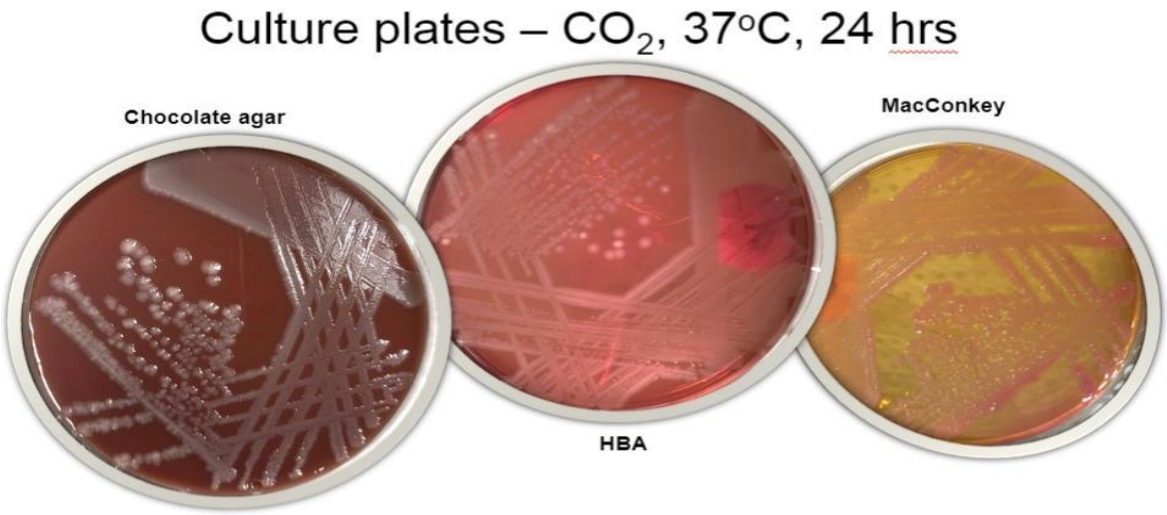


Fig-06 (Sputum culture)

4. Pulse Oximetry :

An oximeter is a small machine that measures the quantum of oxygen in the blood. A small detector is taped or cropped onto a cutlet. When the machine is on, a small red light can be seen in the detector. The test is effortless and the red light doesn't get hot.

5. Chest CT Scan :

This imaging procedure uses a combination of X-rays and computer technology to produce sharp, detailed vertical, or axial, images(frequently called slices) of the body. A CT scan shows detailed images of any part of the body, including the bones, muscles, fat, and organs. CT scans show more details than regular X-rays.

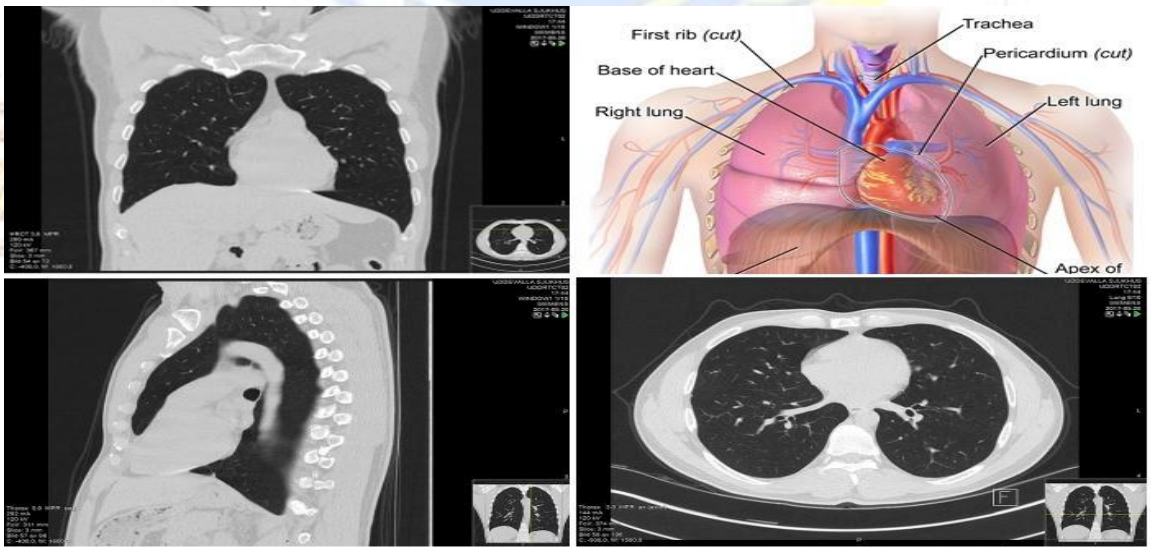


Fig-07 (Chest CT Scan)

6. Bronchoscopy :

This is direct test of the bronchi(the main airways of the lungs) using a flexible tube(called a bronchoscope). It helps to estimate and diagnose lung problems, assess blockages, and take out samples of towel and/ or fluid for testing

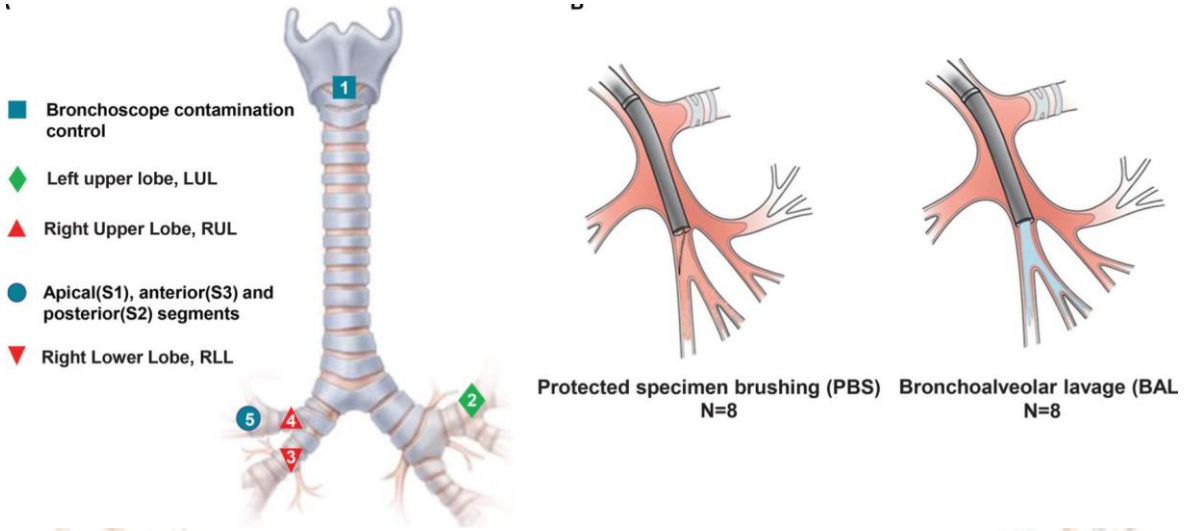


Fig-08 (Bronchoscopy)

7. Pleural Fluid Culture :

In this test, they take a sample of fluid from the pleural space. This is the space between the lungs and casket wall. A long, thin needle is put through the skin between the caricatures and into the pleural space.

