The historic effect of plague

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As palaeopathology appears to have confirmed *Yersinia pestis* as the organism responsible for all three pandemics of plague (Justinian[1,2], Black Death[3] and Modern), arguments for the origin of the disasters have given way to debates on their effects. Records narrate the horrors but barely hint at historical results[4]. This article maintains each pandemic has had a lasting effect and, cumulatively, *Y. pestis* has been more influential than gun powder and could still be explosive.

Y. pestis is a pleomorphic gram-negative bacillus with characteristic 'safety pin' appearance with Giemsa stain. It has a remarkable life cycle through two disparate hosts: a cool flea and a warm rodent. Temperature, however, is not merely one challenge: it is probably one of the external factors that influence gene expression in the different hosts. For survival in the hostile intestine of the flea after being swallowed in rodents' blood, bacterial genes promote enzymes that cause the bacteria to aggregate in biofilm to protect from digestion and excretion[5]. When the biofilm expands to obstruct the oesophagus, hunger causes the flea to bite voraciously and spread the bacteria in regurgitation. Other genes permit the bacteria to digest proteins and lipids contained in blood.

In the warmer mammal, the phenotype changes from passive aggregation to virulent spread, aided by proteins that oppose host clotting and immunity. At first, the small numbers of *Y. pestis* that are injected into the host find refuge in de-activated macrophages in the dermis where they multiply and develop their capacity to avoid killing by neutrophils. They then spread to lymph nodes to induce pain and swelling, known as buboes, which have characterised the disease since its earliest descriptions and lent the name 'bubonic plague'. In the lymph system, metabolism by protein digesting enzymes is downregulated in favour of those digesting polysaccharides[6]. Some bacteria escape into the blood stream, leading to a septicaemic presentation while others travel to the lung and cause an overwhelming pneumonic form in which bacteria may be exhaled in droplets.

The bacteria may cycle from flea to rodent (or other small mammal) in enzootic manner and humans may be incidental victims but, on three grand occasions, the disease has taken hold in human populations with devastating, pandemic results.

Though the last pandemic began in 1894, its bacterial offspring are still causing problems, infecting over 2,000 humans each year, in increasing numbers and in places where the disease has been absent for decades[7]. Plague is a re-emerging disease[8].

The first pandemic

The first pandemic emerged in Egypt in 541 AD during the rule of the Byzantine Emperor Justinian[9] and spread around the Mediterranean to beyond Persia in the east and Gaul in the west. It recurred in waves throughout the following two centuries before acquiescing to forces unknown. The capital of Byzantium, Constantinople, was probably ravaged in each of the 18 onslaughts.

Christian elder, John of Ephesus, returning to Constantinople from Cairo as the disease travelled north through Palestine reports there were 'corpses with their putrefied bellies swollen, their mouths open, eyes staring, and arms stretched upward, that burst open in the streets with their pus running down like water' and there were so many they 'were loaded on ships and cast in the straits or like dung on the opposite shore'. To transport the bodies 'men and women were trodden down, and in the space between them the young and infants were pressed down, trodden with the feet and trampled down like spoilt grapes'[10]. He says 'Houses and farms were abandoned. Animals forgot their domestication. . .Crops of wheat were white and standing but there was no one to reap them and store the wheat. Vineyards, whose picking season came and went, shed their leaves, since winter was severe, but kept their fruits hanging on their vines, and there was no one to pick them or press them'[11].

The slaughter was so great in this first and then the second pandemic there were similar effects. With the loss of a third to a half of populations, labour became scarce and its value increased. Loss of productivity reduced governmental revenue which resulted in increased taxation. Rising prices fuelled inflation. Traditional working relations were challenged: slavery and serfdom were weakened by the rising value of labour, but sought to be strengthened by decree. The ranks of the military were reduced: there was less money for campaigns and even for self defence. Cultures and values were threatened. Some sought to appease divinities and other

ethereal forces, while others retreated to hedonism. Associated famines, wars and earthquakes made everything worse.

Before the first pandemic, the western half of the Roman Empire had succumbed to invaders from its north. Based in the capital of the surviving eastern half, Justinian aspired to resurrect the Empire, and battles had already been won. His forces had reclaimed parts of Africa from the Vandals, and had overcome Goths in the Italian peninsular, but much warfare was needed to restore the Empire. Lombards were laying claim to the peninsular from the north, Slavs were crossing the Danube and seizing the Balkans, and Persians and then Arabs thrusted from the east.

Byzantium succumbed. It failed to resurrect the Empire in the west, permitting the development of states whose independence foreshadowed modern Europe. It also failed to repel Persia from the East, preparing both for Islam.

How much did *Y. pestis* hollow-out Byzantium? How fundamental was it to weakness that permitted historic change? Stathakopoulos concludes it was, at least, catalytic[12].

The second pandemic

The second pandemic emerged in Crimea in 1346 and spread around and inland from the Mediterranean. Its first wave was catastrophic, but its effect was compounded by recurrent outbreaks of varying severity until it, too, mysteriously relented in 1741[13–15]. Narratives are as harrowing as those of the first but variations in presentation, rate of spread and infectivity have generated debate as to whether this 'Black Death' was really *Y. pestis* and not some kind of Ebola-like virus. DNA extracted from the pulp of teeth of skeletons from medieval burial sites has, however, revealed the presence of *Y. pestis* as it has from teeth pulp from Justinian cemeteries[16].

