

# Learning from history in the midst of the COVID-19: epidemics/pandemics of antiquity up to the fall of the Western Roman Empire

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## Abstract

When humans discovered agriculture and livestock, they ceased to be nomads and began to settle in towns until they created large cities. From the first human settlements in Egypt, Mesopotamia, and the Anatolian Peninsula, populations were exposed and susceptible to new infectious agents, leading to epidemics and pandemics. Great civilizations emerged, such as Egypt, the land of Hatti, Israel, Greece, Carthage, and Rome, among others. Contact between different populations through wars or maritime trade is well documented and has been described as a source of epidemics throughout history. Epidemics described as plagues or pestilences, such as those of Egypt, the Hebrews, or the Hittites, are based on biblical texts or evidence such as tablets or hieroglyphic writings. We also reviewed classical books by authors such as Homer, Aeschylus, Herodotus of Halicarnassus, Thucydides, Diodorus Siculus, Dionysius of Halicarnassus, Titus Livius, Suetonius, and others; and described all epidemics/pandemics chronologically. This article describes the epidemics/pandemics for which there is written evidence from ancient Egypt to the fall of the Roman Empire. We should not be surprised when new epidemics/pandemics appear as causes of political and economic collapse, as this has been common throughout history, decimating, blocking, or even destroying cultures and civilizations repeatedly.

**Keywords:** Pandemic. Epidemic. Plague. Pestilence. History. Antonine plague.

## Aprendiendo de la historia en medio del COVID-19: epidemias/pandemias de la antigüedad hasta la caída del Imperio Romano de Occidente

### Resumen

Cuando el hombre descubrió la agricultura y la ganadería, dejó de ser nómada y empezó a asentarse en pueblos hasta crear grandes ciudades. Desde los primeros asentamientos humanos en Egipto, Mesopotamia y la península de Anatolia, las poblaciones estuvieron expuestas y susceptibles a nuevos agentes infecciosos, dando lugar a epidemias y pandemias. Aparecieron grandes civilizaciones como Egipto, la Tierra de Hatti, Israel, Grecia, Cartago y Roma, entre otras. El contacto entre las distintas poblaciones a través de las guerras o el comercio marítimo está muy bien establecido y descrito como focos de epidemias a lo largo de la historia. Las epidemias descritas como plagas o pestilencias, como las que ocurrieron a los egipcios, los judíos, o los hititas, se describen con base en textos bíblicos o mediante evidencias como tablillas o escritos jeroglíficos. También revisamos libros clásicos de autores como Homero, Esquilo, Herodoto de Halicarnaso, Tucídides, Diodoro Sículo, Dionisio de

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Date of reception: 09-11-2022

Date of acceptance: 24-01-2023

DOI: 10.24875/BMHIM.22000147

Available online: 27-10-2023

Bol Med Hosp Infant Mex. 2023;80(5):269-278

www.bmhim.com

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*Halicarnaso, Tito Livio, Suetonio, entre otros. Este artículo describe cronológicamente todas las epidemias/pandemias de las que existe evidencia a través de la escritura desde el antiguo Egipto hasta la caída del Imperio Romano. No debemos sorprendernos cuando aparecen nuevas epidemias/pandemias como causantes del colapso político y económico, ya que ha sido algo común a lo largo de la historia, diezmado, bloqueando o incluso destruyendo culturas y civilizaciones reiteradamente.*

**Palabras clave:** *Pandemia. Epidemia. Plaga. Pestilencia. Historia. Plaga Antonina.*

## Introduction

For an infectious disease to cause an epidemic outbreak, the presence or introduction of an infectious agent into a vector such as humans, contact of that agent with enough susceptible individuals in a population not previously exposed to infection, and effective human-to-human contact and transmission is required.

Primitive man ceased to be a nomad when agriculture and animal husbandry appeared, giving rise to the first populations and great civilizations but also to the first epidemics and pandemics. Diseases are as old as humankind. We have had to live with the coronavirus pandemic since the end of 2019 and the beginning of 2020. However, throughout the ages and since man has lived in society, infectious and contagious diseases have also coexisted with us. Pandemics not only mean an infectious disease but also have several characteristics, such as their global distribution in all latitudes and longitudes, with a high spread and contagiousness, and the number of lost human lives, causing the collapse of societies and their systems.

Some of the epidemics/pandemics that have been documented through writing or other traces are described here, from the earliest civilizations to the Cyprian Pandemic, which marked the collapse of the Roman Empire before its split into the Western Roman Empire and the Eastern Roman Empire.