Fluid is pulled into a hype attached to the needle. It's transferred to the lab where it's tested to find out which bacteria is causing the pneumonia.

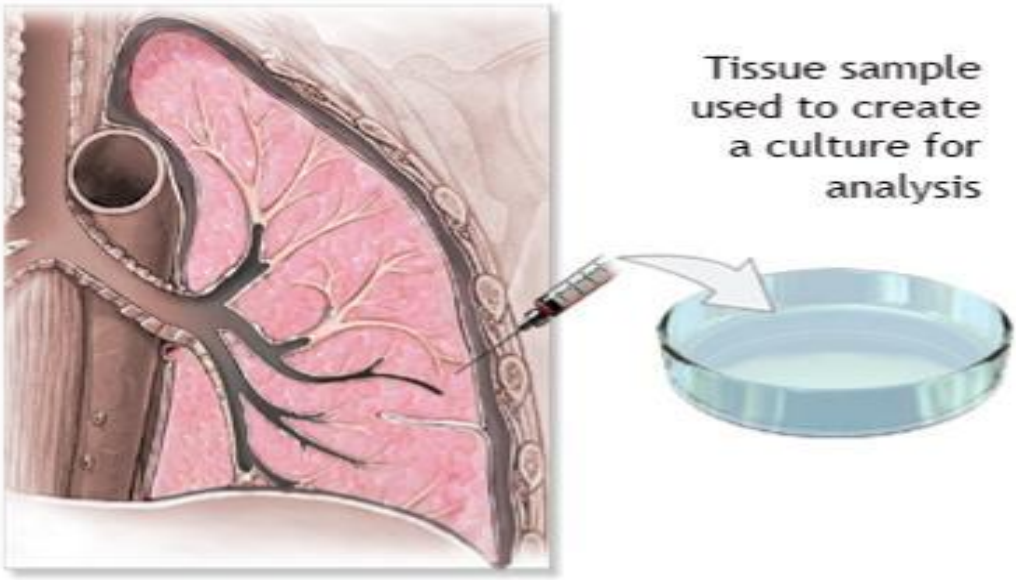


Fig-09 (Pleural Fluid Culture)

1]. CHEST X-RAY. THIS TEST TAKES :

A casketX- shaft is an imaging test that uses X- shafts to look at the structures and organs in your casket. This helps your doctor check how well your heart and lungs are functioning. Certain heart problems can beget changes in your lungs. Certain conditions can beget changes in the structure of the heart or lungs.

Chest X-Rays Can Reveal To Your Doctor The Size, Shape, And Position Of Certain Things.

- Heart
- Lungs
- Bronchi
- Aorta
- Pulmonary arteries
- Middle chest area (mediastinum)
- Bones of your chest

It uses a low amount of radiation to create images of these parts.

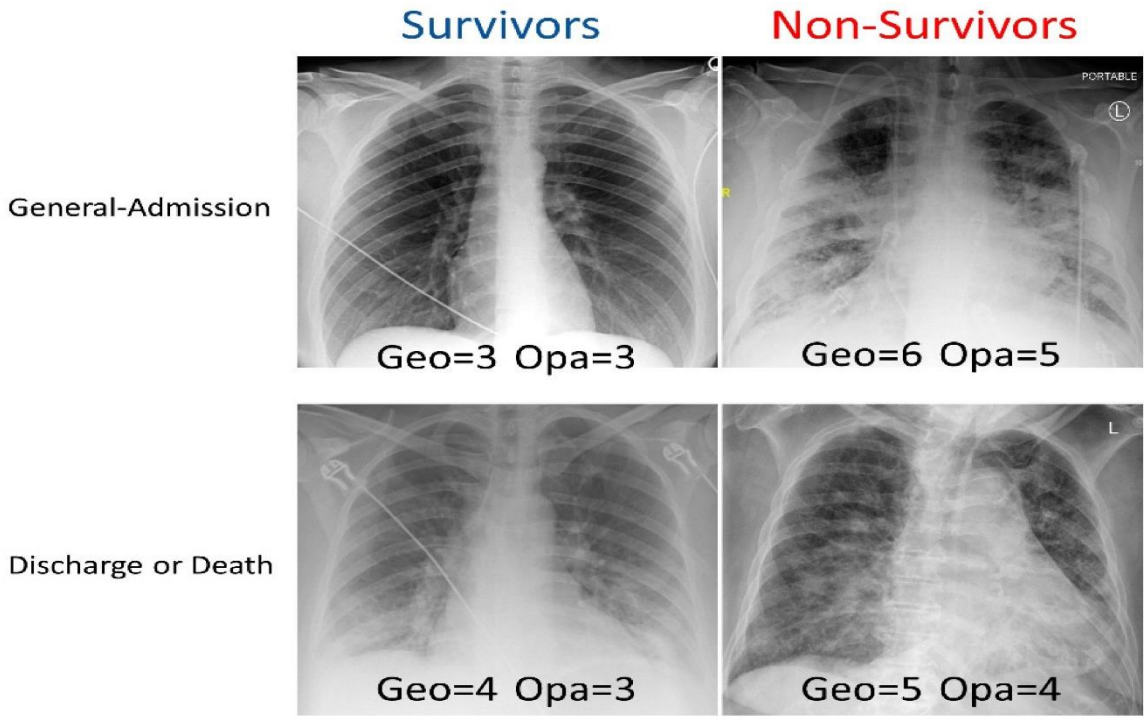


Fig-10 (Chest X-ray)

WHY MIGHT I NEED A CHEST X-RAY :

Your doctor might request a chest X-ray to check the performance of your heart or lungs. You may need one if they suspect you have certain conditions:

- Enlarged heart which can mean you have a congenital heart defect or cardiomyopathy.
- Fluid in the space between your lungs and your chest wall (pleural effusion)
- Pneumonia or another lung problem
- Ballooning of the aorta or another great blood vessel (aneurysm)
- Broken bone
- Hardening of a heart valve or aorta (calcification)
- Tumors or cancer
- Diaphragm that has moved out of place (hernia)
- Inflammation of the lining of the lung (pleuritis)
- Fluid in the lungs (pulmonary oedema) which can mean you have congestive heart failure.

You May Also Need A Chest X-Ray:

- As part of a complete physical exam or before you have surgery
- To check on symptoms related to the heart or lungs
- To see how well treatment if working or how a disease is progressing
- To check on your lungs and chest cavity after surgery
- To see where implanted pacemaker wires and other internal devices are located.

Other tools like central venous catheters, endotracheal tubes, chest tubes, and nasogastric tubes are also used.

Your healthcare provider may have other reasons to recommend a chest X-ray.

