Horror Of Black Plague Disease

Plague

A plague is an infectious disease caused by Yersinia Pestis, a bacterium that is transmitted from rats to humans by the “oriental rat flea” (Xenopsylla cheopis).Transmission of Yersinia Pestis is possible through any of the following scenarios: droplet contact (coughing or sneezing upon another person), direct physical contact (touching, including engaging in sexual contact with, an infected person), indirect contact (typically the touching of a contaminated surface), airborne transmission (only for organisms that remain in the air for long periods of time), fecal-oral transmission (typically through the consumption of contaminated food or water), vector borne transmission (carried by insects or other animals).

Archeologists have found plasmids of Yersinia pestis in the teeth of seven corpses dating as far back as 3000 BC. In history, there have been three major “plague pandemics.” The “first [plague] pandemic” occurred in the Early Middle Ages. Also known as “The Plague of Justinian,” this plague is the first known recorded instance of a mass bubonic plague outbreak. Thought to have originated in China, the disease went on to kill approximately 5,000 people in Constantinople per day at the plague’s peak.

The second plague pandemic, and ultimately one of history’s most well known disasters, is the 1347- 1351 spread of “The Black Death.” This pandemic was also believed to have originated in China; spread along the Silk Road; and then infected mass populations in all of Asia, Europe, and Africa. As a result of the plague, Africa lost approximately ? of its population, Europe lost approximately ? of its population, and China lost approximately ½ of its population. In the end, approximately 100 million people lost their lives as a result of The Black Death; thus, The Black Death reigns as the obtainer of the largest death toll for any non-viral epidemic in history.

The third major plague epidemic occurred in the 19th and 20th centuries. Once again, the disease began in China (particularly in China’s Yunnan province) in 1855. This pandemic caused the deaths of more than 12 million people in China and India alone. Based upon the casualty patterns of this particular case of plague, infection came in the following two separate waves: bubonic plague and pneumonic plague. Advancements in modern medicine during the 19th and 20th centuries allowed scientific researchers to identify plague vectors and plague bacterium, contributing to the first effective modern treatments of plague.

There are three primary forms of plague infection that depend on the route of infection:

pneumonic plague, septicaemic plague, and bubonic plague. Pneumonic plague (also known as lung-based plague) is the most severe, but least common, of the plague forms. Pneumonic plague is often split into two types: primary pneumonic plague and secondary pneumonic plague. If someone inhales droplets of moisture containing plague bacteria, the result can be primary pneumonic plague. Primary pneumonic plague can happen when an infected host coughs or sneezes into the air. Cats are typical contractors of pneumonic plague and can transmit it to humans when they cough or sneeze.

When a case of pneumonic plague is due to the spread, from infection, of an initial bubonic plague form, this form of plague is called secondary pneumonic plague. Secondary pneumonic plague is typically not as contagious as primary pneumonic plague because those who contract primary pneumonic plague have a tendency to be healthy and active. Due to such vitality, these seemingly-healthy contractors of primary pneumonic plague can produce a cough with enough strength to propel disease-infected droplets of moisture through the air, infecting others. Meanwhile, hosts with secondary pneumonic plague are increasingly sick by the time the bubonic plague infection has reached their lungs, thus, their cough's are not as strong enough to propel the disease-infected particles of moisture into the air to infect others. Pneumonic plague causes the typical symptoms of pneumonia such as high fever and a bloody sputum-producing cough.

Due to its highly contagious nature, pneumonic plague, in theory, would be the most likely disease used as a biological weapon. It has even been reported that during World War II, the Japanese military dropped bombs of infected Xenopsylla cheopis over China's mainland. And untreated pneumonic plague has a very high case-fatality ratio.

The second primary form of plague is the septicemic plague. The septicemic plague occurs when infection spreads directly through the bloodstream without forming a bubo. It is very likely that cases of septicaemic plague result from not only bites, but direct contact with infective material through cracks in the skin. Septicaemic plague can also be formed by advanced stages of bubonic plague that have lead to the direct spread of Yersinia Pestis through in the host's blood. In instances of septicaemic plague, plague bacteria and toxins in the blood overwhelm the body's immune defences, causing high fever, abdominal pain, and general exhaustion. When left untreated, this form of plague can leave the immune system with irreparable damage, organ failure, and death.

The final, and most common, form of plague is the bubonic plague (also referred to as "The Black Death" by those of mediaeval Europe). This form of plague is caused by the bite of a host infected Xenopsylla cheopis. After invading the host, the Yersinia Pestis bacteria then travels to the lymph node (an oval-shaped organ that occurs in the area closest to where the bacteria entered the skin) in closest proximity to itself using white blood cells to transport. The lymph

node will then begin to experience swelling due to the overwhelming presence of bacteria and the endotoxins (a toxin that is present inside a bacterial cell and is released when the cell disintegrates) within their cell walls. The lymph node then becomes increasingly painful and turns into an egg-sized bubo (an inflammed lymph node) over a matter of days. It is after the occurrence of buboes that the body's natural immune defences finally begin to act, causing high fever, chills, muscle pains, and overall weakness in an attempt to kill the infecting bacteria.