For this review, the following concepts have been considered:

### Endemic

From the Greek *endemos*, native, plus *demikos*, relating to people or population. It means present in a community or group of people. It refers to diseases that are prevalent with a high number of cases continuously in a region compared to others. Sanitary phenomenon unlimited in time and limited in space<sup>1</sup>.

### Epidemic outbreak

Two or more cases epidemiologically linked. The presence of a single case under surveillance in an area

where the disease did not exist is also considered an outbreak. An outbreak occurs when there is an unusual increase in the number of cases of a disease above normal; it may be localized in a specific area or extend to several countries. It may last for days, weeks, or years<sup>2</sup>.

### Epidemic

From the Greek words *epi*, about, *demises*, referring to people or population. A disease affects many people in a community simultaneously, when it is not normally present continuously, or when there is a temporary increase in the number of cases of an endemic disease. The usual rates of the disease must be known to detect a significant increase and determine the occurrence of an epidemic. It occurs in a specific geographical area, and generally implies the occurrence of a large number of new cases in a short period, greater than the expected number<sup>1,2</sup>.

### Pandemic

From the Greek words *pan*, whole, and *demos*, *demikos*, people. A widespread epidemic covering large groups of countries and several continents. It is the expansion of the territory of the epidemic worldwide. It must meet at least two criteria: the first, as mentioned above, is that it affects several continents, and the second is that the cases in each country are no longer imported but caused by community transmission<sup>1,2</sup>.

### Plague

We must also mention “pests,” a synonym for pestilence, when discussing epidemics and pandemics. It refers to an epidemic disease, almost always related to the famous plague caused by *Yersinia bacillus*. The terms pests, pestilence, and plague are used in various classical or medieval sources, not always used to refer to a single and specific etiology. Either term refers to the condition of many people with epidemic characteristics and high mortality<sup>3</sup>.

## Epidemics and pandemics before Christ

The group of people that constituted humanity between the years 10,000 and 5000 B.C. (before Christ) was distinguished into those that progressed to build great archaic and ancient cultures, such as the Sumerian, Assyro-Babylonian, Egyptian, Chinese, Iranian, Indian, Israelite, and pre-Hellenic, among others; and those whose progress was minimal or absent, remaining stagnant, for which they became extinct by themselves or were conquered by human groups stronger than them. Epidemic diseases have occurred in all civilizations. In the ancient cultures, they were approached first with a magical-religious nature and secondly with scientific knowledge through the physicians of that time<sup>4</sup>.

A chronological order of the various epidemics/pandemics has been established, beginning in Egypt and almost simultaneously in the Hittite Empire, the Hebrews, and the Philistines, which could be documented as the first major pandemic. Then, the epidemics in Athens, Carthage, and Rome are documented.

## The plague of the Egyptians: Egyptian, Hebrew, or Hittite origin

Civilization in North Africa began about 13,000 years ago when the Sahara was a savannah inhabited by gathering and hunting groups. However, the changing climate gave way to desert, and people were forced to settle around the Nile, the region's main water source. The earliest settlements were located in the northernmost part of the country, known as Lower Egypt, and include three major sites: Beni-Salama, Fayum, and Omari (4600-4400 B.C.). During the following periods, sedentarization began, and with the appearance of the desert, agriculture, and livestock became the primary food source. Furthermore, during this period, foreign marketing began with Lebanon, Mesopotamia, and Sumer<sup>5</sup>.

Along with the great Egyptian history, the arrival of the Jews in Egypt and their relationship with plagues and pestilence should also be mentioned. Historically, this fact may be related to the Asian migration to the Nile Delta of the Hyksos (foreign rulers from the Middle East). Then, the Egyptians started a war against them until they were driven back to Canaan<sup>6</sup>. This part of the story happened at the time of Amnosis, but it is not known if they were Jews. Regarding the plagues in Egypt, the book of Exodus in the Old Testament of the Bible describes that Moses and his brother Aaron went

to Pharaoh's court to warn him that if he did not let his people leave, Yahweh would unleash a terrible plague on Egypt, and so it happened: blood in the waters of the Nile, frogs, mosquitoes, and plague until the Jews were permitted to leave Egypt. According to various film scripts, Ramses II is mentioned as the protagonist pharaoh of this exodus<sup>7</sup>; however, the historical facts point to perhaps a longer period in history.

