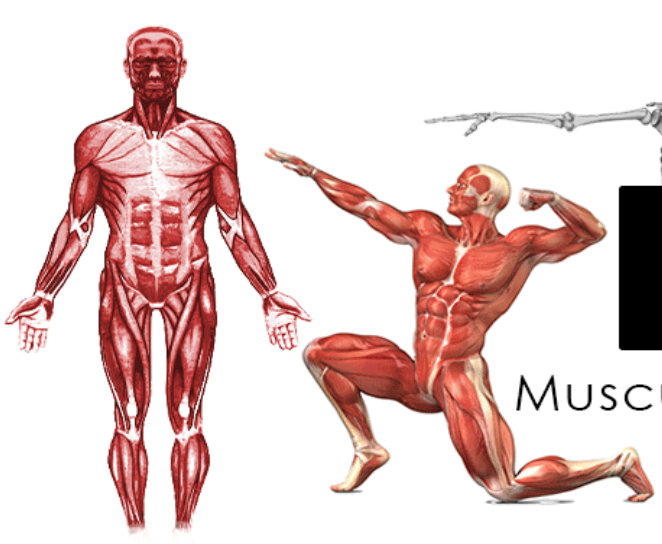
Compliment
'leishmania'



# MSS

Musculoskeletal System

# Pharmacology

Doctor 2018 | Medicine | JU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Hello there! this is going to be an extra sheet for the rest of the skin material the doctor didn't get to cover in all sections, ***Good luck!*** 🙂

Record 3: section 3. Min 28:30

## ❖ Drugs for Leishmania:

- Leishmania is an **infective disorder** that can be caused by species species of parasites and can accordingly occur in three different forms of the disease **leishmaniasis**

  *L.tropica* causes: **Cutaneous leishmaniasis** or oriental sore. Here the infection affects only the skin.

  *L. brazeliensis* causes: **Mucocutaneous leishmaniasis.** In this case the infection affects the skin AND the mucous membranes**.**

  *L. Donovani* causes: **Visceral leishmaniasis.**

The **sandfly** is the vector of leishmania. If present in an area, it can bite multiple individuals and the disease can disseminate between individuals quickly.

### Now the real deal, Drugs:

- Sodium Stibogluconate

Drug description: Pentravalent antimonial

Mechanism of action: It binds to -SH groups on proteins (cysteine residues of proteins for example).

It binds to these proteins in the parasite and causes damage of their 3D structure leading to the death of these parasites.

It inhibits phosphofructokinase.

Dosage: Typical preparations contain **30% to 34%** pentavalent antimony by weight as well as m-chlorocresol added as a preservative.

by weight means: the percentage of the active ingredient of the drug to the other constituents-which are chemicals that help dissolve this compound in the form of that cream for example- so when we say 30% we man that 30% of every mg in the preparation is **stibogluconate.**

Administration: Can be given local, IM or IV (in the case of IV, it's given SLOWLY because it's irritant)

- Duration: Given for a long period of time (20-28 days).

Why such a long time? The problem is that we don't know at what stage the parasite is (egg, intermediate, mature), so we give the treatment for thirty days to make sure that we kill the parasite in all its developing stages.

Drug of choice for all forms of leishmaniasis.

However, Resistance to Sodium Stibogluconate is increasing, especially in areas like India so we have to develop other drugs.

Side effects: Cough, Vomiting, Diarrhea, myalgia, arthralgia, ECG changes, Rash, Pruritus.

- Amphotericin:

Drug description: It's an **antifungal** agent, which can also be used to treat this **parasitic infection.**

- But we shouldn't forget that it's difficult to use (only given intravenously) and very toxic.

It's an alternative therapy for **visceral leishmaniasis**, especially in areas with high resistance to other therapies.

- Miltefosine:

Drug description: Mainly used For **visceral leishmaniasis**.

NOTE: visceral leishmaniasis is the most severe form of leishmaniasis.

Although leishmaniasis is a skin disorder it can sometimes go the liver and other cells in the body, which can easily be lethal.

Administration: Given orally, for at least 1 month (28 days)

Used for visceral leishmaniasis.

Side effects: Causes Vomiting & Diarrhea, hepatotoxicity, nephrotoxicity, and it is teratogenic.

- Pentamidine:

Mechanism of action: Inhibits DNA replication → By intercalating in the replicating DNA chain in the parasite.

It's also Dihydro Folate (DHF) reductase inhibitor, so it'll prevent the synthesis of pyrimidines that are important for the DNA replication

(connect pentamidine to pyrimidine)

Administration: Given IM or IV injection and Inhalation (problem with inhalers is that we can't adjust it well, or monitor the dose)

Plus points: Binds avidly to tissues which is beneficial in the case of leishmaniasis, but does not cross to the CNS because it's not very lipid soluble

Adverse effects:

- If it's given in a Rapid Infusion: **Hypotension, tachycardia, dizziness**.
- **Pain** at the injection site.
- Others: Pancreatic toxicity, Renal (nephrotoxic), and Hepatic toxicity.

Other uses of the drug to treat infections the doctor didn't mention but are in the slides:

**Leishmaniasis:** Alternative to Na stibogluconate

**Pneumocystis jiroveci:** Treatment and prophylaxis of patients who cannot tolerate or fail other drugs.

**Trypanosomiasis:** For early hemolymphatic stage.

## ❖ Antilepromatous Drugs: (used to treat leprosy)

- Dapsone and Sulphones:

Mechanism of action: they're related to sulfonamides (antibacterial), which work by inhibiting (DHF synthase) folate synthesis.

☹ Resistance has developed to these agents and in order to overcome this resistance, they're Combined with other drugs like Rifampin and Clofazimine.

– Also used for Pn. Jeroveci in AIDS patients (doctor didn't mention it)

Notes:

- Well absorbed and distributed.
- Retained in the skin, muscle, liver and kidney.

Side effects: (FOCUS ON THEM)

- **Hemolysis, particularly in G-6-PD patients** (don't give it in this case!!)
- GIT intolerance (nausea, vomiting, diarrhea)
- Fever, Pruritus, Rashes.
- **Erythema Nodosum Leprosum** an allergic reaction in the skin, in patients with leprosy towards **dapsone**, we suppress that allergic reaction by steroids (glucocorticoids) or thalidomide.

- ## Rifampin:

It's MAINLY used to treat tuberculosis (anti-tuberculous drug)

One important detail you're required to know is:

Rifampin is an inducer of cytochrome p450,

*for example:* If I give it with warfarin which is metabolized through the activity of cytochrome p450, it'll **increase the metabolism** of it, and the concentration of the drug will drop to levels sometimes below the effective therapeutic concentration, which in turn increases the risk in patients on warfarin to get thrombosis or thromboembolic events.

- ## Clofazimine:

Mechanism of action: works by intercalating in the (Binding to) DNA.

Notes:

- Stored widely in reticuloendothelial system (RES) and skin.
- Released slowly from storage sites, t1/2 = 2 months.

Indication: Given for dapsone or sulphone- resistant or intolerant cases.

side effects:

Causes skin discoloration (red-brown to black) and GIT intolerance.

That's all

*Good luck*