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COURSE TITLE: INTRODUCTORY PHARMACOLOGY AND TOXICOLOGY II**

**ASSIGNMENT QUESTION**
1. Write on a named bacterial protein synthesis inhibitor, stating its mechanism of action, indication for use, toxicity, and adverse effects.

**ANSWER

STREPTOMYCIN
Streptomycin** is an [antibiotic](https://en.wikipedia.org/wiki/Antibiotic) used to treat a number of bacterial infections. This includes [tuberculosis](https://en.wikipedia.org/wiki/Tuberculosis), [*Mycobacterium avium* complex](https://en.wikipedia.org/wiki/Mycobacterium_avium_complex), [endocarditis](https://en.wikipedia.org/wiki/Endocarditis), [brucellosis](https://en.wikipedia.org/wiki/Brucellosis), [*Burkholderia* infection](https://en.wikipedia.org/wiki/Burkholderia_infection), [plague](https://en.wikipedia.org/wiki/Plague_%28disease%29), [tularemia](https://en.wikipedia.org/wiki/Tularemia), and [rat bite fever](https://en.wikipedia.org/wiki/Rat_bite_fever). For active tuberculosis it is often given together with [isoniazid](https://en.wikipedia.org/wiki/Isoniazid), [rifampicin](https://en.wikipedia.org/wiki/Rifampicin), and [pyrazinamide](https://en.wikipedia.org/wiki/Pyrazinamide). It is given by [injection into a vein](https://en.wikipedia.org/wiki/Intravenous) or [muscle](https://en.wikipedia.org/wiki/Intramuscular).

Common side effects include [feeling like the world is spinning](https://en.wikipedia.org/wiki/Vertigo), vomiting, numbness of the face, fever, and rash. Use during [pregnancy](https://en.wikipedia.org/wiki/Pregnancy) may result in permanent [deafness](https://en.wikipedia.org/wiki/Deafness) in the developing baby. Use appears to be safe while [breastfeeding](https://en.wikipedia.org/wiki/Breastfeeding). It is not recommended in people with [myasthenia gravis](https://en.wikipedia.org/wiki/Myasthenia_gravis) or other [neuromuscular disorders](https://en.wikipedia.org/wiki/Neuromuscular_disorders). Streptomycin is an [aminoglycoside](https://en.wikipedia.org/wiki/Aminoglycoside). It works by blocking the ability of [30S ribosomal subunits](https://en.wikipedia.org/wiki/30S_ribosomal_subunits) to make proteins, which results in [bacterial death](https://en.wikipedia.org/wiki/Bactericidal).

Streptomycin was discovered in 1943 from [*Streptomyces griseus*](https://en.wikipedia.org/wiki/Streptomyces_griseus). It is on the [World Health Organization's List of Essential Medicines](https://en.wikipedia.org/wiki/WHO_Model_List_of_Essential_Medicines), the safest and most effective medicines needed in a [health system](https://en.wikipedia.org/wiki/Health_system). The World Health Organization classifies it as critically important for human medicine.

**MECHANISM OF ACTION**

Streptomycin is a [protein synthesis inhibitor](https://en.wikipedia.org/wiki/Protein_synthesis_inhibitor). It binds to the small 16S rRNA of the 30S subunit of the bacterial ribosome, interfering with the binding of [formyl-methionyl-tRNA](https://en.wikipedia.org/wiki/Formyl-methionyl-tRNA) to the 30S subunit.This leads to codon misreading, eventual inhibition of protein synthesis and ultimately death of microbial cells through mechanisms that are still not understood. Speculation on this mechanism indicates that the binding of the molecule to the 30S subunit interferes with 50S subunit association with the [mRNA](https://en.wikipedia.org/wiki/MRNA) strand. This results in an unstable ribosomal-mRNA complex, leading to a frame shift and defective protein synthesis; leading to cell death.Humans have ribosomes which are structurally different from those in bacteria, so the drug does not have this effect in human cells.

At low concentrations, however, streptomycin only inhibits growth of the bacteria by inducing prokaryotic ribosomes to misread mRNA.Streptomycin is an antibiotic that inhibits both Gram-positive and Gram-negative bacteria,and is therefore a useful broad-spectrum antibiotic.

