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# Origin of Infectious Diseases and Covid – 19

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***Abstract:*** Mankind has faced infectious diseases repeatedly throughout its evolutionary history. Some of these diseases that recently affected human populations are black plague, smallpox, tuberculosis, Spanish flu, Russian flu, AIDS, Ebola, Asian flu, Avian flu, Hong Kong flu, SARS, swine flu, MERS, Zika, and finally human coronavirus disease (COVID-19). Bacteria, viruses, fungi, and worms/helminths are among the pathogens that cause infectious disorders (Kotra, 2007). For humans, pathogens transmission may occur by other people, animals, or environmental sources. As infective organisms, like humans, benefit from modern transportation facilities, infectious diseases are much faster and imminent dangers than before. In the classification of infectious diseases, the concepts of endemic, outbreak, epidemic, and pandemic appear. The amount of disease found only in a particular population is called the endemic level of the disease. An outbreak is defined as an unpredictable increase in the number of people showing a health condition or the occurrence of cases in a new region. When the disease spreads over a wider geographical area, the concept of epidemic emerges. When the epidemic spreads all over the world, the disease is now defined as a pandemic disease (Piret and Boivin, 2020). Throughout human history, epidemics and pandemics have constantly changed people's lifestyles due to their striking effects and still continue to do so. The COVID-19 pandemic we are currently experiencing is also changing everyone's lives in a remarkable way, and its effects on the future cannot be fully predicted. Learning about the factors, progress, and 6 Recent Advances In Biological Sciences effects of COVID-19 and past epidemics will at least help us to be prepared for infectious diseases.

## I. INTRODUCTION

The first records of infectious diseases that caused great epidemics in human history go back to 430 BC. In this section, information about some of the major pandemics that have occurred to date is given. These pandemics are given in Figure 1. Figure 1: Some Of The Major Pandemics That Have Occurred In The World The first pandemic in human history was the plague of Athens, which appeared in 430 BC during the Peloponnesian War between Athens and Sparta and lasted for five years. According to the records, 100,000 people, who make up 25% of the city's population, died during this epidemic. As a result of the researches, this epidemic may have been caused by smallpox or typhus (Littman, 2009).

The Antonine Plague, also known as the Plague of Galen between 165 and 180 BC, is an ancient epidemic that was carried into the Roman Empire by soldiers returning from expeditions. Symptoms of the disease included fever, diarrhea, vomiting, thirst, swollen throat, and cough. It was stated that during this epidemic, which is considered one of the biggest plague epidemics, 2 thousand people per day and 30 7 percent of the total population of the empire (5 million) died (Littman and Littman, 1973).

The plague of Cyprian, seen between 249-270, was recorded as a type of hemorrhagic fever that probably affected the entire Roman Empire. During this epidemic, 1 million people lost their lives all over the world (Alfani and Murphy, 2017).

The plague of Justinian, which occurred between 541 and 543 and is traditionally regarded as the first of three human plague pandemics, traveled over the Mediterranean basin from Central Asia or Africa to Europe, killing an estimated 100 million people. This pandemic is thought to be caused by the bacterium Pasteurellapestie (later referred to as Yersinia pestis) (Wagner et al., 2014).

In more recent history, a significant epidemic disease known to spread from China to the world is the Black Death (14th century) (Benedictow, 1992). This epidemic, which caused the death of approximately 75-125 million people between 1347 and 1351 in North Africa and Europe (Shaw and Taylor, 2020). The plague is caused by a bacterium called Y. pestis, the main source of which is wild rodents (Wheelis, 2002). Bacteria carried by fleas can affect both humans and animals. A variant of bubonic plague is named after the swollen lymph nodes (bubs) caused by the disease (Hinnebusch, 1997). From China, the plague also traveled west, reaching Crimea, Istanbul, then spreading to the Balkans, and from there to the Adriatic, Italy and the rest of Europe, and Africa, and Damascus. Plague spread from here to Anatolia (Ayalon, 2015).

## II. MATERIAL AND METHODS

### 1. Methodology

In the Ottoman landscape, the Black Death affected the Ottomans until the middle of the 19th century. Ten thousand people died in Istanbul in the year 1409/1410 (Marien, 2009). The water vole, shore vole, ground squirrel, and maybe the Persian jird, known in Iran, were all mentioned as plague carriers by the seventeenth-century Ottoman travelerEvliyaÇelebi.

