TETRACYCLINE

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The four-ringed compound, tetracycline, was first discovered in 1948 under the name chlortetracycline. It was produced and derived from actual bacterial cells from Streptomyces and Actinobacteria cultures. Years following this discovery, new analogues were developed. These include tetracycline, demeclocycline, doxycycline and minocycline, which are now widely used today. Just recently, a new class of tetracycline was introduced which exhibits broad-spectrum anti-bacterial coverage. This new medication, tigecycline was discovered while attempting to develop various tetracycline analogues for use with multi-drug resistant organisms.

**Mechanism:** Tetracycline antibiotics function to inhibit protein synthesis within bacterial cells. Protein synthesis is vital to the integrity of all cells and when halted, causes cell death. This contributes to the eradication of bacterial infections and leads to clinical improvement in patients with signs and symptoms of infection. Once ingested, the tetracycline compound enters the cell wall of the bacteria and binds to the 30S ribosome. The 30S ribosome is responsible for attaching to RNA genetic material essential to the process of protein synthesis. The body’s response to tetracycline is inhibitory to the bacteria and stops replication. This inhibition is usually reversible upon discontinuing the medication and may contribute to reinfection if the course of tetracycline is not completed.

Non-antimicrobial uses of tetracyclines have gained attention recently. Many dermatologists have experimented with the use of tetracycline for its proposed anti-inflammatory effects in treatment of skin diseases. This is explained by recent research that has found tetracycline to have a significant effect on matrix metalloproteinases (MMPs). MMPs are enzymes that are responsible for the destruction of connective tissue proteins in the body. It was found that MMP levels were significantly elevated in inflammatory conditions involving the skin. By inhibiting this enzyme, tetracycline has the ability to reduce the connective tissue destruction associated with the elevation of metalloproteinases (MMPs) during skin inflammation. Tetracycline has also been found to inhibit inflammatory regulators called cytokines. Cytokines are responsible for recruiting inflammatory cells to the site of skin injury. For example, rosacea is primarily an inflammatory reaction rather than from an infectious cause. Overactive inflammation contributes to the redness and swelling associated with rosacea and this inflammation is decreased when treated with tetracycline.

**Uses:**

**Infectious causes**

- Acne
- Rocky Mountain Spotted Fever
- Lyme disease
- Gastritis
- Balantidiasis
- Q Fever
- Psittacosis
- Lymphogranuloma venereum
- Genital chlamydia infection
- Cholera
- Mycoplasma pneumonia

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Non-infectious causes

- Rosacea
- Pyoderma gangrenosum
- Bullous pemphigoid

All four analogues of the tetracycline family have the same mechanism of action within the cells, but there are slight differences among these medications. Minocycline is the most active of all the tetracyclines due to an increase in fat solubility, allowing it to enter cells more readily. This increased solubility may contribute to vertigo (dizziness) symptoms mainly due to the increase in absorption by the brain. Minocycline is also used for treatment of patients infected with MRSA (methacillin-resistant staphylococcus aureus). Doxycycline is effective in treating patients infected with nongonococcal urethritis and second line treatment for patients infected with genital chlamydia infections. Minocycline and doxycycline are frequently the first line medication for patients with moderate to severe acne. Tigecycline, a newer analog of tetracycline, has a much broader spectrum of activity and covers many gram positive and negative organisms. Demeclocycline has been used for the off-label treatment of hyponatremia due to a condition call SIADH. SIADH is defined as a syndrome of inappropriate antidiuretic hormone release. Demeclocycline functions to block the reabsorption of water from the kidney, therefore increasing the concentration of sodium in the blood. This off-label use relies on a side effect of demeclocycline, which causes a condition termed nephrogenic diabetes insipidus. This condition reduces the absorption of water from the kidney.

Resistance: Tetracyclines cover a broad spectrum of bacteria including aerobic, gram positive and gram negative organisms. Previously sensitized organisms are now developing resistance to this medication including Staphylococcus, Streptococcus and Neisseria. Unfortunately, Pseudomonas and Proteus bacteria display strong resistance to all tetracyclines and require other antibiotic coverage to completely eradicate these organisms. This resistance is caused by bacterial processes that prevent the accumulation of the medication inside the cell. Upon developing resistance to any one type of tetracycline usually confers that the organism will be resistant to all 4 analogs of the drug. If this occurs, another form of antibiotic should be started in place of a tetracycline.

Side Effects: The most common side effect in patients taking tetracycline is abdominal discomfort, nausea, vomiting, and loss of appetite. These effects may be diminished with food ingestion when taking the medication. However, food may reduce the absorption of the medication as much as 50 percent. Doxycycline absorption is not affected by food and may be better tolerated in patients with gastrointestinal complaints. Diarrhea is another concern and may be caused by reduction in the body’s normal gut bacteria in response to the antibiotic. If diarrhea occurs, consult your physician immediately.

Other side effects that may occur with tetracycline use include:

- Phototoxicity (demeclocycline, skin easily burns with sun exposure)
- Allergic reactions (hives, rash, and/or shortness of breath)
- Teeth and bone discoloration
- Hepatic and renal toxicity (liver and kidney damage)
- Vertigo (minocycline, dizziness)
- Nephrogenic diabetes insipidus

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