Antiprotozoal Agents

Drug	MOA	Administration	Uses	Side Effects	Notes
Antimalarial Agents					
Chloroquine	**Specific** uptake mechanism is present in the parasite, the drug accumulates in the parasite to inhibit polymerization of heme into hemozoin and thus parasite is poisoned by heme	-Given orally (convenient) immediately after diagnosis -Other doses are given after 6 hours, 24 hours and last dose after 48 hours *Total: 4 doses can eliminate the erythrocytic form of all parasites (except in resistance)	-Used for suppressive treatment (clinical) & radical cure -**Schizonticide** for all four types of malaria -Drug of choice in the treatment of **non-falciparum** and **sensitive falciparum malaria** -Does not eliminate **dormant liver forms** of P. vivax and P. ovale → **Primaquine** must be added for their radical cure -Also effective in: Rheumatoid arthritis, LE, Amebic liver abscess, Photoallergic reactions & Clonorchis sinensis	-Headache, dizziness, Itching and rash -Nausea, vomiting, anorexia -Unmasking of LE, psoriasis and porphyria -Corneal deposits, blindness, blurring of vision ***Resistance**: Very common with P. falciparum and increasing with P. vivax (Due to mutation in P170 glycoprotein (PfCRT) which works as a drug-transporting pump mechanism)	**-**Synthetic 4-Aminoquinolone **-**Well absorbed, distributed, bound to tissues -Very practical, convenient(oral), rapid action, low cost, and safe
Quinine & Quinidine	General protoplasmic poison: will affect the feeding mechanism of the parasite		Effective rapid **schizonticide** therapy for severe falciparum, chloroquine-resistant malaria, usually in combination with another drug (e.g. Doxycycline or Clindamycin) to **shorten** duration of use (less exposure to quinine = less side effects) -Effective for **Babesia microti** infection -For **nocturnal leg muscle cramps** (Arthritis, DM, thrombophlebitis, arteriosclerosis, varicose veins)	-***Cinchonism syndrome***: Tinnitus, headache, nausea, dizziness, flushing, visual disturbances. Later, auditory abnormalities, vomiting, diarrhea, and abdominal pain -Blood dyscrasias, hypersensitivity, hypoglycemia, uterine contractions. -Hypotension, QT prolongation -Blackwater fever	-Was discovered from cinchona tree - Resistance is uncommon ***Blackwater fever**: hemolysis, hemoglobinemia, hemoglobinurea, and renal failure

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Mefloquine		Oral use	- Blood schizonticide, not for liver forms -Used for resistant P. falciparum (**single oral dose**) -For suppressive and prophylactic treatment (**weekly doses**)	-Nausea, vomiting, diarrhea, pain -Vertigo, dizziness, headache, rashes and visual alterations -Psychosis, hallucinations, confusion, anxiety, depression	
Primaquin	Unknown MOA		- Drug of choice; the only available one, for eradication of **exoerythrocytic** forms of malaria after treatment with chloroquin	- Hemolysis in G6PD deficient patients. -Nausea, distress, headache, pruritis, leukopenia and agranulocytosis	-8-aminoquinolone
Atovaquone & Proguanil (=Malarone)			- Recommended drug for **prophylaxis** - Atovaquone also approved for P. jiroveci pneumonia, although has lower efficacy than Trimethoprim-sulfamethaxazole combination	-Can cause fever, rash, nausea, vomiting, diarrhea, headache, and insomnia	
Pyrimethamine	Inhibits DHF Reductase (Preferential binding to parasitic enzyme)		- Effective on erythrocytic forms of all species -Not for severe malaria -For Toxoplasmosis (in higher doses), and P. jeroveci - No longer recommended for prophylaxis	- Anorexia, Vomiting, Leucopenia, Thrombocytopenia, glossitis -CNS: Stimulation, Convulsions -Allergic reactions including Stevens-Johnson Syndrome	-Usually combined with Sulfadoxine, combination is called “Fansidar” or Sulfones which inhibit Dihydropteroate synthase
Halofantrine & Lumefantrine			-Rapidly effective against erythrocytic forms of all species -Usually for chloroquine-resistant strains	-Well tolerated, except for cardiac toxicity (QT prolongation)	