WHAT ARE THE RISKS OF A CHEST X-RAY :

You should inquire with your doctor about the radiation dose in the test and any specific risks for you. It's a good idea to keep a record of all your X-rays, including previous ones for different health issues. Show this list to your healthcare provider. The risks from radiation exposure can increase with the number of X-rays and treatments you receive over time.

If you're pregnant or might be, inform your doctor because radiation can harm the baby. Depending on your health, you might have other risks, so discuss your concerns with your healthcare provider before the procedure.

WHAT DANGERS ARE ASSOCIATED WITH A CHEST X-RAY:

You can get a chest X-ray as an outpatient or during a hospital stay. How the test is done may vary based on your condition and your healthcare provider's practices.

In General, A Chest X-ray Involves The Following Steps:

1) You will be asked to remove any clothing, jewellery, or other objects that may get in the way of the test.
2) They will give you a gown to wear.
3) You may be asked to lie down, sit, or stand. The technologist's choice of your position depends on the images needed.
4) For a standing or sitting image, you will stand or sit in front of the X-ray plate. You'll need to hunch your shoulders, breathe in deeply, and keep your breath in place while the X-ray is taken. If you are unable to hold your breath, the technologist will take the picture by watching how you breathe.
5) You will need to stay still during the X-ray. Moving while getting the X-ray can impact the image's quality.
6) To get a side view of your chest, they will ask you to turn sideways and lift your arms over your head. You'll be instructed to take a deep breath and hold it while they take the X-ray.
7) The technologist will step behind a special window while the images are being made.

The chest X-ray is not painful. If you've had recent surgery or an injury, changing positions for the X-ray may cause discomfort or pain. The technologist will take steps to make you as comfortable as possible and complete the scan quickly to reduce any discomfort or pain.

2]. PULSE OXIMETRY :

Pulse oximetry is a test that checks the oxygen level in your blood. It's a simple and painless way to see how well oxygen is reaching areas far from your heart, like your arms and legs. A device called a probe, similar to a clip, is placed on a body part, like a finger or earlobe, and it uses light to measure the blood's oxygen level.. This information helps the healthcare provider decide if a person needs extra oxygen.

Fig-11 (Pulse Oximetry)

WHY MIGHT I NEED PULSE OXIMETRY :

Pulse oximetry can check if there's sufficient oxygen in your blood. This information is needed in many kinds of situations. It may be used:

- During or after surgery or procedures that use sedation
- You can use pulse oximetry to check if lung medicines are effective.
- To check a person's ability to handle increased activity levels
- To see if a ventilator is needed to help with breathing, or to see how well it's working
- To check a person has moments when breathing stops during sleep (sleep apnea)

Pulse oximetry is used to check the health of people with conditions that affect blood oxygen levels, such as:

- Heart attack
- Heart failure
- Chronic obstructive pulmonary disease (COPD)
- Anemia
- Lung cancer

Your doctor may recommend pulse oximetry for various other reasons.

THE RISKS OF PULSE OXIMETRY :

All procedures have some risks. This procedure can have potential risks, which may include:

- Incorrect reading if the probe falls off the earlobe, toe, or finger
- Skin irritation from adhesive on the probe . The risks can differ based on your overall health and other factors. Ask your doctor which risks are relevant to your situation and discuss any concerns you may have.

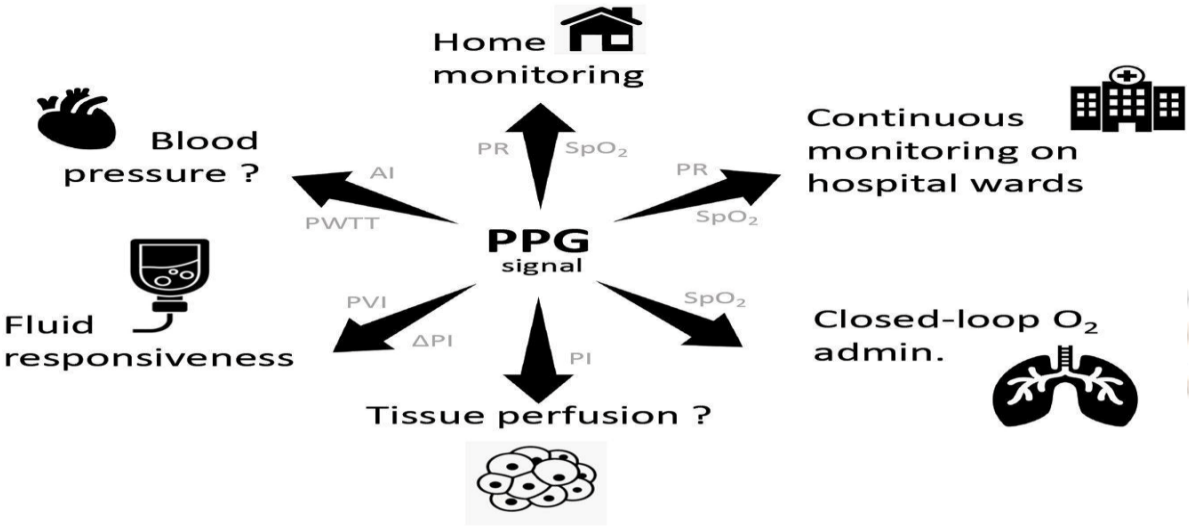


Fig-12 (Risks Of Pulse Oximetry)

WHAT HAPPENS DURING PULSE OXIMETRY :

You may have your procedure as an outpatient. This means you'll be able to go home on the same day. This can be done during a hospital stay, and how it's done can vary. It depends on your condition and your healthcare provider's methods. Usually, pulse oximetry will involve these steps:

1) A clip-like device called a probe will be placed on your finger or earlobe. A probe with sticky adhesive can be placed on your forehead or finger.

2) You can keep the probe on for continuous monitoring.

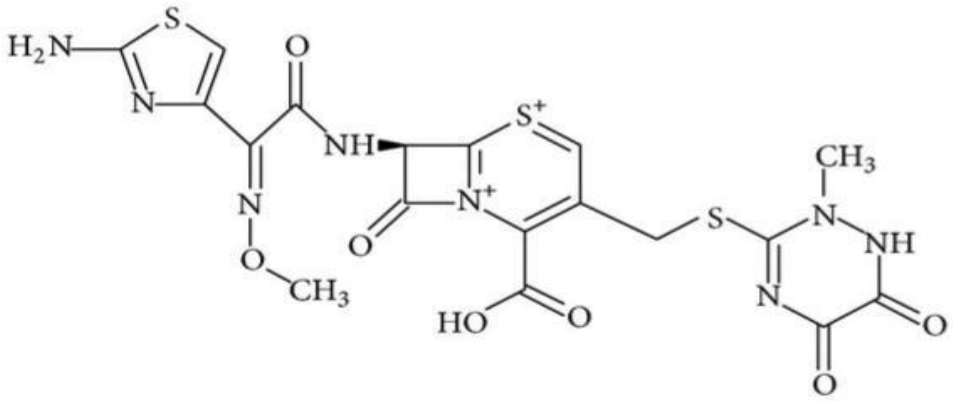
3) Or it may be used to take a single reading. The probe will be taken off once the test is done.

