

LARGE EPIDEMICS OF HEMORRHAGIC FEVERS IN MEXICO 1545–1815

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Abstract. In 1545, twenty-four years after the Spanish conquest of the Aztec empire, an epidemic of a malignant form of a hemorrhagic fever appeared in the highlands of Mexico. The illness was characterized by high fever, headache, and bleeding from the nose, ears, and mouth, accompanied by jaundice, severe abdominal and thoracic pain as well as acute neurological manifestations. The disease was highly lethal and lasted three to four days. It attacked primarily the native population, leaving the Spaniards almost unaffected. The hemorrhagic fevers remained in the area for three centuries and the etiologic agent is still unknown. In this report we describe, and now that more information is available, analyze four epidemics that occurred in Mexico during the colonial period with a focus on the epidemic of 1576 which killed 45% of the entire population of Mexico. It is important to retrieve such diseases and the epidemics they caused from their purely historical context and consider the reality that if they were to reemerge, they are potentially dangerous.

INTRODUCTION

In 1545, twenty-four years after the Spanish conquest of the Aztec empire, a disease that had never before been seen appeared in the highlands of Mexico. The illness was characterized by an acute onset of fever, vertigo, and severe headache, followed by bleeding from the nose, ears and mouth; it was accompanied by jaundice and severe abdominal and thoracic pain as well as acute neurological manifestations. The disease lasted three to four days, was highly lethal, and attacked mainly the native population, leaving the Spanish population almost untouched. The epidemic of 1545 covered Mexico, lasted four years, and was responsible of approximately 800,000 deaths in the Valley of Mexico alone. At that time, Mexico had a population of 6.4 million inhabitants. The impact of this epidemic was immense; approximately 80% of the Indian population died during this epidemic.^{1–9} The disease was called *cocoliztli*, the word for pestilence in Nahuatl, a Uto-Aztecan language widely spoken in central and western Mexico.¹⁰ Both Aztec and Spanish physicians recognized that the disease differed from smallpox, measles, epidemic typhus, pertussis, and malaria. This hemorrhagic fever epidemic was the first in a series that ravaged Mexico from 1545 to 1815, a period that spans almost the entire colonial period.^{11–21}

The word and concept of *cocoliztli* appeared after the arrival of the Spaniards. Post-Hispanic Indian manuscripts represented the *cocoliztli* epidemics as a large number of dead bodies linked to a particular year.²⁰ *Cocoliztli* was also depicted as a skull over the glyph of a year, connected by a line to the figure of a dead Indian upside down, bleeding from the nose and mouth.²¹ During the Sixteenth and the first half of the Seventeenth Centuries, *cocoliztli* was associated with epidemics of hemorrhagic fevers. Reports of eleven more outbreaks of *cocoliztli* can be found, but the information about them is scarce. Those epidemics occurred in 1555, 1559, 1566, 1587–1588, 1592–1593, 1601–1602, 1604–1607, 1613, 1624–1631, 1633–1634, and 1641–1642.^{8,17}

One of the largest epidemics of *cocoliztli*, reviewed in detail below, began in 1576, causing at least two million deaths in Mexico, out of a total population of 4.4 million, representing a 45% mortality in the entire population.^{6,7} By

the time of the third large epidemic in 1736, the term *matlazahuatl* was in use, and it is unclear whether the use of a different name corresponds to a different disease. The epidemic of 1736 originated in the town of Tacuba, now part of metropolitan Mexico City. It killed 40,000 people in the city alone, out of 130,000 inhabitants; 30.76% of the city's entire population died. As before, this epidemic affected primarily the Indian population as it spread across the country.^{13,14}