Though its long term effects are as debated as those of the first pandemic, there is consensus the recurrent outbreaks of plague reduced agricultural manpower in Western Europe and led to the end of manorial production: serfdom gave way to mobilised wage labour. Governments were able to restrict the process in Eastern Europe but in the West there emerged an independent 'yeoman' who could be described as the fore runner of the wage earner of the Industrial Revolution'.

Less measurable but of no less historical importance may have been a weakening in the religious culture in the West. Disillusion in established Catholicism as mediator with a punishing God, and disgust with the cowardice of many of its self-serving priests, encouraged a critique that was expressed in the Reformation and the reactionary birth of Protestantism. If social philosopher Max Weber is to be believed[17], the work ethic and financial determination of Protestanism would become responsible for the spirit for capitalism that went on to transform the world.

If plague lead to the Reformation, did its momentum lead to the questioning of all religion in the Renaissance? How much did this intellectualism contribute to the conviction that plague was an objective, contagious entity that could be actively combatted rather than passively accepted? Is Dols correct in arguing plague caused more suffering under Islam because of passive acceptance of divine will[18]? The Black Death altered the mind of man as much as his working relations.

The third pandemic

The third pandemic emerged in eastern China, reaching Hong Kong from 1894. From that port *Y. pestis* spread to distant parts of the world where its offspring continue to reside within various mammals, from whence to infect several thousand humans each year. Though narratives from this pandemic are more often expressed in the colder language of a medical profession at war with a now recognisable enemy, the horrors remain even if better understood. With Alexandre Yersin unveiling the bacteria in Hong Kong in 1894 and Paul Simon incriminating the rat and its fleas in 1896, the force of public health was unleashed on rat infested slums to the bewilderment and resentment of their inmates who rejected the germ theory in commitment to ethereal origins of disease. But, slums were razed, quarantines imposed, migration opposed and the disease was at least contained in Hong Kong. In India, the enthusiasm of the colonial government abated when opposition was so great it threatened civil war[19]. Perhaps 12 million Indians joined the hundreds of thousands of Chinese victims in those early years of the third pandemic. Did their deaths affect the history of the millions who remained?

The man who would lead the revolution that overthrew the Qing dynasty and establish the Republic of China in 1912, Sun Yat Sen, graduated from the College of Medicine for the Chinese in Hong Kong in 1892 when plague was emerging in southern China. He had been schooled in Hawaii and had studied in a Christian hospital in Canton before transferring to Hong Kong and, along the way, had become committed to political reform. He objected to the restrictions of traditional Chinese culture and was inspired by the scientific method (and political freedoms) he had observed in western culture[20]. The extent the germ theory and the application of public health influenced his determination for liberation from traditional bondages is unknown but he was intimately associated with the colony that was employing them against the plague that had broken out in his home territories.

Plague erupted again in China, in 1910, when the Republic was being born. It emerged in the north, in Manchuria, where three powers were contesting for natural resources and their management[21]. Chinese citizens died of plague under their infantile government. Western powers were weak and overstretched in their efforts to contain the epidemic, but the Japanese were strong. They had

already humiliated Russia in the war of 1905 and were in China in organised, determined force, and they controlled the outbreak in their regions with military precision. Did the weakness of their opponents in the face of the plague encourage the Japanese to believe they could invade China in 1937 and the rest of Asia in 1941? One lasting effect of that invasion of China was the exhaustion and subsequent defeat of its Nationalist government (the Kuomintang of Sun Yat Sen) by the Communists. Then, under Mao, millions, died. Did the flea set those dominoes off?

The future

Could the flea do it again? History shows *Y. pestis* can vary its presentation from the more indolent bubonic to the highly contagious pneumonic form. But, either way, antibiotics and insecticides are now available and science may prevail over grossest ignorance.

In 1967, I was the doctor in a refugee camp in South Vietnam after graduating the previous year with no knowledge of many things including plague. I assumed my patients with fevers, prostration and large suppurating lumps in their groins were suffering from staphylococci and wielded streptomycin, the only antibiotic we had. Plague, of course, is sensitive to that drug: No one died, no workers were infected and the contagion subsided[22].

As long as we have antibiotics to which *Y. pestis* is sensitive, and in sufficient amounts, we should not face a new Black Death. But resistance is being reported[23] and both Nature and human beings retain a capacity for rupturing medical supply in disasters and warfare.

Human beings also have an unlimited capacity for mendacity and, though most killings have been inflicted with chemicals or explosives, bacteria have been considered. There are anecdotes that plague was inflicted by catapulting corpses over 14th century city walls but spread by fomites is uncommon and fleas abandon cooling hosts. The Japanese air-force dispersed infected fleas over civilians in Manchuria in WW2 but the effects were limited[24]. In the Cold War, both US and USSR sought better ways to deliver and disperse plague as a weapon that would both demoralise and deplete their opponents. Reportedly, USSR ultimately developed strains that were resistant both to antibiotics and to certain vaccines, and factories that could produce them in tons until at least the 1990's[25]. Aware of the potential for disaster in 1970, WHO declared the effects of dropping 50 kg of aerosolised plague on a city of 5 million could be 150,000 cases of pneumonic plague with 36,000 deaths[26]. Does Russia still possess these facilities?

Could plague be inflicted in a terrorist attack? An expert committee in the US believed there was 'great concern' in 2000[27], over a year before terrorists demonstrated their ability to hi-jack airliners.

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Biography

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