Some historical facts, such as the Amarna Letters (correspondence between Egypt and foreign countries of the Near East), indicate that some of these facts can be related to the reign of Akhenaten. For example, one of these letters reports a plague that spread from Canaan to the Hittite kingdom and from there to Cyprus and the capital of Egypt. Previously, during the description of the Hittite Empire, an epidemic was mentioned that almost devastated the entire kingdom of the country of Hatti, coming from Egyptian slaves in the years close to the reign of Akhenaten. Therefore, will the first pandemic described in history be this one that encompassed several empires of antiquity? In fact, in 2004, the archaeological discovery of the inhabitants of Akhenaten identified a high frequency of fleas and other fossilized parasites, all containing the bacterium that produces the plague (*Yersinia pestis*)<sup>8</sup>.

For centuries in antiquity, the numerous epidemics and pandemics were called "plagues" and caused great mortality. Various ancient sources mention a terrible plague that spread throughout the Mediterranean in the fourteenth century B.C., during the time of Akhenaten. Various medical papyri attest to an epidemic that probably began during the reign of Amenhotep, Akhenaten's father. During his reign, an extraordinary number of statues of Sekhmet, the goddess of plagues, were made to appease the goddess and thus rid Pharaoh and Egypt of disease. In 1344 B.C., it is documented that King Tushratta of Mitanni sent an embassy to Egypt with the statue of the goddess Ishtar, which had healing properties and could fight plagues. It is possible that this plague affected members of Akhenaten's royal family, such as the princesses Maketaton, Neferneferure, and Setepenre, the royal wife Kiya, and Akhenaten himself. The plague spread and persisted during Akhenaten's reign, where archaeological evidence shows the appearance of fleas and bedbugs, vectors that spread parasites and were ideal for epidemic diseases. Simultaneously, in other places outside of Egypt, such as Cyprus, Canaan, Sumur Amurru, and Megiddo, it is mentioned in letters to the Pharaoh that an epidemic and pestilence ruined the cities. Another region also severely affected was Anatolia, previously

mentioned by King Mursili II, in the heart of the Hatti Empire. Other papyri refer to a possible Asian origin of the pandemic (18<sup>th</sup> Dynasty: 1539-1292 B.C.): “The body is blackened with black spots.” They mention plagues spread by rodents, which could be tularemia or “rabbit fever,” but others support malaria or bubonic plague<sup>9</sup>.

### **Hittite Empire at the time of Mursili II: the great plague of the Hittites**

The region of Anatolia, corresponding to modern Turkey and the northern parts of Syria and Iraq, is an area where various civilizations developed over several millennia, including the Hittite Empire, the Hurrians, and the Mitanni.

In the last quarter of the 3<sup>rd</sup> millennium B.C., the Anatolian Peninsula was occupied by indigenous population centers confined to small geographical areas. In the center of the plateau, small kingdoms formed a coalition to stop the expansion of the Akkadian King Naram-Sin (2260-2223 B.C.), giving rise to an indigenous group known as the Hattians, for whom the region became known as the “Country of Hatti.” Indo-European migrations during the next two centuries mixed with the local population, giving rise to the Hittites. This empire reached its peak during the reign of Suppiluliuma I (1344-1322 B.C.), conquering Assyria, Mitanni, and even Egypt. This King defeated the Pharaoh Amenhotep IV (Akhenaten). This triumph over the Egyptian Empire came with a heavy tribute. According to the Hittite annals written on tablets, an epidemic of plague spread among the thousands of captives the Hittites made in Egypt, and “when the captives entered the land of Hatti, and from that day on, death reigned in the kingdom.” Emperor Suppiluliuma I died soon after, and Arnuwanda, his successor, also fell ill (1321 B.C.). He was succeeded by his younger brother Mursili II (1321-1295 B.C.), who took power in a country on the verge of collapse. In the annals of Mursili II, the episode of the plague epidemic is very illustrative of the Hittite mentality. It is known as the “Plague Prayer” and reads as follows: “What is this, oh gods? What are they doing? They have allowed a plague in the land. The land of Hatti, all of it, is dying: so no one prepares the sacrificial loaves and libations for us.” The plague was believed to be a divine punishment for the King’s sake. The entire population had to observe a series of religious protocols to ensure divine blessing; if any of them were violated, the wrath of the gods would be directed against it, and if the King committed the fault, the gods’

punishment was worse, and it fell on all the people. The plague that devastated the empire was considered the result of the fact that Suppiluliuma I, after his victories, stopped making offerings to certain gods, so they sent him the plague that ended his life and that of his son<sup>10</sup>.