❖ **CEFTRIAXONE :**

Ceftriaxone is an antibiotic medication used to treat a variety of bacterial infections. It belongs to a class of drugs known as cephalosporin and is often administered through injection or intravenous (IV) infusion.

Ceftriaxone is effective against a wide range of bacteria and is commonly used to treat conditions such as respiratory tract infections, skin and soft tissue infections, urinary tract infections, and more serious infections like sepsis and certain types of meningitis. It is typically prescribed by healthcare professionals when other antibiotics may not be effective against the specific bacteria causing the infection.

Ceftriaxone is a type of antibiotic called cephalosporin. It's used to kill bacteria or stop their growth. But it won't treat colds, flu, or viral infections. You need a doctor's prescription to get this medicine.



Sacture Of Ceftriaxone

Brand Names	**Rocephin**
Generic Name	**Ceftriaxone**
Drug Bank Accession Number	**DB01212**
Type	**Small Molecule**
Groups	**Approved**
Weight	**Average: 554.58** **Monoisotopic: 554.04605704**
Chemical Formula	**C18H18N8O7S3**
Synonyms	**Ceftriaxona** **Ceftriaxone** **Ceftriaxonum** **Rocephin**
External IDs	**DRG-0071** **Ro 139904**
IUPAC name	**(6R,7R)-7-{[(2Z)-2-(2-amino-1,3-thiazol-4-yl)- >2-(methoxyimino)acetyl]amino}-3-{[(2-methyl-5,6-dioxo-1,2,5,6 tetrahydro-1,2-triazin-3-yl)thio]methyl]-8-oxo-5-thia-1- azabicyclo[4.2.0]oct-2-ene-2-carboxylic**

MECHANISM OF ACTION:

Ceftriaxone is a broad-spectrum antibiotic that belongs to the cephalosporin class. Its mechanism of action involves inhibiting bacterial cell wall synthesis. Here's a simpler explanation of how it works :

1. **Cell Wall**

Synthesis:

Bacterial cells have a rigid outer structure called the cell wall, which provides stability and protection. This wall is composed of peptidoglycan, a complex molecule.

2. **Transpeptidase Inhibition:**
   Ceftriaxone interferes with the final steps of peptidoglycan synthesis by binding to and inhibiting an enzyme called transpeptidase (also known as penicillin-binding protein or PBP). Transpeptidase is essential for cross-linking the peptidoglycan chains, which is crucial for the integrity of the bacterial cell wall.

3. **Weakening the Cell Wall:**
   As a result of transpeptidase inhibition, the bacterial cell wall becomes weak and cannot maintain its structural integrity.

4. **Cell Lysis:**
   Without a strong cell wall, the internal pressure of the bacterial cell causes it to burst or lyse. This causes the bacterium to die.

Ceftriaxone is effective against a wide range of bacteria, both Gram-positive and Gram-negative, making it a valuable tool in the treatment of various bacterial infections.

It is administered intravenously or intramuscularly and is often used for serious infections like pneumonia, meningitis, and certain types of gonorrhea. It's important to note that antibiotics should only be used under the guidance of a healthcare professional to ensure proper diagnosis and treatment.

Fig-13 (Ceftriaxone For injection,USP)

PHARMACOKINETIC: Of Ceftriaxone :

Absorption :

When given through injection into muscles (IM), Ceftriaxone gets fully absorbed, and its highest levels in the blood happen around 2 to 3 hours after the dose. If you take multiple doses through injection or **intravenously (IV**), spaced 12 to 24 hours apart, there can be 15% to 36% more Ceftriaxone in your system compared to a single dose.

Distribution :

Ceftriaxone goes into tissues and body fluids effectively, including the cerebrospinal fluid, to treat central nervous system infections.

Ceftriaxone is reversibly bound to human plasma proteins and the binding of ceftriaxone decreases with increasing concentration from a value of 95% at plasma concentrations less than 25 mcg/mL to 85% at plasma concentration of 300 mcg/mL. Over a 0.15 to 3 g dose range in healthy adult subjects, the apparent volume of distribution ranged from 5.8 to 13.5 L.

Metabolism :

33–67% of ceftriaxone is renally excreted as unchanged drug, but no dose adjustments are required in renal impairment with dosages up to 2 grams per day. The restis excreted in the bile as unchanged drug which is ultimately excreted in feces as inactive compounds from hepatic and gut flora metabolise .

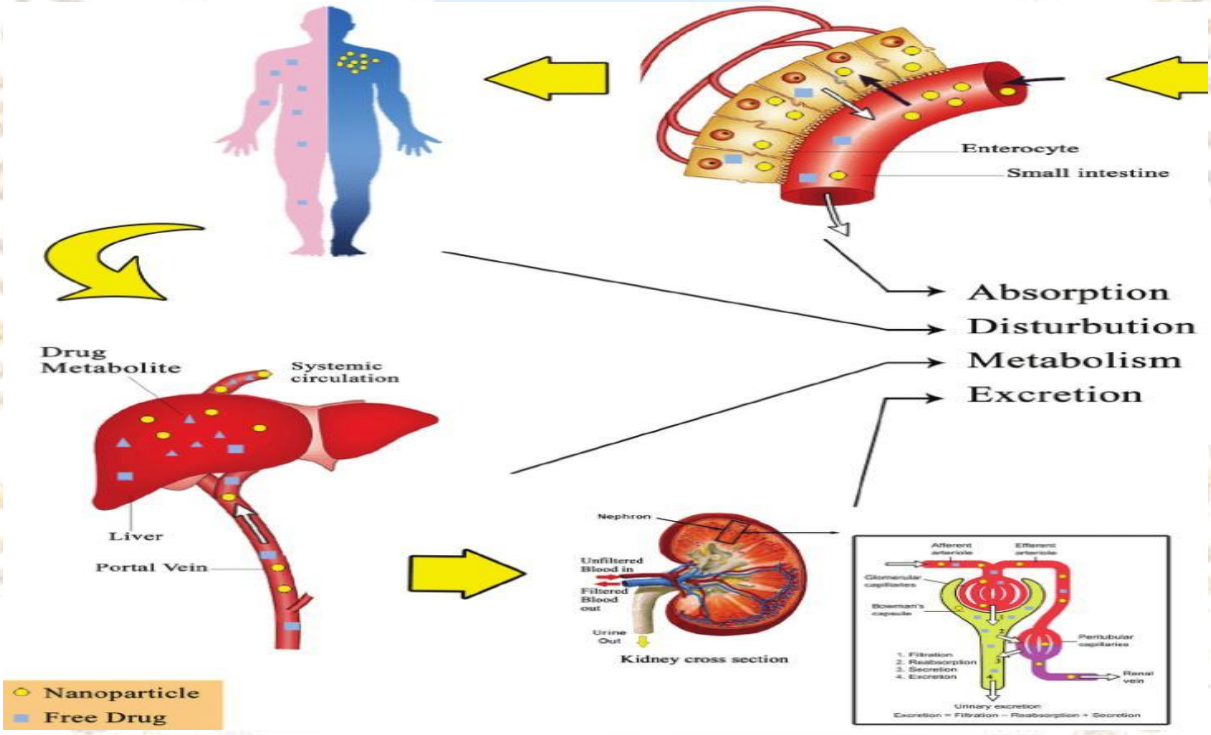
Elimination :

In healthy adults, Ceftriaxone is typically removed from the body in about 5.8 to 8.7 hours, with an average of 6.5 hours. In some cases, it can take up to 10 hours to be eliminated. In people with renal impairment, the average elimination half-life increases to 11.4–15.7 hours.

