



Medicine for Managers

Dr Paul Lambden BSc MB BS BDS FDSRCS MRCS LRCP DRCOG MHSM

The End of the World

Since Coronavirus (Covid-19) first made its appearance in China in late 2019, it has infected over 70 million people and killed over 1.6 million of them (as of mid-December 2020). We now have vaccines which will hopefully herald the end, or at least the beginning of the end of this virus. Some Christian groups, however, have claimed it as the Biblical plague heralded in the book of Revelations.

The **Book of Revelations** is the last book in the Bible New Testament and conjures up vivid claims of disaster, death and suffering.

The world has certainly been confronted with disasters in the lifetimes of most of us and some theologists have evoked the increase in floods, failures of crops and global warming as the predicted end of the world which Revelations describes. Others have cited the development of AIDS and even the proliferation of nuclear power plants and armaments as the 'plague'.

Revelations was written by John of Patmos, who was believed to have been a Jew from Palestine.

The text displays John's anger and is thought to be a reflection of his loathing for the Romans who persecuted the early Christians, partly because Nero blamed them for the fire of 64BC in Rome, and partly because of their rejection of Roman Gods, worship of which was regarded as idolatry.



John refers to the Four Horsemen of the Apocalypse, previously described in the Old Testament book of Zachariah and in the book of

Ezekiel, where they are named as punishments from God.

The four horsemen have been widely represented in a host of paintings and each horse is symbolic. The white horse symbolises vengeance, the red horse war and destruction, the black horse famine, and the pale horse symbolises death.

Armageddon is a place in modern Israel, the site of many battles and it is likely that, because it had been a place of such bloodshed, John saw it as the place where the final battle between good and evil would occur. The place has given rise to suggestions of 'facing Armageddon' to describe a potentially catastrophic event.

The purpose of Revelations is regarded as inciting Christians to oppose Rome and to affirm that their faithfulness would be rewarded.

Have we had documented serious infections before in the history of the world? Yes, we certainly have. As far back as 1200 BC there is a recorded outbreak of infection, written by scholars in Sanskrit and describing symptoms similar to those of influenza. It reportedly spread through central Asia. Numbers of deaths are unknown but were probably very high.

In more recent history, perhaps the best known of the plagues has been the '**Black Death**', caused by a bacterium called *Yersinia pestis*.

It has caused epidemics from pre-Christian history and the first pandemic spread through Asia, India and Uganda to China and from there to Europe between 1348 and 1355.

However, it was a devastating second pandemic, which swept across large parts of the world in the mid-fourteenth century causing severe recurrent episodes lasting several years at a time between the 1360s and the 1660s.

In England the disease was probably endemic during that period and may have killed over two million people.

It started in a south coast port brought in from overseas by ship and spread to Bristol as a **bubonic form** in about 1348 and it is said to have struck with 'shocking force'.

It spread from the south northwards mutating into the **pneumonic form** as it went. When the

disease reached London, it is thought to have killed 50% of the population. It reached Scotland in 1350 and was known as the "foul death of England". Many populations of 3-500 people were either completely decimated or wiped out.

Globally the second pandemic probably killed around 150 million people, thereby reducing the world population by around 30%. The population numbers did not recover to pre-plague levels for over 200 years.

A third pandemic struck China in around the 1850s, which spread through Asia and is said to have killed ten million people in India alone. Similar outbreaks were reported in major cities throughout Europe.



Outbreaks of other diseases with large numbers of fatalities have occurred during recorded history.

In Athens typhoid or typhus is believed to have killed 100,000 people in about 429-426 BC.

Smallpox may have killed anything up to 10 million people in the Roman empire during the first half of the second century BC.

The disease killed one third of the Japanese population in the eighth century, 7-8 million in Mexico and a quarter of the population of Chile during the sixteenth century.

It ravaged Iceland in the early 1700s killing a third of the population and some years later it decimated France. An outbreak in New South Wales in the late eighteenth century probably killed up to three quarters of the Aboriginal population.

In Europe half a million died in five years from 1870. There have been outbreaks with fatal consequences throughout North America over three hundred years from the sixteenth century. Smallpox was officially eradicated in 1980.