It is now known that the Hittites attacked the Egyptian frontier at Amka, east of Byblos and Simira. The spoils and prisoners of war left a contaminated trail, as evidenced by the letter RS 4475 from Ugarit, ruled by Nipmaddu II, one of the states of the Hittite Empire. It was a plague that lasted 35-40 years, infecting humans and animals, causing fever, disability, and death, spread by rodents on board ships. This disease points to *Francisella tularensis*, the etiologic agent of tularemia. The description from the Hittite records, such as weak knees and internal burning sensation, is consistent with tularemia. It has been shown that the geographical area has been a reservoir of the etiologic agent since the 2<sup>nd</sup> millennium B.C. in the Canaan area, later spreading to Egypt in the 18<sup>th</sup> century B.C. and later with the war on Hittite lands<sup>11</sup>.

### **The Philistines, enemies of the Hebrews: the plague of Azoth**

In the Bible, the Philistines are enemies of the Israelites and can be connected to Old Testament stories such as the story of Goliath<sup>12</sup> or Delilah<sup>13</sup>. They were originally a people of the Late Bronze Age, as evidenced by Egyptian, Hebrew, and Assyrian sources. In Egyptian documents, they are referred to as part of the Sea People, who were called the *Peleset*<sup>14</sup>. After their confrontation with the Egyptians, they settled on the coast of Canaan, today’s Gaza Strip (Palestine). The Book of Genesis mentions that they were of Egyptian origin, although it is also mentioned that they could have been descendants of the Cretans, the Aegean, or Minor Asia<sup>14</sup>. Recent studies of the DNA of a group of individuals from Ashkelon have provided definitive evidence of the European genetic origin of the Philistines, supporting the theory that they were foreigners who arrived in the Middle East in the 12<sup>th</sup> century B.C. from Greece, Crete, Sardinia, or even the Iberian Peninsula, as evidenced by ceramics similar to Greek, the use of Aegean rather than Semitic writing, and the consumption of pork<sup>15</sup>.

The French Baroque oil painting entitled “The Philistines Struck by the Plague” or “The Miracle of the Ark” shows the Old Testament story of Samuel in which he describes how the Philistines steal the Ark of the Covenant and take it to the Philistine city of Ashdod or

Azoth after defeating the Israelites. They place the Ark in a temple dedicated to the god Dagon, for which Yahweh sends a great plague on the inhabitants of Ashdod and other Philistine cities. “God punished all the inhabitants, from the smallest to the largest, causing them to grow tumors, a disease that lasted until the Ark was returned. There is an atmosphere of desolation, panic, and death in this work, reflecting the fate of those who face God”<sup>16</sup>. According to the descriptions, the Philistines grew tumors or buboes, and according to some translations, the fields were invaded by mice and rats, which could carry flea bites and thus the bubonic plague. However, it is more accurate to consider that the Middle East was free of plague epidemics until the early years of our era. An alternative scenario is that the disease could be dysentery with severe diarrhea, ulcers, and swelling in the perianal area. According to some Hebrew texts, the tumors could be hemorrhoids or dysenteric abscesses, but this is a very weak hypothesis, and anything related to contaminated water or diarrheal diseases is not reported in the biblical text. A new hypothesis has been described, which maintains that the Ark of the Covenant, because of its size, could accommodate more mice than rats and that these animals suffered the disease and transmitted it to humans, forming tumors and, in severe cases, causing death. Tularemia is caused by *F. tularensis* and is a zoonotic disease that presents with glandular ulcers that can be confused with bubonic plague and can have a mortality rate of over 15%. Around 1715 B.C., tularemia was known as the “Asian disease,” believed to have originated in Canaan and spread to Egypt through contaminated ships. Tularemia would have occurred more than once in Canaan, and this recurrence suggests that this geographic area was a reservoir for *F. tularensis* in the 2<sup>nd</sup> millennium B.C.<sup>17</sup>.

The Bible also mentions in its Old Testament the plague that punished David’s sin of ordering a census of his people and killed about 70,000 men out of 1,300,000 people who inhabited Israel and Judah<sup>18</sup>. It also mentions a plague that wounded an Assyrian camp of 185,000 men in one night, causing the Assyrian king Sennacherib to withdraw from Judah without taking Jerusalem<sup>19-22</sup>.

### **Greek polis: the plague of Athens**

The particular orography of the Greek territory, consisting of numerous islands, beautiful mountains, valleys, and gorges on the coasts, led to the creation of the first polis in Greece and a new economic and social structure

after the disappearance of the Mycenaean culture during the 8<sup>th</sup>-6<sup>th</sup> centuries B.C. During the 5<sup>th</sup> century B.C., the century of Pericles (495-429 B.C.), the great statesman of the polis, Athens reached its maximum splendor, making it a center of innovation and progress, including the various arts, philosophy, historiography, and engineering, among others<sup>23</sup>.