Exceration :

Around one-third to two-thirds of the drug is eliminated in the urine without any changes, while the rest is released in the bile and eventually ends up in the feces. as microbiologically inactive compounds. When given as an intramuscular injection, Ceftriaxone is quickly and fully absorbed by the body.

Fig-14 (General Pharmacokinetic: Of Ceftriaxone)



SIDE EFFECTS :

Besides its intended effects, a medication can have unwanted side effects. While not everyone will experience these side effects, if they do happen, it's important to seek medical advice. Contact your doctor or nurse right away if any of the following side effects happen.

More common ,

- Black, tarry stools
- Chest pain
- Chills
- Cough
- Fever

- Painful or difficult urination
- Shortness of breath
- Sore throat
- Blisters, ulcers, or white spots on the lips or inside the mouth.
- Swollen glands
- Unusual bleeding or bruising
- Unusual tiredness or weakness

Less common :

- **Diarrhea.**

Rare ,

- Abdominal or stomach cramps or tenderness
- Back, leg, or stomach pains
- Bleeding gums Shortness
- Bloating
- Blood in the urine or stools
- Bloody nose
- Bluish color
- Changes in skin color
- Clay-colored stools
- Convulsions
- Cough or hoarseness
- Pinpoint red spots on the skin
- Swelling around the eyes, face, lips, or tongue, causing puffiness.
- Rash
- The face, neck, arms, and sometimes the upper chest may become red.
- of breath
- Skin rash
- Swelling of the foot or leg
- Swollen lymph nodes , Soreness , Feeling pressure in the chest , Difficulty breathing during ,physical activity , Bad breath odor , Unexpected weight loss ,Throwing up blood, Watery or bloody diarrhea , Wheezing , Yellowing of the eyes or skin .

❖ **PHENOXYMETHYLPENICILLIN AND NETILMICIN :**

Phenoxymethylpenicillin is an antibiotic that belongs to the penicillin class. It is often used to treat bacterial infections, including strep throat and skin infections.

Netilmicin, on the other hand, is an antibiotic from the aminoglycoside class. It is used to cure different bacterial infections, especially those caused by gram-negative bacteria.

Both of these antibiotics work by targeting and inhibiting the growth of specific types of bacteria, but they belong to different classes and have different mechanisms of action. They may be prescribed for different types of infections based on the specific bacteria causing the infection and their susceptibility to these antibiotics. You should obey your doctor’s advice when using antibiotics.

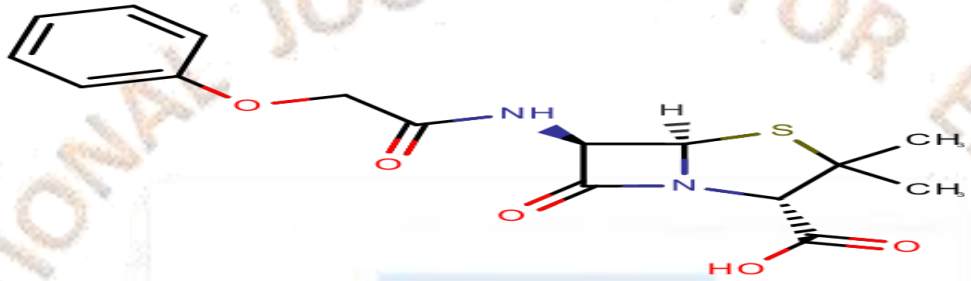
Phenoxymethylpenicillin and Netilmicin are sometimes used in combination to treat certain severe bacterial infections. This combination is often prescribed when the infecting bacteria are resistant to single antibiotics or when a broad-spectrum approach is needed to cover a wide range of bacteria.

The combination of Phenoxymethylpenicillin (a penicillin antibiotic) and Netilmicin (an aminoglycoside antibiotic) can have a synergistic effect, meaning that they work together to enhance their antibacterial activity against a broader spectrum of bacteria. However, the use of combination antibiotics is typically reserved for

serious infections, and it should be prescribed and monitored by a healthcare professional, as there can be potential side effects and considerations when using multiple antibiotics together.

❖ PHENOXYMETHYLPENICILLIN : (Penicillin V)

Phenoxymethylpenicillin, also known as penicillin V, is a type of antibiotic medication in the penicillin class. It is commonly used to treat various bacterial infections, including strep throat, tonsillitis, and some skin infections. Like other penicillin, it works by inhibiting the growth of bacteria by interfering with their cell wall formation. However, it's important to use this medication as prescribed by a healthcare professional, and for the full prescribed course, to ensure the infection is properly treated and to prevent antibiotic resistance.



Phenoxymethylpenicillin

MECHANISM OF ACTION: (Phenoxymethylpenicillin)

Phenoxymethylpenicillin, **also known as penicillin V**, works through the following mechanism of action:

1) **Inhibition of Cell Wall Synthesis:** Bacterial cells have a rigid cell wall made up of a substance called peptidoglycan. Phenoxymethylpenicillin interferes with the synthesis of peptidoglycan by inhibiting the activity of enzymes known as transpeptidase (also called penicillin-binding proteins or PBPs). These enzymes are essential for cross-linking the peptidoglycan strands in the bacterial cell wall.