### INDICATION FOR USEMedication

* [Infective endocarditis](https://en.wikipedia.org/wiki/Infective_endocarditis) caused by enterococcus when the organism is not sensitive to [gentamicin](https://en.wikipedia.org/wiki/Gentamicin)
* [Tuberculosis](https://en.wikipedia.org/wiki/Tuberculosis) in combination with other antibiotics. For active tuberculosis it is often given together with [isoniazid](https://en.wikipedia.org/wiki/Isoniazid), [rifampicin](https://en.wikipedia.org/wiki/Rifampicin), and [pyrazinamide](https://en.wikipedia.org/wiki/Pyrazinamide).It is not the first-line treatment, except in medically under-served populations where the cost of more expensive treatments is prohibitive. It may be useful in cases where resistance to other drugs is identified.
* [Plague](https://en.wikipedia.org/wiki/Plague_%28disease%29) ([*Yersinia pestis*](https://en.wikipedia.org/wiki/Yersinia_pestis)) has historically been treated with it as the first-line treatment. However streptomycin is approved for this purpose only by the [U.S. Food and Drug Administration](https://en.wikipedia.org/wiki/U.S._Food_and_Drug_Administration).
* In [veterinary medicine](https://en.wikipedia.org/wiki/Veterinary_medicine), streptomycin is the first-line antibiotic for use against [gram negative](https://en.wikipedia.org/wiki/Gram_negative) bacteria in large animals ([horses](https://en.wikipedia.org/wiki/Horse), [cattle](https://en.wikipedia.org/wiki/Cattle), [sheep](https://en.wikipedia.org/wiki/Sheep), etc.). It is commonly combined with procaine [penicillin](https://en.wikipedia.org/wiki/Penicillin) for intramuscular injection.
* [Tularemia](https://en.wikipedia.org/wiki/Tularemia) infections have been treated mostly with streptomycin.

Streptomycin is traditionally given [intramuscularly](https://en.wikipedia.org/wiki/Intramuscular_injection), and in many nations is only licensed to be administered intramuscularly, though in some regions the drug may also be administered [intravenously](https://en.wikipedia.org/wiki/Intravenous_injection).

### Pesticide

Streptomycin also is used as a pesticide, to combat the growth of bacteria beyond human applications. Streptomycin controls bacterial diseases of certain fruit, vegetables, seed, and ornamental crops. A major use is in the control of [fire blight](https://en.wikipedia.org/wiki/Fireblight) on apple and pear trees. As in medical applications, extensive use can be associated with the development of resistant strains. Streptomycin could potentially be used to control [cyanobacterial](https://en.wikipedia.org/wiki/Cyanobacteria%22%20%5Co%20%22Cyanobacteria) blooms in ornamental ponds and aquaria. While some antibacterial antibiotics are inhibitory to certain eukaryotes, this seems not to be the case for streptomycin, especially in the case of [anti-fungal](https://en.wikipedia.org/wiki/Fungicide) activity.

### Cell culture

Streptomycin, in combination with penicillin, is used in a standard antibiotic cocktail to prevent bacterial infection in cell culture.

### Protein purification

When purifying protein from a biological extract, streptomycin sulfate is sometimes added as a means of removing nucleic acids. Since it binds to ribosomes and precipitates out of solution, it serves as a method for removing rRNA, mRNA, and even DNA if the extract is from a prokaryote.

**TOXICITY

Nephrotoxicity** is [toxicity](https://en.wikipedia.org/wiki/Toxicity) in the [kidneys](https://en.wikipedia.org/wiki/Kidney). It is a [poisonous](https://en.wikipedia.org/wiki/Poison) effect of some [substances](https://en.wikipedia.org/wiki/Chemical_substance), both toxic chemicals and [medications](https://en.wikipedia.org/wiki/Pharmaceutical_drug), on [kidney function](https://en.wikipedia.org/wiki/Kidney_function). There are various forms, and some drugs may affect kidney function in more than one way. **Nephrotoxins** are substances displaying nephrotoxicity.