The first evidence of an epidemic in Greece is described in the first book of Homer’s Iliad: “The Greeks plundered Crise in the Troad and sent Briseis, the daughter of Chryses, Apollo’s priest, as a gift to Agamemnon, who made her his concubine and refused to return her to her father. He invoked Apollo, who shot arrows into the midst of the Greeks for 9 days, killing first mules and dogs and later the Greek armies”; the text is interpreted as an epidemic of plague in the Greek camp<sup>24</sup>. According to Williams, it is believed to be related to the depopulation and destruction of Greece around the year 1200 B.C. This author believes that a great epidemic was the cause, and the Dorians, seeing how weak the Greeks were, were able to invade them. Apollodorus, a Greek writer from the 1<sup>st</sup> century A.D., describes this event as occurring 80 years after the Trojan War<sup>25</sup>. Herodotus also briefly mentions that after the Cretans returned from Troy, a plague struck Crete, affecting both cattle and humans: “...let us return to Crete, where many people, especially the Greeks, came to live as in an inhabited country. In the third age, after the death of Minos, the expedition against Troy took place, in which the Cretans did not appear because of their pain and their neglect to revenge Minos; after returning from Troy, they were attacked by hunger and plague, both men and cattle...”<sup>26</sup>. Herodotus also mentions a plague of dysentery that struck Xerxes on his return to Persia after the First Persian War in 479 B.C. (Xerxes’ plague)<sup>27</sup>. Herodotus mentions other plagues: “When a choir of 100 young people was sent to Delphi, only two returned, the other 98 were snatched away by a plague that struck them unexpectedly”<sup>28</sup>. He also described: “...in addition to the plague that broke out in the army, it was decimated along the way. And he left the sick...”<sup>29</sup>. Aeschylus, a Greek tragedian, mentions the plague in the “Suppliants” (never can the plague empty the city of its men) and in the “Persians” referring to the shadow of Darius (did a plague scourge or civil war come?)<sup>30,31</sup>.

During the Peloponnesian War, an epidemic is described that changed the war’s course. In 430 B.C., Athens was at war with Sparta for control of all of Greece. Athens had conquered the Greek seas and islands with its large navy; however, control of the land was dominated by the

Spartans, who had reached Athens with a large army. Because of this naval dominance, the Athenians could be under siege for years, as they received grain and food by sea. What they did not expect was that one of the ships coming from Egypt would bring a deadly disease that would devastate the city and weaken the army and its fleet for the rest of the war. The plague is said to have started in Ethiopia and spread to Egypt, Libya, and most of Persia before suddenly descending on Athens. Athenian doctors began to document the first cases among sailors and unloaders at the docks, and it was suspected that the Spartans were poisoning the water. The cases multiplied rapidly, and the population began to die of the plague while the healers and priests could do nothing. Thucydides himself, who wrote about the events, fell ill and mentioned that “the disease ended in a few days with all the physicians in the city because, not knowing how to treat it, they fell in droves”<sup>32</sup>. In this way, the infected were neglected, their relatives and friends avoided contact for fear of becoming infected, and the few compassionate souls who came to their aid died of the disease, contributing to its greater and faster spread throughout the city. Symptoms included a burning fever and irritation of the throat and tongue, which, according to Thucydides himself, produced fetid and unnatural breath. This was followed by vomiting and choking, which led to loss of strength and bedriddenness. Later, ulcers appeared all over the body, along with hyperthermia. All these ulcers were very painful, and the patients always had a great thirst, which was never quenched. The end, on the 7<sup>th</sup> day of the disease, consisted of a stomach ulceration that caused diarrhea, which led to greater weakness and inability to eat<sup>33,34</sup>. Conventionally, this has been called an outbreak of bubonic plague, but based on the symptoms and evolution of the disease, some researchers have concluded that it could have been an epidemic of smallpox or even typhus. The unusual number of corpses overwhelmed the burial services, and many people abandoned their dead in the streets. Even the initiator of the war, Pericles, died during the epidemic<sup>35</sup>. It is estimated that between 70,000 and 100,000 people, a quarter of the population, died in two waves of epidemics between 430 and 427 B.C. The military power of Athens was quite limited, but the war continued until 404 B.C. when the final surrender was given<sup>36</sup>.