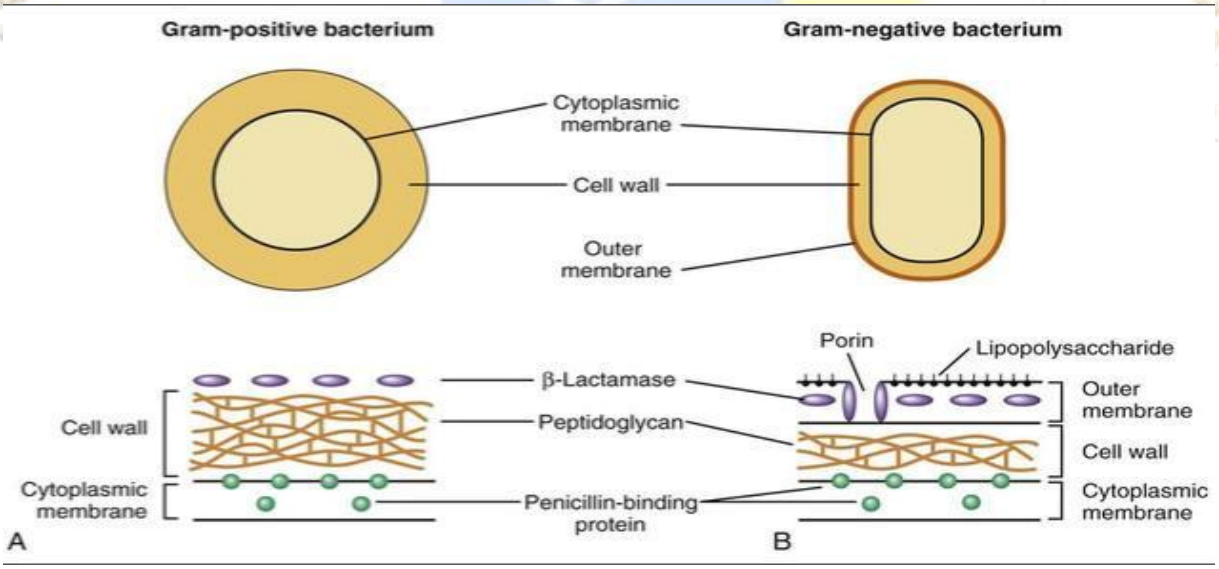


Fig-15 (Inhibition of Cell Wall Synthesis)

2) **Weakening the Cell Wall:** By inhibiting transpeptidase enzymes, Phenoxymethylpenicillin prevents the formation of strong cross-links in the bacterial cell wall. This results in a weakened and structurally compromised cell wall.

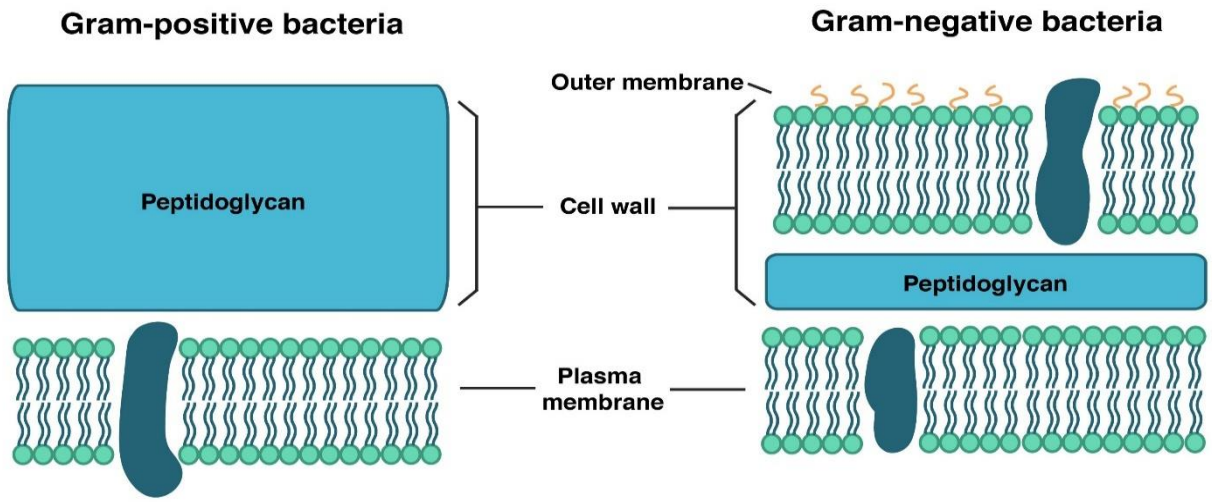


Fig-16 (Weakening the Cell Wall By Inhibiting Transpeptidase Enzymes)

3) **Osmotic Lysis:** As a consequence of the weakened cell wall, the bacterial cell becomes susceptible to osmotic pressure changes. The cell wall cannot withstand the pressure difference between the cell's interior and its external environment. This leads to the influx of water into the bacterial cell, causing it to swell and ultimately burst, leading to bacterial cell death.

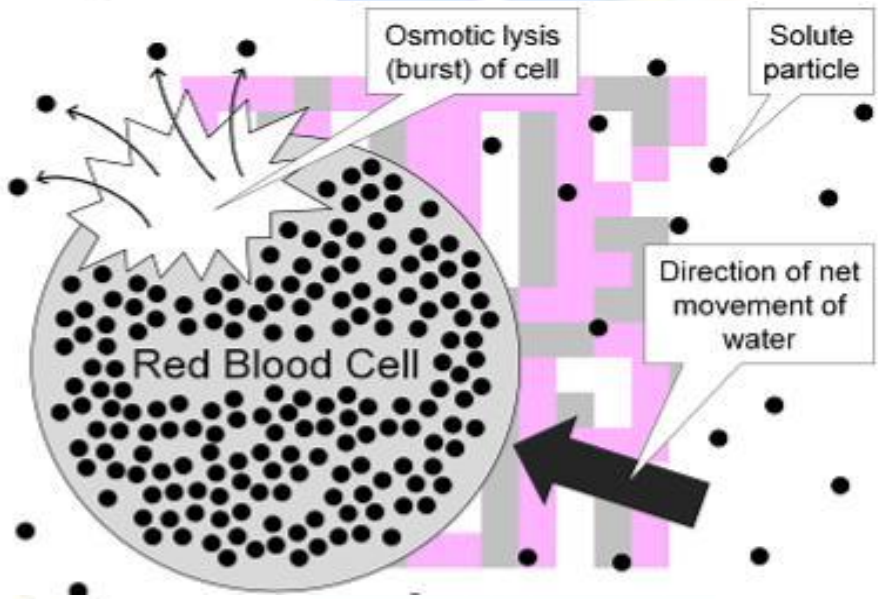
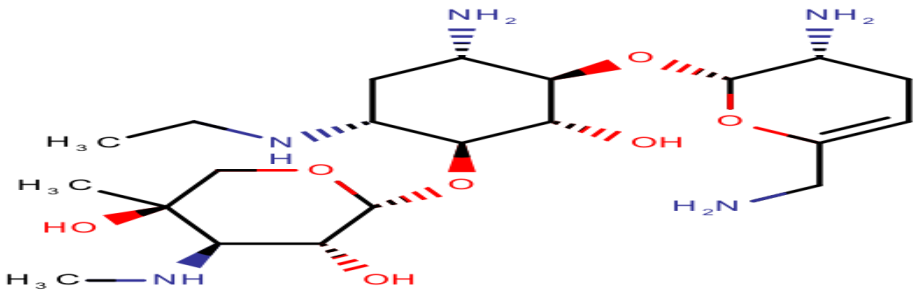


Fig-17 (Osmotic Lysis)

In summary, Phenoxymethylpenicillin mechanism of action revolves around interfering with the formation of the bacterial cell wall, ultimately causing bacterial cells to rupture and die due to osmotic lysis. This antibiotic is particularly effective against a range of Gram-positive bacteria that have peptidoglycan-rich cell walls.