Smallpox, a viral epidemic that caused the death of 300 million people in the last 100 years before being eradicated in 1979 in the 20th century, spread from China to the world in the 1500s (Needham and Lu, 2000). This disease is caused by the variola virus and causes pus-filled blisters (pustules) to form on the skin (Lofquist et al., 2003). This cureless disease as a biological weapon against Native Americans in the 18th century (Patterson and Runge, 2002). The inoculation against smallpox has been applied for centuries in Ottoman lands (first vaccine usage), the wife of the British ambassador was observed in Istanbul in 1721, then send the method to England. The modern smallpox vaccine was developed in the 20th century (Plotkin, 2011).

Despite the use of vaccines and various antibiotics worldwide, tuberculosis (TB), one of the oldest diseases of humanity, is still the leading cause of death among infectious diseases (Smith, 2003; Talbot and Raffa, 2015; Fitzgerald and Haas, 2005;

Moule and Cirillo, 2020). Every year, two million people die due to tuberculosis, an epidemic that causes the death of millions of people. The microorganism that causes TB is Mycobacterium tuberculosis. While Mycobacterium species were originally found in the soil, some species evolved to live 9 in mammals such as cows and were transmitted to a new host, humans, due to the domestication of cattle (Smith, 2003).

A vaccine strain attenuated by the successful passage of a virulent M. bovis strain was produced by Calmette and Guerin in Paris in 1920, which later introduced the BCG vaccine, but these vaccines failed to eradicate TB (Smith, 2003).

## 2. Result and Discussion

- **Antibacterial Drugs**

The discovery of antibiotics was one of the greatest achievements of the 20th century. Antibiotics are chemicals that inhibit bacterial growth by stopping bacterial cell division or killing them. Antibiotics are used for the treatment or prevention of infectious diseases in humans and animals (Dugassa and Shukuri, 2017). Antibiotics show their effects by targeting protein synthesis, nucleic acid synthesis, metabolic compound synthesis, bacterial cell wall, and cell membrane (Zaman et al., 2017). The mechanisms of action of antibiotics are shown in Figure 2. Figure 2: The Mechanisms of Action of Antibiotics 12 Recent Advances In Biological Sciences .

- **Antibiotics Targeting Cell Wall**

Bacterial cell wall components are attractive antibacterial targets due to the lack of analogs in human cells, thereby ensuring target selectivity. Various antibacterial drugs make cells more susceptible to osmotic lysis by blocking different steps in the biosynthesis of peptidoglycan. Peptidoglycan, which is the basic element of the bacterial cell wall, is synthesized of four stages: synthesis of precursors in the cytoplasm, transport of these lipid-dependent precursors across the cytoplasmic membrane, glycan units attached to the cell wall, and transpeptidation binding and maturation (Mc Dermott et al., 2003). β-lactams, glycopeptides, and bacitracin are among the antibiotics that inhibit different stages of the cell wall biosynthesis of bacteria (Dowling et al., 2017). Drugs inhibiting bacterial cell wall synthesis are divided into 3 main groups according to their mechanism of action. Antibiotics in the first group interact with penicillin-binding proteins (PBPs) and inhibit transpeptidase activity. Antibiotics in the second group inhibit transglycosylation and transpeptidation. The antibiotics in the third group inhibit the transport of peptidoglycan subunits across the cytoplasmic membrane.

- **Antibiotics Targeting Cell Membrane**

Cyclic polypeptides (colistins and polymyxins) in this group are branched polypeptides containing both hydrophobic and cationic amino acids. Due to this amphipathic feature, polymyxin and colistins change the permeability of the cell membrane and act as detergents. They are more effective on Gram-negative bacteria as they can hardly pass through the thick peptidoglycan layer on the Gram-positive cell wall (Epand et al., 2016).

- **Antibiotics Targeting Protein Synthesis**

Bacterial ribosomes consist of two subunits of rRNA (the 30S and 50S) and proteins. Antibiotics that inhibit protein synthesis generally show their effect by binding to these subunits. Antibiotics in this group are aminoglycosides (binds to the 30S subunit of the ribosome), tetracyclines and alkylaminocyclines (inhibits the binding of aminoacyltRNA to the A site of the ribosome), fusidic acid (inhibits 14 Recent Advances In Biological Sciences the transport of peptidyltRNA from the A site of the ribosome to the P site), mupirocin (inhibits protein synthesis by binding to bacterial isoleucyltRNAsynthetase), macrolides (targets 50S subunit of ribosome), lincosamides (targets 50S subunit of ribosome), streptogramins (targets 50S subunit of ribosome), chloramphenicol and thiamphenicol (targets 50S subunit of ribosome) (McCoy et al., 2011).