A fourth large epidemic began in 1813 in the state of Morelos, in the city of Cuautla when the it was under siege during the Independence War. From there, the disease extended quickly throughout the country. In Mexico City out of a population of approximately 240,000, the epidemic caused 53,916 cases of disease with 8,271 deaths. Thus, 22% of the inhabitants became sick, and 3.4% of the population died. This epidemic was called “the mysterious fevers of the Year 13” because physicians did not recognize the disease, even though many of them were familiar with yellow fever which had been endemic-epidemic in the coastal region of the Gulf of Mexico from at least 1699.^{11,14,16}

In this report we describe the general aspects of four large epidemics of hemorrhagic fevers that occurred in Mexico during the colonial period and analyze the outbreak now that more information is available. These epidemics were highly lethal and damaged the Mexican population enormously for three centuries. The etiologic agent that caused this disease and its possible present-day persistence in the area are yet to be discovered. Today, there is no assurance that the hemorrhagic fevers will not return, making it compelling to retrieve these diseases and the epidemics they caused from their purely historical context, and to consider the reality that their possible reemergence makes them potentially dangerous.

HEMORRHAGIC FEVER EPIDEMICS IN MEXICO

Only information provided by contemporaneous witnesses was considered for this report. The characteristics of the epidemics of 1545, 1576, 1736, and 1813 are presented in Table 1. The fact that they share some characteristics and yet differ in other aspects has generated considerable confusion and controversy.^{8,12,22–24} The illnesses of all four epi-

TABLE 1.
Comparison of the characteristics of four large epidemics of hemorrhagic fevers in Mexico

Characteristics	Year of Epidemic ^{References}			
	1545 ^{3-6,9,46}	1576 ^{13,15,32-41}	1736 ¹³	1813 ¹⁶
Strong winds in the months before	Yes*	N.D.†	Yes	N.D.
Month first reported	August	June	April	April
Duration	4 years	2 years	3 years	2 years
Mortality (% of total population)	80.0	45.5	30.8	3.4
Affected Indians preferentially	Yes	Yes	Yes	Yes
Affected mainly young adults	N.D.	Yes	N.D.	N.D.
No sex preference	Yes	Yes	N.D.	N.D.
Death within 7 days	Yes	Yes	Yes	Yes
Acute onset	Yes	Yes	Yes	Yes
Recurrences	N.D.	Yes	Yes	Yes
High fever	Yes	Yes	Yes	Yes
Intense headache	N.D.	Yes	Yes	Yes
Chills	N.D.	N.D.	Yes	Yes
Bleeding from nose, mouth, ears	Yes	Yes	Yes	Yes
Jaundice	Yes	Yes	Yes	N.D.
Injected eyes	N.D.	Yes	Yes	N.D.
Abdominal pain	N.D.	Yes	Yes	N.D.
Chest pain	N.D.	Yes	Yes	N.D.
Intense thirst	N.D.	Yes	N.D.	N.D.
Dysentery	N.D.	Yes	N.D.	N.D.
Rigor	N.D.	Yes	N.D.	N.D.
Dark urine	N.D.	Yes	N.D.	N.D.
Retroauricular nodules	N.D.	Yes	N.D.	N.D.
Tremor	N.D.	Yes	N.D.	N.D.
Great anxiety	N.D.	Yes	N.D.	N.D.
Lip and genital ulcers	N.D.	Yes	Yes	N.D.
Rash	N.D.	N.D.	Yes	N.D.
Acute mental disorders	N.D.	Yes	N.D.	N.D.
Abdominal distention	N.D.	Yes	N.D.	N.D.
Constipation	N.D.	N.D.	N.D.	Yes
Diarrhea	N.D.	N.D.	N.D.	Yes
Nausea and vomiting	N.D.	N.D.	N.D.	Yes
Sweating	N.D.	N.D.	N.D.	Yes
Hepatomegaly	N.D.	Yes	N.D.	N.D.
Splenomegaly	N.D.	Yes	N.D.	N.D.
Lung hemorrhage	N.D.	Yes	N.D.	N.D.
Survivors were thin and weak	N.D.	Yes	N.D.	N.D.

*Yes = described as present.