❖ **NETILMICIN :**

Netilmicin is a modified form of sisomycin, an antibiotic like gentamicin but with less harm to the ears and kidneys. It works by stopping bacteria from making proteins, and the exact way it kills bacteria is not completely clear.



Netilmicin

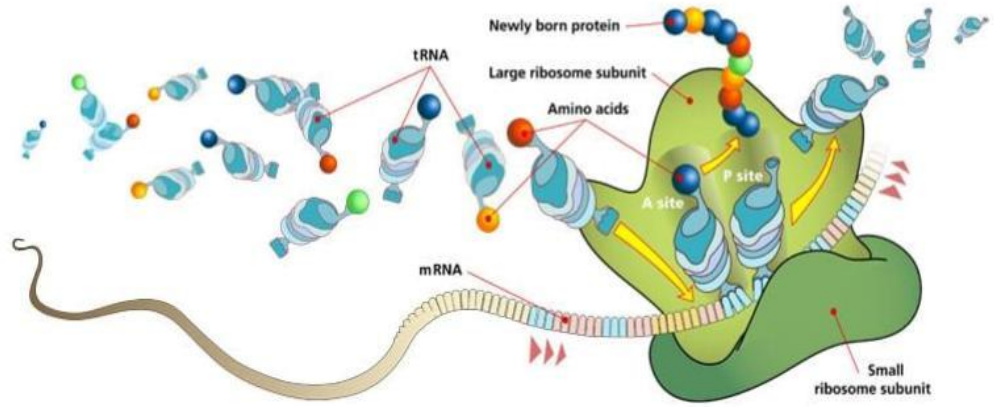
MECHANISM OF ACTION : (Netilmicin)

Netilmicin is an antibiotic that belongs to the aminoglycoside class of antibiotics. It stops bacteria by blocking their protein production. Here's how it works:

Binding To Ribosomes: Netilmicin binds to the bacterial ribosomes, specifically the 30S subunit of the bacterial ribosome.

Interference With Protein Synthesis: By binding to the ribosome, Netilmicin disrupts the normal process of protein synthesis in bacteria. It causes misreading of the genetic code on the mRNA, leading to the incorporation of incorrect amino acids into the growing protein chain. Inhibition of proteins synthase.

Fig-18 (Interference with Protein Synthesis By binding To The Ribosome)



Translation: This interference with protein synthesis ultimately results in the inhibition of bacterial translation, preventing the synthesis of essential proteins that bacteria need to grow and multiply.

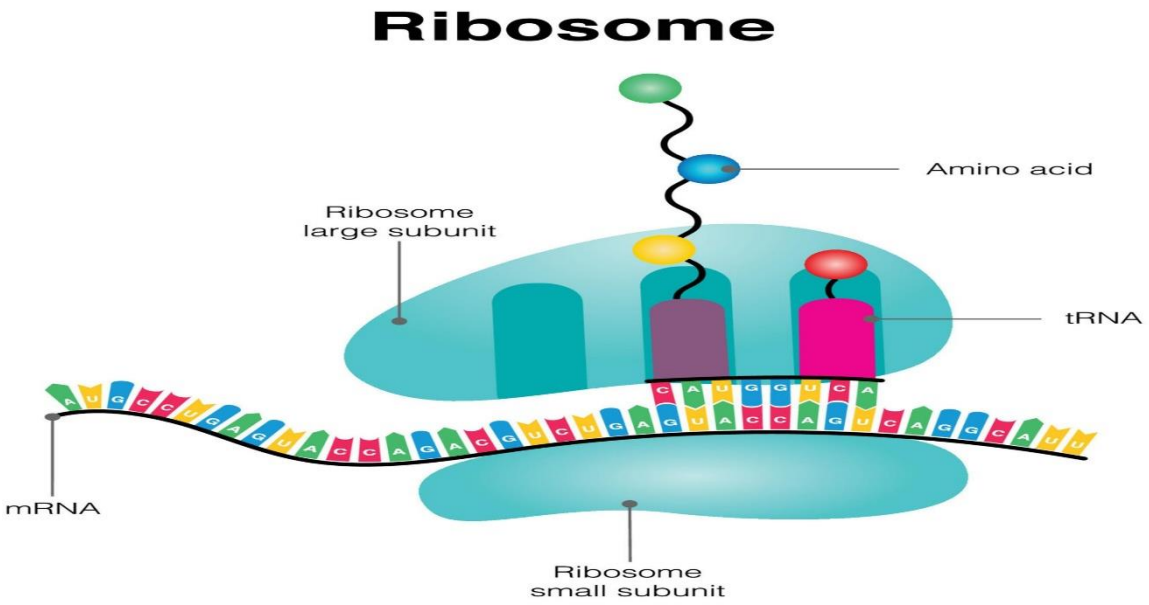


Fig-19 (Translation)

Bactericidal Activity: Netilmicin's disruption of protein synthesis is bactericidal, meaning it kills bacteria rather than just inhibiting their growth. It is effective against a wide range of Gram-negative bacteria, including some strains that are resistant to other antibiotics.

Overall, netilmicin's mechanism of action makes it an important antibiotic for treating infections caused by susceptible bacteria. However, it's important to note that its use should be guided by susceptibility testing to ensure it is effective against the specific bacteria causing the infection, and its use should be carefully monitored due to the potential for side effects, especially on kidney function and hearing .

ADVANTAGES OF CEFTRIAXONE :

Ceftriaxone is an antibiotic with several advantages:

1) **Broad-Spectrum:** Ceftriaxone is effective against a wide range of bacteria, making it useful for treating various infections.
2) **Long Duration Of Action:** It has a long half-life, allowing for once-a-day dosing in many cases, which can improve patient compliance.
3) **High tissue penetration:** Ceftriaxone can penetrate into tissues effectively, making it suitable for treating infections in different parts of the body.
4) **Injectable And Oral Forms:** It is available as an injectable and, in some cases, oral medication, providing flexibility in treatment options.
5) **Low Risk Of Resistance:** Ceftriaxone has a low likelihood of bacterial resistance compared to some other antibiotics, making it a valuable choice for empiric therapy.
6) **Suitable For Serious Infections:** It's commonly used for treating serious infections like pneumonia, meningitis, and septicaemia.
7) **Pediatric Use:** Ceftriaxone is safe for use in children, which is crucial for pediatric healthcare.
8) **Minimal Side Effects:** While all medications have potential side effects, ceftriaxone is generally well-tolerated when used appropriately.

9) **Synergy With Other Drugs:** It can be used in combination with other antibiotics to enhance its effectiveness against certain bacterial infections.

EFFECTIVENESS OF CEFTRIAXONE IN PNEUMONIA :

Ceftriaxone can be effective in treating pneumonia, particularly when the causative bacteria are susceptible to it. Pneumonia can be caused by various pathogens, including Streptococcus pneumoniae, Haemophilus influenza, Klebsiella pneumoniae, and others. Ceftriaxone's broad-spectrum activity makes it effective against many of these bacteria.

