Trypanosoma brucei and Sleeping Sickness

Trypansoma brucei is a flagellated protozoan parasite that causes the disease African Trypanosomiasis, also known as Sleeping Sickness, in humans. The organism is a single-celled eukaryotic organism approximately the size of a red blood cell. As with all trypanosome organisms, *T.brucei* has a single large mitochondria that is attached to the basal body of its flagella and is spanned through the entire body. Within this large mitochondria is a mass of DNA material aggregated at the site called the kinetoplast. A great majority of the parasitic organism's cytoskeleton is composed of microtubules. Its unstable nature allows *T.brucei* to manipulate its body and squeeze between cells and the blood-brain barrier. Perhaps the most unique characteristic of *T.brucei* is its Variable Surface Glycoprotein or VSG coat which allows it to evade the host's inflammatory and immune defenses.

Two subspecies of *T.brucei* cause unique forms of sleeping sickness. *T.b. rhodesiense*, which causes East African sleeping sickness, invades the central nervous in as few as a couple weeks. *T.b. gambiense*, causing West African sleeping sickness, progresses more slowly as it takes 1-2 years before nervous system invasion occurs. *T.brucei* is transmitted to a human host by a bite from an infected tsetse fly, which contains the pathogen in its salivary glands. The pathogen is directly injected into the subcutaneous tissue of the host where it begins to make its way to the blood stream and the lymph system. In this hemolymphatic stage, *T.brucei* begins to replicate via binary fission and makes its way to the blood-brain barrier. The only sign of hemolymphatic invasion is swelling of the body at lymph node sites due to aggregation of *T.brucei* in system. Due to host inflammation the cell junctions between the blood-brain barrier are weakened allowing *T.brucei* to enter the cerebral-spinal regions. As more and more organisms enter these compact regions swelling of the nearby vessels occur which in turn signals *T.brucei* to release the sleep-inducing compound tryptophol. As a result the typical symptoms of a neurological invasion occur like confusion, paralysis, poor coordination and disturbance of sleep cycle.

Treatment of sleeping sickness is most effective during the hemolymphatic stage as drugs can easily circulate the blood and lymphatic systems where the parasites reside. However, treatment success in the neurological stage depends on the drug crossing the blood-brain barrier where is *T.brucei* are accumulating. If left untreated, the concentration of parasites in the brain tissue regions reach a critical mass leading to progressive mental deterioration, coma and death.