The formation of buboes differ depending on the location of the initial flea bite. If bitten on the arm or hand, the buboes form in the axillary lymph nodes beneath the arm; if bitten on the leg or foot, the buboes form in the inguinal lymph nodes in the groin; if bitten on the head, the buboes are formed in the neck and jaw; and if bitten on the torso, the buboes are able to form, undetected, in the abdominal cavity of the host.

Xenopsylla cheopis has a particular physical trait that allows it to efficiently transmit plague bacteria--- the flea's digestive system can become blocked by a large mass of plague bacteria.. When a blocked flea bites a host, it often then regurgitates plague-infested blood back into the bite wound that it has created. Even if the flea's digestive system is not experiencing blockage, the flea is still capable of transmitting bacteria to the host it bites if carrying bacteria on the areas surrounding its mouth at the time. The bacteria then suppresses the host's body's natural inflammatory response and uses proteins to protect itself, thus making the host (and its internal system) unaware that anything is wrong.

In humans, the infectious dose of Y. pestis has been estimated to range from 100 organisms to 20,000 organisms. The incubation period of the bubonic, septicemic, and pneumonic plague types ranges from 2-6 days. Y. pestis colonizes macrophages, reaches lymph nodes, escapes the macrophages, and proliferates extracellularly. Left untreated, Y. pestis is able to spread to the bloodstream and cause secondary infection as well as septicemic plague in rare cases. Y. pestis is also able to colonize lung tissue as pneumonic plague.

The majority of mammals are capable of being infected with plague. Colonization and growth of Yersinia pestis in the flea proventriculus (the valve between oesophagus and midgut) blocks the passage of food, it is this blockage that gives way to an efficient transmission by means of the flea bite. Though Phospholipase D is not exported, it assists the bacteria in withstanding immunity in the flea midgut. Haemin storage locus (hms) is necessary for colonization and for the formation of biofilm within the flea. Yersinia pestis disseminated from the infection site within macrophages (which requires a plasminogen activator) encoded by pPst plasmids. Once phagocytized (having ingested the bacteria or other material by phagocytes and amoeboid protozoans), the disease progresses. There are two stages of Yersinia pestis rapid production within the host. Neutrophils kill the bacteria, but macrophages phagocytize them but do not kill them and there it grows intracellularly within spacious vacuoles.

The reason that dogs are unaffected by plague is because dog macrophages fail to release the bacteria from the spacious vacuole. In susceptible hosts, infected macrophages are carried to the lymph nodes --hence, buboes-- and the liver and spleen, where the bacteria cause the macrophages to lyse. Then, the bacteria grow extracellularly. Extracellular growth requires plasmid pCD/pYV encoded TTSS and translocation of YOPs. Yops interfere with immune cell function and can cause immune cell death by apoptosis. LcrV (V antigen) has anti-inflammatory activity via CD14 and TLR-2 to raise IL-10 levels. pFra capsule is anti-phagocytic, preventing extracellular bacteria from being phagocytosed. LPS is less toxic than other Enterobacteriaceae to facilitate high grade bacteremia. Collectively, these virulence factors allow massive extracellular proliferation of the bacteria in affected tissues.

“A 70-kb virulence plasmid (sometimes called pYV) enables Yersinia spp. to survive and multiply in the lymphoid tissues of their host. It encodes the Yop virulon, a system consisting of secreted proteins called Yops and their dedicated type III secretion apparatus called Ysc. The Ysc apparatus forms a channel composed of 29 proteins. Of these, 10 have counterparts in almost every type III system. Secretion of some Yops requires the assistance, in the bacterial cytosol, of small individual chaperones called the Syc proteins.These chaperones act as bodyguards or secretion pilots for their partner Yop. Yop proteins fall into two categories. Some are intracellular effectors, whereas the others are ‘‘translocators’’ needed to deliver the effectors across the eukaryotic plasma membrane, into eukaryotic cells. The translocators (YopB, YopD, LcrV) form a pore of 16–23 Å in the eukaryotic cell plasma membrane. The effector Yops are YopE, YopH, YpkAyYopO, YopPy YopJ, YopM, and YopT. YopH is a powerful phosphotyrosine phosphatase playing an antiphagocytic role by dephosphorylating several focal adhesion proteins. YopE and YopT contribute to antiphagocytic effects by inactivating GTPases controlling cytoskeleton dynamics. YopPyYopJ plays an anti-inflammatory role by preventing the activation of the transcription factor NF-kB. It also induces rapid apoptosis of macrophages. Less is known about the role of the phosphoserine kinase YopOyYpkA and YopM.”

Though plague appear to simply be a disease of the past, it is still rather relevant in today’s society and poses as a severe disease for humans. In the year 2013, 783 cases of plague were reported from around the world with a death toll of 126. The most recent reporting of a plague victim occurred in Portland, Oregon on October 24th, 2015 in which a 16-year-old girl likely acquired the disease from a flea bite during a hunting trip five days before her hospital admittance. It is due to modern medicine, sanitation, and general awareness that plague pandemics do not occur on a widespread and severe scale.