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Antibiotics: **Tetracycline** **Doxycycline** **Clindamycin** **Azithromycin** **Fluoroquinolone**			-Active against erythrocytic forms of all species -Usually for chloroquine-resistant strains -Also effective against other protozoal diseases		
Artemisnin = Qinghaosu (Artesunate & Artemether)	Work by free radical formation or ATP inhibition		Rapidly acting schizonticides against all species -Only drugs reliably effective against quinineresistant and multi-drug resistant strains	-Nausea, vomiting, diarrhea and neurotoxicity in animals	-Derivatives of Artemisia (الشيح) used by Chinese -No documented resistance -High cost, unavailable
Drugs for Leishmania					
Sodium Stibogluconate (Pentavalent Antimony)	- Binds to SH groups on proteins -Also, inhibits phosphofructokinase	- Locally (IM) → for cutaneous leishmaniasis -Slow IV (irritant) → for visceral leishmaniasis -Given for 20-28 days	- Drug of choice for all forms of leishmaniasis	- Cough, Vomiting, Diarrhea, myalgia, arthralgia, ECG changes, Rash, Pruritus -Resistance is increasing, especially in India	- Contains 30% to 34% pentavalent antimony by weight as well as m-chlorocresol added as a preservative
Amphotericin B	Antifungal agent	-IV	-Alternative therapy for **visceral** leishmaniasis, especially in areas with high resistance	-Difficult to use and toxic	
Pentamidine	-Inhibits DNA replication -Inhibits DHF reductase	- Given by IM or IV injection and Inhalation	-**Leishmaniasis**: alternative to Na-stibogluconate -**Pneumocystis jiroveci:** treatment & prophylaxis (who cannot tolerate or fail other drugs) -**Trypanosomiasis**: for early hemolymphatic stage	-Rapid Infusion: Hypotension, tachycardia, dizziness -Pain at the injection site -Others: Pancreatic, Renal, and Hepatic toxicity	- Binds avidly to tissues, but not to the CNS

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Miltefosine		- Given orally, for 28 days	-For visceral leishmaniasis	- Causes vomiting, diarrhea, hepatotoxicity, nephrotoxicity, and teratogenicity	
Drugs for Filariasis					
Di-ethylcarbamazine	-Immobilizes microfilariae and alters their surface structure, displacing them from tissues and making them more susceptible to destruction by host defense mechanisms (kills them **indirectly**) -The mode of action against adult worms is unknown		- The drug of choice in the treatment of filariasis, loiasis, and tropical eosinophilia. -May also be used for mass treatment and chemoprophylaxis	- Reactions to **dying microfilariae** are usually **mild** in W. bancrofti, more **intense** in B. malayi , and occasionally severe in L. loa infections (fever, malaise, papular rash, headache, gastrointestinal symptoms, cough, chest pain, and muscle or joint pain, leukocytosis, eosinophilia, proteinuria) in patients with heavy loads of microfilariae. -Retinal hemorrhages and, rarely, encephalopathy have been described	- Plasma half-life is 2–3 hours in the presence of acidic urine but about 10 hours if the urine is alkaline -Allergic reactions **aren't caused by the drug**, but by the death of the microfilariae - Antihistamines and corticosteroids might be needed to reduce allergic reactions
Ivermectine	-Appears to paralyze nematodes and arthropods by intensifying γ-aminobutyric acid (GABA)		- Filariasis -Onchocerciasis -Strongyloidiasis -Also for scabies, lice, and cutaneous larva migrans	- Occasionally induces severe reactions and appears to be more dangerous than diethylcarbamazine	
Doxycycline	-Acts indirectly, by killing Wolbachia		- Against W. bancrofti -Onchocerciasis -For both treatment of active disease and in mass chemotherapy campaigns		-Has significant macrofilaricidal activity against W. bancrofti → better than any other drug against adult form

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