However, the choice of antibiotic for treating pneumonia depends on several factors, including the severity of the infection, local antibiotic resistance patterns, and individual patient factors. Ceftriaxone is often used as an empiric treatment for community-acquired pneumonia, especially in hospitalized patients, due to its broad coverage.

It's crucial to note that in severe cases of pneumonia or cases where the causative bacteria are known to be resistant to ceftriaxone, alternative antibiotics may be required. The choice of antibiotic should always be guided by the recommendations of a healthcare professional and, ideally, supported by microbiological testing to identify the specific bacteria causing the infection and their susceptibility to antibiotics.

ADVANTAGES OF PHENOXYMETHYLPENICILLIN :

Phenoxymethylpenicillin, also known as penicillin V, is an antibiotic with several advantages:

1. **Effective Against Common Infections:** It is effective against a wide range of common bacterial infections, including streptococcal throat infections, dental infections, and skin infections.
2. **Low Cost:** Phenoxymethylpenicillin is a cost-effective antibiotic, making it accessible to a broad population.
3. **Well-Tolerated:** It is generally well-tolerated with a low incidence of serious side effects, making it suitable for use in many patients, including children and pregnant women.
4. **Narrow Spectrum:** While it is effective against various bacteria, it has a narrower spectrum compared to some other antibiotics, reducing the risk of disrupting the body's natural microbiota.
5. **Oral Form:** It is available in oral tablet or liquid forms, making it convenient for outpatient treatment.
6. **Minimal Drug Interactions:** Phenoxymethylpenicillin has fewer interactions with other medications compared to some other antibiotics, reducing the risk of complications in patients taking multiple drugs.
7. **Low Risk Of Antibiotic Resistance:** Its narrow spectrum and limited use in comparison to broader-spectrum antibiotics contribute to a lower likelihood of bacterial resistance development.

EFFECTIVENESS OF PHENOXYMETHYLPENICILLIN IN PNEUMONIA :

Phenoxymethylpenicillin, also known as penicillin V, is not typically the first-choice antibiotic for treating pneumonia. Pneumonia can be caused by a variety of bacteria, including Streptococcus pneumoniae, Haemophilus influenzae, and others. Penicillin V has a more limited spectrum of activity and may not effectively target all the bacteria responsible for pneumonia, especially in cases of more severe or atypical pneumonia.

In many cases, healthcare professionals may prescribe broader-spectrum antibiotics such as amoxicillin, amoxicillin-clavulanate, or macrolides like azithromycin or clarithromycin for the treatment of pneumonia. These antibiotics provide better coverage for the range of bacteria commonly associated with pneumonia

The choice of antibiotic for pneumonia should be based on several factors, including the suspected causative pathogens, the severity of the illness, local antibiotic resistance patterns, and individual patient factors. It's essential to consult a healthcare professional who can make an appropriate antibiotic selection based on these considerations and, ideally, guided by microbiological testing to determine the specific bacteria causing the infection and their susceptibility to antibiotics.

While penicillin V has its place in treating certain bacterial infections, it's not typically the first-line choice for pneumonia due to its narrower spectrum of activity.

ADVANTAGES OF NETILMICIN :

Netilmicin is an antibiotic that belongs to the aminoglycoside class and has several advantages:

1. **Effective Against A Wide Range Of Bacteria:** Netilmicin is effective against many Gram-negative bacteria, including Escherichia coli, Klebsiella pneumoniae, and Pseudomonas aeruginosa. It is particularly useful in treating serious infections caused by these bacteria.

2. **Bactericidal Action:** It has a bactericidal (kills bacteria) mode of action, which can be highly effective in rapidly reducing bacterial loads in severe infections.

3. **Low Resistance Development:** Netilmicin has a lower likelihood of resistance development compared to some other antibiotics, making it valuable in combating multidrug-resistant strains of bacteria.

4. **Synergy With Other Antibiotics:** It can be used in combination with other antibiotics to enhance the overall effectiveness of treatment, especially in severe or complicated infections.

5. **Suitable For Serious Infections:** Netilmicin is often used to treat serious infections like sepsis, urinary tract infections, and respiratory tract infections when the causative bacteria are susceptible to it.

6. **Parenteral Administration:** It is typically administered intravenously or intramuscularly, allowing for rapid delivery of the medication, making it suitable for hospitalized patients with severe infections.

7. **Clinically Established:** Netilmicin has a history of successful clinical use in a variety of healthcare settings, which contributes to its reliability in treating bacterial infections.

EFFECTIVENESS OF NETILMICIN IN PNEUMONIA :

Netilmicin is not typically a first-line antibiotic choice for treating pneumonia. Pneumonia can be caused by various bacteria, including both Gram-negative and Gram-positive species. While netilmiicin is effective against some Gram-negative bacteria, it may not cover the full spectrum of pathogens that commonly cause pneumonia, especially community-acquired pneumonia.

First-line antibiotics for treating pneumonia often include drugs like amoxicillin or amoxicillin-clavulanate for mild to moderate cases, or broader-spectrum antibiotics like ceftriaxone or cefuroxime for more severe or hospital-acquired pneumonia. These antibiotics provide coverage for a wider range of bacteria associated with pneumonia.

The choice of antibiotic for pneumonia should be based on several factors, including the suspected causative pathogens, the severity of the illness, local antibiotic resistance patterns, and individual patient factors.

It's essential to consult a healthcare professional who can make an appropriate antibiotic selection based on these considerations and, ideally, guided by microbiological testing to determine the specific bacteria causing the infection and their susceptibility to antibiotics.

While netilmiicin has its place in treating certain bacterial infections, it's not typically the first-choice antibiotic for pneumonia due to its narrower spectrum of activity.

CONCLUSION:

I can provide a brief conclusion based on the information available up to my last training data in September 2021, but keep in mind that medical research may have evolved since then.

The effectiveness of ceftriaxone versus combined Phenoxymethylpenicillin and Netilmicin in severe pneumonia management may vary depending on factors like the specific pathogens involved, patient characteristics, and local antibiotic resistance patterns. It is essential to consider individual patient cases and consult with a healthcare professional for the most current and appropriate treatment recommendations.

The effectiveness of ceftriaxone In severe pneumonia management is generally well-established. Ceftriaxone is an effective broad-spectrum antibiotic often used to treat severe pneumonia, especially when the causative pathogens are susceptible to this drug. However, the appropriateness of ceftriaxone may depend on factors such as the patient's specific condition, local antibiotic resistance patterns, and individual patient characteristics. Consultation with a healthcare professional is crucial to determine the most suitable treatment for a patient's severe pneumonia.

The effectiveness of combined Phenoxymethylpenicillin and Netilmicin In severe pneumonia management can be positive in specific cases, particularly when dealing with pathogens that are susceptible to these antibiotics. However, the choice of this combination therapy should be based on factors such as the patient's condition, microbial susceptibility, and local antibiotic resistance patterns. It's essential to consult with a healthcare professional to determine the most appropriate treatment for severe pneumonia in a particular patient. Medical guidelines and research may also evolve, so the most up-to-date information should be considered.

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