A host of other illnesses have caused epidemics and pandemics, often resulting in six or seven figure numbers of deaths, including malaria, measles and diphtheria, yellow fever, scarlet fever, polio, typhoid and typhus, as well as a host of other infections.

Cholera killed over a million people in Russia in the 1850s and, in 1854, there was the cholera outbreak in the Broad Street area of London where over 600 people died.

The physician John Snow, who investigated cholera, did not accept the widely-held theory of 'miasma' (something in the air) causing the disease but had a germ theory about contaminated water.

Over some years he mapped every case of cholera in his area and found it was less common where the water was cleaner and better filtered. During the Broad Street outbreak, Snow traced the source of infection to the public water pump in Broad Street (now Broadwick Street). The pattern of the disease was sufficiently persuasive to convince the St James parish authorities to disable the pump. The number of deaths immediately dropped dramatically.

Encephalitis lethargica is an atypical form of encephalitis. It was first described in 1917. The pandemic lasted from 1917-1927. It was at its most virulent during the winter of 1918-19. It affected 5 million people, nearly a third of whom died. Many of those who survived never fully recovered.

The symptoms were strange. Sufferers would sit motionless, apparently profoundly indifferent to everything, lacking energy, with no affect or

desire even to eat. The cause of the disease is uncertain. It may have been an auto-immune response, perhaps consequent on viral or bacterial infection.

Unfortunately the disease coincided with the 1918 influenza pandemic and undoubtedly the influenza virus potentiated the effects of the encephalitis increasing its impact and raising the death rate. The encephalitis pandemic disappeared in 1927 as mysteriously and abruptly as it had appeared.

In more recent times, more localised epidemics of infection have occurred such as an Ebola outbreak in the Congo between 2018 and 2020 and Lassa fever between 2019 and the present day.

Then, of course, there is coronavirus. This virus was first identified in the 1920s in domestic chickens in the United States.

The human form of coronavirus was identified in the 1960s. When acquired, it usually results in relatively mild upper respiratory symptoms, including a runny nose, cough, sore throat and fever.

For the immunologically weak and other vulnerable groups, the virus can spread down to the lungs causing respiratory pneumonic disease which can be deadly. Most of us will have had a Coronavirus infection at some time.

The world has seen three significant outbreaks of coronavirus this century.

In 2002 SARS (Severe Acute Respiratory Syndrome) was identified in Guangdong in Southern China. Over 8,000 people were infected during 2003, of whom 774 died. Overall the death rate was about 10% although for people over age 65, it may have been as high as 50%. The disease was able to be managed

because it had a short incubation period, it was identifiable because all sufferers quickly developed symptoms and isolation could be carried out at speed.

In 2012 MERS (Middle East Respiratory Syndrome) was diagnosed in Saudi Arabia where 80% of subsequent cases have developed.

It has since been found in 27 countries in the Middle East, South Africa and in Asia. It may have started in bats, transmitted to Camels and subsequently to humans. It can pass from person to person but seems relatively unusual in a family setting, although more common in healthcare facilities.

The symptoms are like those of other coronaviruses and are worse in vulnerable groups. The data suggests there have been about 860 deaths with an estimated mortality rate of 35%. The virus still exists in some communities.

In 2019, a novel coronavirus (2019-nCoV, Covid-19) appeared in Wuhan in China, which gave it its other name of Wuhan virus.

It is believed to have originally come from bats. In the UK, getting on for 2 million cases have been identified with over 74,000 deaths. It has spread world-wide.

It causes symptoms like the other coronaviruses and is more serious or fatal in the more vulnerable groups. It has been more difficult to control because of the relatively long incubation period of up to 10-12 days, and that a large number of people have minimal or no symptoms and can unknowingly spread the disease. Vaccines are now available and hopefully, during the next 6-9 months, Covid-19 will be brought under control as people are protected and a herd immunity develops.

The latest complication is the mutations, which undoubtedly increase infection rates and which may affect virulence.

The world has therefore had to deal with many epidemics and pandemics and, one way or another, over time, they have been overcome. Some have died out naturally, some have been overcome with avoidance and cleanliness mechanisms and some with appropriate treatments; antibiotics for bacterial infections and vaccines for bacterial and viral infections.