New methods, such as forensic DNA analysis, have shed new light on the problem of solving the cause of the epidemic in Athens. The highly contagious epidemic presented with a pustular rash, high fever, and diarrhea originated in Ethiopia and spread throughout the

Mediterranean. The epidemic broke out in 430 B.C., with further waves in 428 B.C. and 426 B.C., and lasted about 5 years. In 2001, a mass grave was discovered that belonged to the plague years. DNA was extracted from ancient microbial typhoid (*Salmonella enterica* serovar typhi) from three skeletons; however, since typhoid was endemic in the Greek world, it is unlikely to have been the cause of this epidemic (Littman, 2009)<sup>37</sup>. In a recent report analyzing all of Thucydides’ clinical descriptions, smallpox or measles are the ones that best explain what could have happened in Athens at the beginning of the Peloponnesian War, and the preponderance of clinical features favors measles as the explanation for this epidemic<sup>38</sup>. In very recent reports, there are those who defend the hypothesis that it could have been an influenza epidemic<sup>39</sup> or even Ebola<sup>40</sup>, but the reality is still unknown.

### Carthage: epidemics of the Carthaginian army

Born as a colony of Tiro toward the end of the 9<sup>th</sup> century B.C., Carthage inherited the commercial network of its metropolis when the Assyrians and Neo-Babylonians dominated Phoenicia. It dominated the former Phoenician colonies in the south of the Iberian Peninsula (Gadir, Abdera, and Malacca), the Maltese archipelago, Western Sicily, Sardinia, and Ibiza. This eventually caused friction with the Magna Graecia, and with Rome, a promising city-state that was expanding southward in Sicily, where Carthaginian colonies were established<sup>41</sup>.

According to history, Carthage had to fight not only against Syracuse in Sicily but also against epidemics. The first epidemic is mentioned in 409 B.C.; after a series of victories that brought them to the gates of Syracuse, the Carthaginian army was decimated by an epidemic, and the Carthaginian troops had to abandon the siege<sup>42</sup>. The historian Diodorus Siculus said: “Dionysius the Elder (tyrant of Syracuse), taking advantage of the fact that the epidemic of the Punic army had spread to Africa, established his power and took over practically all of Sicily. However, a new Carthaginian general named Himilcon regained the territory for Carthage at the command of 300,000 men. During this siege, a new epidemic struck his land army, and 150,000 died of disease, prompting Dionysius to attack again and forcing Himilcon to ask for a truce and retreat. Once in Africa, the epidemic spread among the Carthaginians and their allies, greatly reducing the population of Carthage<sup>42,43</sup>. In the years 378 and 368 B.C., two new outbreaks of epidemics spread rapidly and shook Carthage, a situation used by its neighbors Libya and Corsica to revolt<sup>44,45</sup>.”

## Foundation of Rome and its republic: epidemics in the Roman Republic

According to legend, the founder of Rome was Romulus in 751 B.C., a descendant of Aeneas, a hero of Troy who fled the destruction of the city, taking with him dozens of Trojans<sup>46</sup>. During the 4<sup>th</sup> century B.C., Rome expanded southward, conquering practically the entire peninsula, establishing contact with the Greek cities of Magna Graecia, and spreading along the coasts of the Ionian and Tyrrhenian Seas<sup>41</sup>. Years later, the Romans launched a preventive war called the First Punic War (punicus from the Latin: Phoenician), which conquered Sicily and ended with the defeat of Carthage, which was forced to sign peace in 241 B.C.<sup>47</sup>.

The first epidemics in Italy can be dated precisely thanks to the references of Dionysius of Halicarnassus and Livy. Halicarnassus's first reference to an epidemic dates back to the time of Romulus in a war of conquest against Cameria: "The Camerins had attacked the Roman people at a time when the city of Rome suffered an epidemic of plague"<sup>48</sup>. In the year 638 B.C., Marcio Anco was elected king, and he called for a meeting where he mentioned that religious beliefs must be neglected, so the gods punished with many pestilences, causing a large part of the population to die<sup>49</sup>. Livy's first reference to epidemics is in 466 B.C. when Quintus Servilius Priscus (consul) was sent against the Aequi, but his army was infected by an epidemic, forcing him not to attack<sup>50</sup>. In 463 B.C., elections were held, and Lucius Eburcius Helva and Publius Servilius Priscus were elected consuls. Livy mentions that "that year was notable for the great pestilence that swept through both the city and the countryside, affecting both cattle and men. The virulence of the epidemic was aggravated by the overcrowding of the city by rural people and their cattle frightened by enemies. The constant contact between them contributed to the spread of the disease. While Rome was attacked by the Aequi and the Volscians, who ravaged its borders with a huge army, the city of Rome was ravaged by the plague sent by the wrath of the gods. The enemy went to destroy the fields of Rome. However, they were already devastated without having suffered war; the enemies found no one, not even an unarmed peasant, and after touring the country, they abandoned it, as its defenders had already abandoned it. Both consuls died, and most of the leading men were affected, as well as the senators and military men"<sup>51</sup>. In 451 B.C., Dionysius of Halicarnassus reported an epidemic in which almost all the slaves of the city and about half of the Roman citizens died. The plague

lasted for a year and was spread by throwing the infected corpses into the sewers and the river, contaminating the drinking water and the air instead of burying them<sup>52</sup>. Livy mentions that in 436 B.C., "the armies were led into the Veientine and Faliscan territory, but there was no enemy in the open field and no reason to fight. Their cities were not attacked because they were suffering from a new epidemic; the following year, the epidemic worsened"<sup>53</sup>.