- **Antibiotics Targeting Nucleic Acid Synthesis**

Fluoroquinolones in this group show their effect by inhibiting topoisomerase activity. Ansamycins, on the other hand, inhibit the initiation step of transcription by acting on RNA polymerase (Bhattacharjee, 2016).

- **Antibiotics Targeting Biological Metabolic Compound Synthesis**

Sulfonamides, the most important antibiotics in this group, are derived from p-aminobenzenesulfonamide, which is a necessary factor for folic acid synthesis in bacteria. In this way, it shows its effect by inhibiting the synthesis of tetrahydrofolate (Kapoor et al., 2017).

## 3. Spreading of Infections

Viruses spread in different ways. Some viruses spread through the air droplets like influenza, while others by contact with an object that has viruses on it. Another way is spreading the infections through body fluids and blood such as HIV, hepatitis B, and hepatitis C. Some germs are spread from contaminated food or water, such as Salmonellosis, Listeriosis, and Toxoplasmosis. Some germs are transmitted by insects or other animals. The diseases spread by the insect are yellow fever, chikungunya virus, dengue fever), bacteria (plague, Lyme disease), parasites (malaria, filariasis, leishmaniasis, sleeping sickness).

Many recent infectious diseases are caused by viruses, and their origin is nonhuman host reservoirs that are usually mammalian and sometimes avian (Taylor et al., 2001). The recent emerging infectious disease outbreaks are the Ebola virus disease (EVD) epidemic in West Africa, the Zika virus disease epidemic in America (Woolhouse et al., 2016), and SARS CoV-2 in the World. Domesticated and wild animals can carry harmful viruses and germs that can spread to people and cause illnesses called zoonotic diseases. Generally, Carnivora and Chiroptera spread RNA viruses to other hosts, while wild and domesticated species transmit both RNA and DNA viruses to other hosts (Wells et al., 2020). The novel coronavirus originated from the seafood market in Wuhan where racons, dogs, bats, snakes, and other animals sold and spread the world (Hafeez et al., 2020). The main 19 transmission route of COVID-19 is respiratory droplets (Sheeren et al., 2020).

RNA viruses have higher mutation rates than DNA viruses. (Lauring and Hodcroft, 2021). COVID-19 is rapidly changing due to virus genome type and replication enzyme characteristics. CT images of the lungs are used to aid in the diagnosis of COVID-19, but real-time polymerase chain reaction made from samples from the upper and lower respiratory tract is used for definitive detection of the virus.

**4. How does the Coronavirus Infect?**

It enters the body through the mouth or nose, invading cells in the throat and lungs. Normally, when the virus enters the body, the defense system starts to work. However, this virus somehow makes copies of itself by blocking the defense system. Even if it is late, the small chemical weapons in our bodies begin to be secreted for defense. Therefore, our fever increases. Our germ-eating white blood cells rush to the occupied place.

The virus uses everything that does not belong to itself in the cell, for its benefit, the cell tries to commit suicide to get rid of it, but the virus prevents it. After making thousands of viruses, it kills the cell itself and invades neighboring cells with its new viruses. In the cell it enters, the message in the virus is read and the proteins necessary for the continuation and reproduction of the virus are made in line with the message. The virus has 24 proteins, versus 100,000 different proteins in the human cell, and these make many people helpless. Some of 20 Recent Advances In Biological Sciences these proteins work like photocopiers and make copies of the virus, while others act like scissors. Thus, it allows the proteins to be released and do their work. Normally, the human defense system stands up to the virus, but the viruses camouflage and prevent the attacks of the defense system. During an innate immune response to a viral infection, dendritic cells, adaptive T and B lymphocytes, macrophages, natural killer cells, and produce cytokines. Pattern recognition receptors (PRRs) identify the virus's numerous molecular structures. When PRRs attach to them, the inflammatory reaction against the virus that has entered the body is triggered, and some signaling pathways and, as a result, transcription factors are activated. Pro-inflammatory cytokines are produced for the expression of genes encoding adhesion molecules, inflammatory cytokines, and chemokines. Plasma proteins and leukocytes, which will fight the infection, come to the area where the virus is located (Ragab et al., 2020). During the cytokine storm, the level of proinflammatory cytokines IL-6, IL-1, TNF-α, and interferon increases. This increase results in acute respiratory distress syndrome, a systemic inflammatory response, multi-organ failure, and ultimately death. When the virus infects the body, a strong cytokine storm resulting from an unbalanced response can be very damaging to patients, although the inflammatory response plays an antiviral role (Shimizu, 2019).