Nephrotoxicity should not be confused with the fact that some medications are predominantly excreted by the kidneys and need their dose adjusted for the decreased kidney function (e.g., [heparin](https://en.wikipedia.org/wiki/Heparin), lithium).

The nephrotoxic effect of most drugs is more profound in patients already suffering from [kidney failure](https://en.wikipedia.org/wiki/Kidney_failure).

 **Ototoxicity** is the property of being [toxic](https://en.wikipedia.org/wiki/Toxicity) to the [ear](https://en.wikipedia.org/wiki/Ear) (*oto-*), specifically the [cochlea](https://en.wikipedia.org/wiki/Cochlea) or [auditory nerve](https://en.wikipedia.org/wiki/Vestibulocochlear_nerve) and sometimes the [vestibular system](https://en.wikipedia.org/wiki/Vestibular_system), for example, as a side effect of a drug. The effects of ototoxicity can be reversible and temporary, or irreversible and permanent. It has been recognized since the 19th century.There are many well-known ototoxic drugs used in clinical situations, and they are prescribed, despite the risk of hearing disorders, to very serious health conditions. Ototoxic drugs include [antibiotics](https://en.wikipedia.org/wiki/Antibiotic) such as [gentamicin](https://en.wikipedia.org/wiki/Gentamicin), [streptomycin](https://en.wikipedia.org/wiki/Streptomycin), [tobramycin](https://en.wikipedia.org/wiki/Tobramycin), [loop diuretics](https://en.wikipedia.org/wiki/Loop_diuretic) such as [furosemide](https://en.wikipedia.org/wiki/Furosemide) and [platinum](https://en.wikipedia.org/wiki/Platinum)-based [chemotherapy](https://en.wikipedia.org/wiki/Chemotherapy) agents such as [cisplatin](https://en.wikipedia.org/wiki/Cisplatin%22%20%5Co%20%22Cisplatin), [carboplatin](https://en.wikipedia.org/wiki/Carboplatin), and [vincristine](https://en.wikipedia.org/wiki/Vincristine). A number of [nonsteroidal anti-inflammatory drugs](https://en.wikipedia.org/wiki/Nonsteroidal_anti-inflammatory_drug%22%20%5Co%20%22Nonsteroidal%20anti-inflammatory%20drug) (NSAIDS) have also been shown to be ototoxic. This can result in [sensorineural hearing loss](https://en.wikipedia.org/wiki/Sensorineural_hearing_loss%22%20%5Co%20%22Sensorineural%20hearing%20loss), [dysequilibrium](https://en.wikipedia.org/wiki/Dysequilibrium%22%20%5Co%20%22Dysequilibrium), or both. Some environmental and occupational chemicals have also been shown to affect the [auditory system](https://en.wikipedia.org/wiki/Auditory_system) and interact with noise. **ADVERSE EFFECTS**
The most concerning side effects, as with other [aminoglycosides](https://en.wikipedia.org/wiki/Aminoglycosides), are [kidney toxicity](https://en.wikipedia.org/wiki/Nephrotoxicity) and [ear toxicity](https://en.wikipedia.org/wiki/Ototoxicity). Transient or permanent deafness may result. The vestibular portion of cranial nerve VIII (the [vestibulocochlear nerve](https://en.wikipedia.org/wiki/Vestibulocochlear_nerve)) can be affected, resulting in [tinnitus](https://en.wikipedia.org/wiki/Tinnitus), [vertigo](https://en.wikipedia.org/wiki/Vertigo), [ataxia](https://en.wikipedia.org/wiki/Ataxia), kidney toxicity, and can potentially interfere with diagnosis of kidney malfunction.

Common side effects include [vertigo](https://en.wikipedia.org/wiki/Vertigo), vomiting, numbness of the face, fever, and rash. Fever and rashes may result from persistent use.

Use is not recommended during pregnancy.Congenital deafness has been reported in children whose mothers received streptomycin during pregnancy.Use appears to be okay while [breastfeeding](https://en.wikipedia.org/wiki/Breastfeeding). It is not recommended in people with [myasthenia gravis](https://en.wikipedia.org/wiki/Myasthenia_gravis).