The Romans believed in a divine religious origin and punishment as the cause of these epidemics. This is how Dionysius described it: "The cause of the epidemic was the loss of virginity of a vestal (priestess dedicated to the household goddess Vesta), who was then persecuted so that the gods were pacified and the epidemic could end." To appease the divine punishments of the epidemics, the Romans also established the Lectisternium, a huge banquet to which the deities represented by statues were invited. In 363 B.C., a new epidemic broke out, which spread for several years and caused many deaths. Rome initiated a ritual called "the Dictator of the Nail," which consisted of driving a nail on September 15 to the temple of Jupiter (the main god of Roman mythology), specifically in the wall that faced the temple of Minerva (goddess of wisdom and the arts in Roman mythology), to appease the divine wrath that manifested itself with an epidemic<sup>54</sup>. The Roman chronicles describe two other occasions in which this ritual was used; the first was carried out by the general Gaius Petelio Libo Visolo in 313 B.C. in the face of an epidemic that arose during the war against the Samnites. A second was carried out in 263 B.C. by Fulvio Máximo Centumalo to contain an epidemic during the displacement of the Roman armies to Sicily during the first Punic War<sup>55</sup>. Around 300 B.C., an epidemic was recorded that may be the earliest evidence of the existence of the bubonic plague<sup>56</sup>. In the year 212 B.C., during the Second Punic War, Livy reported an epidemic in the city of Achradina (in Sicily), which was besieged by the Roman general Marcellus: "At first, it was the climate and the location that caused sickness and death, but soon the disease spread by contagion or by caring for the sick. The population could not keep up with the burials, and some chose suicide as a way out. The armies were aware of the contagion. The Carthaginian army dispersed and returned to their cities; the Romans were also affected but to a lesser extent. The Carthaginian general Himilco and the Syracusan rebel Hippocrates died of the plague, which contributed to the successful capture of Syracuse in 211 B.C.<sup>57</sup>. In 205 B.C., and again in 178 and 174 B.C., there was a plague in Italy: "It killed the cattle last year, but now

it began to attack man. Many people died, especially slaves, and the streets were littered with unburied corpses. In 125 B.C., a similar attack occurred in Cyrene<sup>58-60</sup>.

### Rise of the Western Roman Empire: Antonine plague and Cyprian plague

In 63 B.C., Caesar Octavius, known as Octavian and later as Augustus, was born, establishing the Principality form of government and becoming the first Roman emperor. During the reign of Emperor Nero, Suetonius wrote that there were 30,000 deaths caused by a plague in a single fall<sup>61</sup>. In 69 A.D., a general named Vespasian took power and founded the Flavian dynasty, creating one of the Empire's greatest symbols, the Flavian Amphitheater or Colosseum<sup>62</sup>. During the early reign of Titus, son of Vespasian, there were great disasters such as the eruption of Vesuvius in 79 A.D., which destroyed Pompeii and Herculaneum, a fire in Rome in 80 A.D. and an epidemic of the plague<sup>63</sup>. After these events, the whole Empire was governed with virtue and wisdom, it was called the time of the "Good Emperors" or the "Antonine Dynasty," from Nerva to Commodus<sup>64</sup>. During this dynasty, in 161 A.D., Marcus Aurelius, known as the "wise emperor," came to the throne. During his reign, he triumphed in the Parthian wars between 162 and 166 A.D. This war brought two consequences: a weakening of the Danubian border with the beginning of the Marcomanni war, and a plague that entered the Empire<sup>65</sup>.

The first post-Christian pestilence of which we have sufficient information refers to a plague brought by the legions on their return from the East after a military victory against the Parthian Empire (155 A.D.). The magnitude of the disaster is unknown, but it must have affected Rome so severely that in the year 167 A.D., it is described as follows in the Augustan History: "The dead were carried away in carts, the plague killed thousands of people, including aristocrats." It is known that this plague lasted for a long time, claiming victims even 10 years after its initiation<sup>66</sup>. It is considered the first pandemic because it affected all the provinces of the Roman Empire and even caused the death of the Emperor Marcus Aurelius. The emperor requested the intervention of Galen, who cited this plague and compared it to the one described by Thucydides<sup>67</sup>. Roman cities were densely populated and closely interconnected, facilitating the spread of infectious diseases. This first major pandemic to affect the Roman complex was called the "Antonine Plague" (165-180 A.D.) or "Galen's Plague," which occurred in several waves.