So, will the world end with a catastrophe or will it still be surviving in many millennia. There is, of course, a possibility of global destruction.

Famine exists and could become a much more major issue with the consequences of global warming, leading to destruction of crops.

With increasing competition for food, invasion and war is a likely sequel with the horrifying consequences which could be expected. The potential terrifying actions of Kim Jung Un and other tyrannical fanatics round the globe are desperately dangerous and nuclear war must remain a prospect as megalomaniacs play out their vengeances.

So John of Patmos was justified in highlighting potentially apocalyptic events, albeit he saw them more locally when he wrote Revelations and the real risks are now much more international.

So where does disease and pestilence fit into all this.

As I said, we have antibiotics and we have vaccines. We can hope that they will become more effective, act more quickly and protect us ever better over time. The question is, are we indulging in a fantasy? Will be bacteria and viruses beat us in the end?

We depend on antibiotics to defeat **bacterial infections**, but there are increasing problems with the availability of effective drugs to destroy bacteria, principally because of the development of **resistance**.

So why is this resistance developing? There are a number of reasons

1. Abuse and inappropriate prescribing.

Fleming discovered penicillin in 1928 when he was Professor of Bacteriology at St Mary's Hospital in Paddington. It was greeted with wonder by the medical profession and the population at large, but Fleming himself expressed concern about the rapid increase in public demands for antibiotic for everything. He was, of course, right. The number of prescriptions issued for antibiotics is huge and many are for self-limiting or for viral illness where they contribute little or nothing to recovery.

Antibiotics are abused by many patients who stop their course of treatment prematurely, perhaps because they feel better, or they 'forget'. To do so, fails to destroy the infecting organisms and the sub-lethal exposure affords them the opportunity to learn to survive an attack by the antibiotic.

As if all that wasn't bad enough, in many countries, antibiotics are available on sale over the counter without a prescription.

The result is that many of the antibiotics on which medicine has relied for several decades have now been rendered relatively useless in a range of bacterial infections

because the bacteria have adapted to become resistant to the drugs. Indeed there are now some bacteria which are resistant to virtually all known antibiotics.

As an example, most will know about MRSA (methicillin resistant staphylococcus aureus) which is resistant to many antibiotics and which causes complications, especially in hospital patients who may be debilitated and where the consequences can easily be life threatening.

As the world continues using antibiotics, indiscriminately for minor and inappropriate infections, the problem will continue to escalate until we could end up with infections that we will be able to treat no more effectively than before antibiotics were discovered.

2. Agricultural use. Up to 80% of antibiotics are used in animals. They allegedly improve the health of animals but the drugs used on animals are ingested by humans or are passed out of animals and collect in ground water which ultimately may get into the drinking water. Some antibiotics are sprayed on fruit trees as pesticides. Repeated low dose exposure to antibiotics provides an ideal environment for the development of resistant strains of bacteria.

3. Decline in New Antibiotics. The great period of antibiotic development has gone. Many pharmaceutical companies have ceased research on antibiotics. Research teams have been disbanded. Funding cuts and financial crises have had their effect. Between 1980 and 1984, 19 new antibiotics were introduced; 1990-1994, 11 new antibiotics; 2000-2004, 4 new antibiotics were introduced. Only 3 were introduced in

the four years leading to 2010 although, between 2010 and 2014, the number released was 6. Antibiotics are not now as profitable as drugs for chronic conditions.

4. **Regulation.** Part of the problem in point 3 above relates to increased regulation and difficulties experienced by pharmaceutical companies in their countries of research and manufacture when they try to expand their market across other countries. Factors frustrating antibiotic progress include bureaucracy, differences in clinical trial requirements, regulatory and licensing rules and lack of communication between government agencies.

These and other factors will contribute to the development of more bacteria which are resistant to everything we have got.

A global pandemic of *Staphylococcus aureus* or an *Enterococcus* is perhaps the most likely. Tuberculosis may have a renaissance.

Sexually transmitted diseases may increase out of control. *Campylobacter*, *salmonella* and *streptococci* may all lead to epidemics or pandemics. And yes, *Yersinia pestis*, which completely destroyed those whole populations and left urban areas as ghost towns during the plague, could come back.

