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**Question:**

1. Classify the anti- material agents and state the mechanism of action of each class of drug listed

**Answer :**

1. **4-Aminoquinolines :** The mechanism of action of 4-aminoquinolines is characterized by the concentration of the drug in the digestive vacuole of the intraerythrocytic parasite, the inhibition of the haem polymerase of the parasite, leading to the accumulation of soluble haem toxic for the parasite. The high intravacuolar concentration of chloroquine inhibit the polymerisation of haem. As a result, the haem which is released during haemoglobin breakdown builds up to poisonous levels, thereby killing the parasite with its own toxic waste.
2. **Quinoline Methanol:** These drugs are thought to act by interfering with the digestion of haemoglobin in the blood stages of the malaria life cycle. Mefloquine which is an example of Quinoline Methanol is an antimalarial agent which acts as a blood schizonticide. Its exact mechanism of action is not known. Mefloquine is active against the erythrocytic stages of Plasmodium species
3. **Cinchona Alkaloid:** Interference with the parasite's ability to digest haemoglobin in the blood stages of the malaria life cycle. Quinine and quinidine which are examples of Cinchona Alkaloid also inhibit the spontaneous formation of beta-haematin (haemozoin or malaria pigment) which is a toxic product of the digestion of haemoglobin by parasites.
4. **Biguanides:** Proguanil which is an example of Biguanides works by stopping the malaria parasite, Plasmodium falciparum and Plasmodium vivax, from reproducing once it is in the red blood cells. It does this by inhibiting the enzyme, dihydrofolate reductase, which is involved in the reproduction of the parasite.
5. **Diaminopyrimidines:** Pyrimethamine which is an example of a drug in this class selectively inhibits the plasmodial form of dihydrofolate reductase, reducing the production of folic acid required for nucleic acid synthesis in the malarial parasite
6. **8-Aminoquinoline:** Primaquine which is an example of a drug in this class, has gametocytocidal activity against all plasmodia, including P. falciparum. Primaquine's mechanism of action is not well understood. It may be acting by generating reactive oxygen species or by interfering with the electron transport in the parasite.
7. **Sulfonamides & sulfone:** Sulfadoxine which is an example of drug in this class, competitively inhibits dihydropteroate synthase, interfering with folate synthesis.
8. **Antibiotics:** Although it is known that doxycyline which is a drug in this class, is a blood schizontocide, the exact mechanism of action is not well defined. In P. falciparum, doxycycline has been observed to block the expression of apicoplast genes, leading to nonfunctional apicoplasts in subsequent progeny, and impeding the development of viable parasites. It is also thought that doxycycline's antimalarial actions may be similar to its bacteriostatic actions of binding to ribosomal subunits and inhibiting protein synthesis, but this has only been observed in supra-pharmacologic doses.Doxycycline has also been observed to have some degree of pre-erythrocytic activity in P. falciparum.
9. **Sesquiterpine lactones:** Artesunate which is an example of a drug in this class, is an artemisinin drug capable of killing all erythrocytic stages of the malaria parasite including the ring stage, late schizonts, and the gametocytes responsible for transmission of malaria. It also increases splenic clearance of infected erythrocytes by reducing cytoadherence. Artemether which is also an example of a drug in this class works against the erythrocytic stages of P. falciparum by inhibiting nucleic acid and protein synthesis.
10. **Amino alcohols:** lumefantrine which is an example of a drug in this class inhibits the formation of β-hematin by forming a complex with hemin and inhibits nucleic acid and protein synthesis. The mechanism of action of Halofantrine which is also a drug in this class may be similar to that of chloroquine, quinine, and mefloquine; by forming toxic complexes with ferritoporphyrin IX that damage the membrane of the parasite.
11. **Naphthyridine:** pyronaridine which is an example of a drug in this class acts as an antimalarial with a mechanism of action similar to that of the well-known 4-aminoquinoline chloroquine, namely, it inhibits β-hematin formation in vitro (a process which closely parallels hemozoin formation within the parasite food vacuole)
12. **Naphthoquinone:** Atovaquone which is an example of a drug in this class, selectively inhibits the malarial cytochrome bc1 complex in the parasitic electron transport chain, collapsing the mitochondrial membrane potential.