Claudius Galen described it when he visited the emperor, and today it is considered smallpox. It has been calculated that it had a mortality rate of almost 10% of the population, which means that it claimed the lives of 7 to 7.5 million people in a population of almost 75 million<sup>68</sup>. The symptoms of those infected included vomiting, diarrhea, fever, and ulcers that covered the entire body. Some lost their memory in the final stages of the disease. Galen himself describes it as follows: "Black or dark purple rashes, which dry up and fall off the body after a few days, ulcerative pustules all over the body, diarrhea, fever, loss of voice due to sores on the face; between the 9<sup>th</sup> and 12<sup>th</sup> day after the appearance of the rash, the most severe form of the disease occurs, which is the one that causes the highest mortality rate"<sup>69</sup>. A plague with similar symptoms described in China's Han Dynasty supports the possibility that the pandemic originated in China and traveled east through the Silk Road. In Rome, the situation was so critical that it is said that about 2000 people died every day. The crisis hit the economy of the Empire, there were closures of companies, especially those of construction. This situation encouraged the barbarian invasion of the Rhine<sup>67</sup>. During the reign of Emperor Commodus (son of Marcus Aurelius), another epidemic struck Rome and was called the "Second Plague or Epidemic of Commodus" (189-190 A.D.). It is mentioned that there were more than 2000 daily deaths in Rome in 189 A.D. The death of animals is added to the description, a circumstance for which it is thought that it was another epidemic different from the Antonine, perhaps more similar to the one that occurred in 463 B.C., 428 B.C. described by Titus Livy and the one in 451 B.C. described by Dionysius of Halicarnassus. It was reported that Emperor Commodus fled from Rome to Laurento on the advice of his physicians<sup>70</sup>.

From 198 to 250 A.D., the Roman world was free of epidemics. At the end of the war with the Goths, a new epidemic was described by the Bishop of Carthage, San Cipriano, known as the "Plague of Cipriano" (251-266 A.D.). It is said to have originated in Ethiopia and to have spread throughout the known world, from Egypt to Scotland, lasting 16 years. The best testimony is given by Cipriano, who describes a disease with diarrhea, vomiting, abdominal pain, generalized decay and fatigue, sore throat, necrosis of the limbs, red eyes, and loss of hearing and vision. For years, attempts have been made to determine the etiology, and it has been proposed that it was a hemorrhagic viral disease similar to Ebola, but this has not been proven. Others mention that it may have been the arrival of childhood



diseases such as measles or smallpox in Mediterranean countries. Ancient accounts agree on a high mortality rate. For example, in Alexandria, a city that had about 500,000 thousand inhabitants, almost 60% of the population could have died (300,000 people), while in Rome, Emperor Claudio Gotico died because of this pandemic. Many stories from the time mention that the plague was so great that it threatened the survival of the Empire. The Augustan History mentions that the epidemic was so great in Rome that up to 5000 people died in a single day and that entire cities were left empty for fear of contact, for which distancing was then understood as a measure to avoid catching the disease. After the pandemic, the Empire would never regain its glorious past, and the decline of Rome began<sup>70</sup>.

During the third century A.D., the first instability of the Roman Empire began. Based on a military anarchy, the Godians, the soldiers called soldier emperors, and the Illyrian emperors rose to the throne. Faced with military weakness, the Empire began to suffer border breaches, mainly by the Ostrogoths and Visigoths on the Rhine and Danube and the Sassanid Persians in Syria and Mesopotamia. In 284, Diocletian won a military victory and was proclaimed emperor; he restored the governability of the Empire by establishing what he called the Tetrarchy. This system of government was based on the division of the Empire into four sectors, two of which were ruled by the Augustans and the other two by the Caesars, who were considered their legitimate successors and later became the Western and Eastern Roman Empires<sup>71</sup>.

## Ethical disclosures

**Protection of human and animal subjects.** The authors declare that no experiments were performed on humans or animals for this study.

**Confidentiality of data.** The authors declare that no patient data appear in this article.

**Right to privacy and informed consent.** The authors declare that no patient data appear in this article.

## Conflicts of interest

The authors declare no conflicts of interest.

## Funding

No funding.

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