Overall, emerging resistant bacteria could cause a catastrophe, maybe not next year or the year after or even in twenty years' time, but it will come because bacteria have enormous capacity to mutate.

Bacteria are therefore a huge risk, but the recent epidemics and pandemics have, in large part, been caused by viruses, of which Covid-19 is the most recent.

In the present state of medical knowledge, the treatment of viral illness is generally by supportive measures until the body's natural

immunity successfully overcomes the infection. Why can't we have antibiotics which are effective against viruses?

To answer that question, we have to understand the different way in which bacteria and viruses invade the body to cause infection.

In essence, bacteria are microscopic single-celled organisms which contain **DNA**. They have a capsular covering and they exist in the body **between** the constituent cells in the intercellular fluid. They multiply by **binary fission** (asexual reproduction) where they simply divide into two, a process which often occurs as frequently as every twenty minutes. Bacteria attack by multiplication and the release of toxins.

Viruses are generally much simpler and smaller than bacteria. When a virus attacks the body it actually enters body cells, taking over the cells' metabolism. The cells are prevented from carrying on their own functions and their activity is diverted to the manufacture of further virus particles. The cells become stuffed with virus particles and ultimately the cells die and rupture, releasing the viral particles into the circulation enabling them to infect further cells and replicate the process.

The body identifies bacterial attacks as 'foreign' and the immune system will attack them. White blood cells are able to fight off bacteria and antibodies are manufactured which lock on to the bacteria and destroy them.

The body has more difficulty in trying to overcome viruses because, for most of their time, they are within the body cells and therefore not accessible to the body's immune

system. It is only when the virus bursts out of the cells that the body's defence system has the opportunity to attack and destroy them. The period outside the body cells is short and it gives the body's immune system little time to recognise the virions (virus particles) and to destroy them.

The challenge of viruses is increased by their ability to mutate. We are currently experiencing the Covid mutation which is making the disease more infectious and transmissible.

Mutations are not uncommon and if Covid is not overcome through vaccination, more mutations will develop and the danger is that one will be much more lethal.

Bacteria are susceptible to appropriate antibiotics but the anti-viral drugs which are available are commonly less effective and are generally available only for some specific viruses.

Vaccines, however, can be formulated to combat the risk of bacterial infections and viral infections.

A vaccine against bacterial infection may be formulated from small amounts of weakened or dead organisms that cause the diseases, or from their toxins.

Vaccines against viruses are created using weakened virions, the messenger RNA (mRNA) which is in use in the virus's genetic code or identified proteins on the outside of the virus.

The vaccine creates changes in the immune system which increases its preparedness to combat the disease if the body is later exposed to it.

Most commonly, vaccines are administered by an injection. **Vaccination** and **immunisation** are words used to describe the process of being

treated to become immune to or be protected against a disease

We have seen with the Covid-19 infection new vaccines being created within a year of the first appearance of the disease. This is truly amazing because identifying the bacterial or viral antigens, isolation of suitable material, construction of the vaccine and testing to ensure safety and efficacy usually takes several years.

Will the world end with a bacterial or viral plague?

It is not impossible. If humankind is overwhelmed by a novel organism to which we have no immunity and there is no appropriate treatment or the ability to construct a vaccine quickly enough, then it could effectively happen.

Of course, the factor protecting humanity from complete eradication would be the existence globally of many isolated communities, cut off from the outside, and which would probably avoid exposure.

Perhaps the most effective ways of avoiding another terrible pandemic, based on events in the last twenty years, are:

1. To ensure clean water and effective sewage management
2. To avoid consumption of wild animals, given the suspicions about bats and other undomesticated creatures
3. Ensure that all meat from any source is fully cooked
4. Make sure that all vaccination schedules are fully complied with
5. If an infection is susceptible to an antibiotic, ensure that the whole course is taken, as per the instructions.

Despite all this negativity, one must remember that mankind has enormous ingenuity and can meet the challenges that come its way.

The world may come to an end through a cataclysmic catastrophe, such as an asteroid or global nuclear war, or through a super-infection for which no-one can find an answer.

I prefer to be optimistic and believe that we shall have the ability to overcome even the most serious threats and that the right decisions will be made . . . as long as we don't make too many wrong ones first!

Have a happy and healthy 2021.

paul.lambden@compuserve.com