**5.What are the Disease and its Symptoms?**

Some human symptoms begin to show 5 days after infection, after 12 days most infections appear. People can be removed from quarantine after 14 days if there are no symptoms. Some people can get the virus, show no symptoms, but spread the virus. Fever, dry cough, fatigue, shortness of breath, headache, nausea, and diarrhea may occur. Patients with the most severe symptoms are 60 years of age or older.

**6. Who is in Danger?**

Health workers, caregivers of the elderly and children, etc. Service sector employees, public officials who are intertwined with people such as soldiers and police, and people who cannot benefit from adequate nutrition and health services are more in danger.

**7. How can we be Protected?**

We can protect ourselves from the virus by maintaining social distance, avoiding physical contact, protecting the elderly-chronic patients, washing our hands frequently with soap, not touching our faces, changing our clothes when we come from outside, using disinfectants, and wearing a mask if we have to go out. The most important thing is to get vaccinated.

**8. Vaccine Development for Covid-19**

Vaccination is the first form of protection for the prevention of infectious diseases. Vaccines help reduce disease severity and transmission rates (Klompas, 2021). Under normal circumstances, vaccine development for human infectious agents and obtaining the final product traditionally take 15 to 20 years (Excler et al., 2021; Bregu et al., 2011). However, with the new vaccine platform technologies, this time can be shortened, making it possible to rapidly develop, test, and manufacture vaccines (van Riel and de Wit, 2020). This period has been shortened for vaccines developed for COVID-19, and some vaccines have been approved for emergency use by the FDA. Available human vaccines can be grouped into mRNA-based, virus-based, and protein-based vaccines. Virus-based vaccines are either live attenuated viruses or inactivated viruses that are no longer 24 Recent Advances In Biological Sciences harmful. Since fully inactivated viruses are not replicated, it is necessary to add adjuvants to the content of vaccines to stimulate the immune system. (van Riel and de Wit, 2020). Live attenuated virus vaccines are produced by cell culture. After the virus has lost its pathogenic properties, it is ready for further tests. Recommended vaccines are administered to small animals, usually mice, in preclinical studies, and their immune responses are measured. With these tests, immunity against the virus must be proven, otherwise, the vaccine will not be tested further. Toxicity studies are also carried out on animals to detect safety signals (Edwards and Orenstein, 2021). Once these steps are successful, clinical trials, consisting of three phases lasting another 5-10 years, begin to be tested in humans (Figure 5) (Deb et al., 2020). Figure 5: Vaccine Development Stages 25 No DNA vaccines have been licensed for use in humans, as DNA vaccines are not very good at inducing antibodies. Protein-based vaccines can be purified protein from a virus or virus-like particles. An adjuvant is added to them as well. mRNA vaccines have some advantages such as rapid construction of vaccine, no need for cell or animal substrates to manufacture, no need to enter the nucleus, production of a suitable number of protein antigen molecules per molecule of mRNA delivered, and no integration to DNA (Liu, 2019). Two COVID-19 mRNA vaccines were developed (Pfizer– BioNTech35 and Moderna36), both showing safety and high efficacy and now with US Food and Drug Administration (FDA) emergency use authorization (EUA) (Edwards and Orenstein,2021).

## CONCLUSION

Germ (Bacteria, yeast, virus, etc.) was exist in the past, it will exist in the future. Some viruses infect bacteria, some of them plant, and some of them humans. They cause infectious diseases. The disease may spread from person to person by blood transmission and other body fluids due to unsanitary conditions. Some viral infections can be deadly, some of them cause mild damage. The war against viruses and other germs continues by developing drugs and vaccines. While we fight against the germ, they continue to fight back by gaining resistance and changing their genome. Therefore COVID 19 is not the last, not the least virus humanity will challenge with, other pandemics will be in the future. Therefore, we all have to strengthen our research infrastructure, do planning and preparedness to ensure the capacities for pandemic response.

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