†N.D. = Not described.

demics began with the acute onset of high fever followed by manifestations of bleeding, but may or may not have presented with rash, jaundice, acute mental disorders, or cutaneous ulcers. Since we do not know if the information about the epidemics of 1545, 1736, and 1813 is complete, any attempt to perform a detailed or comparative analysis is potentially flawed. Fortunately, the epidemic of 1576 is particularly rich in data. Many government officials,²⁵⁻³⁵ priests,^{6,14,36-39} historians,⁴⁰⁻⁴² physicians,⁴³⁻⁴⁶ and independent writers⁴⁷⁻⁵⁰ left testimonies with concordant information. Taking advantage of this, we will focus our discussion on this epidemic.

The epidemic of cocoliztli of 1576. The second half of the Sixteenth Century was a time of intense change in Mexico. Diseases such as smallpox, mumps, epidemic typhus, and measles were already circulating.^{48,51} Slaves were brought from Africa; hard work and high taxes were demanded of the indigenous Indian population. The construction of Spanish cities required large amounts of wood, so deforestation was intense. Numerous newly-introduced domestic animals and crops and new industries such as silver mining were widespread. There were constant wars with the

Indians of the North and conversion to the Catholic religion was an ongoing process. Under these general circumstances, cocoliztli reappeared, 31 years after the first outbreak.⁸

The presence of hemorrhagic fever, first reported in June 1576, expanded quickly and three months later was a source of massive mortality all over the country.³³ Reports of terrible human suffering came from all directions, from the sparsely populated dry plains of the north to the thickly populated subtropical valleys of central Mexico. Interestingly, the coastal populations were less affected.^{32,33} The wave of devastation reached from as far as Autlán, approximately 600 kilometers west of Mexico City³² to the city of Jalapa, 240 km east of Mexico City.³⁴ The degree of devastation in the highland cities was not uniform. For example, Tepeaca, 150 km southeast Mexico City, with a pre-epidemic population of 60,000 and a post-epidemic population of only 8,000, lost 86.6% of its citizens.³⁴ Cholula, 95 km east of Mexico City, had 15,000 inhabitants before the epidemic and 9,000 after it, a 40% death toll.³⁴ The town of Nochistlan, 450 km northwest of Mexico City, went from 1,500 inhabitants before the epidemic to approximately 500 after it, a reduction of approximately 66.7%.³² The global mortality

caused by this epidemic was estimated at approximately two million, from an original population of 4.4 million.^{6,37,50} Young Indian adults suffered the heaviest impact of the epidemic. Data from a census of victims of the Cholula epidemic indicate that 75% of deaths were in the age group of 25 years old or older. As a consequence of previous epidemics, only a small proportion of the population of people older than 50 years was left. In contrast, infant mortality was unchanged from previous years.²⁴ The epidemic primarily affected human beings, not other animals, since records show that in many towns only farm animals survived.³³ In most locations, the epidemic appeared and then disappeared more or less suddenly and lasted for approximately one and a half years, the first six months being the most deadly.^{6,14,47} In many places, new outbreaks were reported two years later,^{29,47} whereas in other areas, the disease was unremittingly active for at least six more years.³³ The disease disappeared and reappeared continuously in the whole affected area for at least twelve more years, always targeting the Indian population.³⁰ During the epidemic, the weather was reported to be cloudy, cold, and foul; the rainy season of 1577 started two months before it was expected and was especially intense.^{37,40,47}

Fray Juan de Torquemada, a Franciscan historian, described the magnitude of the epidemic of 1576 in Mexico City as follows:⁶

In the year 1576 a great mortality and pestilence that lasted for more than a year overcame the Indians. It was so big that it ruined and destroyed almost the entire land. The place we know as New Spain was left almost empty. It was a thing of great bewilderment to see the people die. Many were dead and others almost dead, and nobody had the health or strength to help the diseased or bury the dead. In the cities and large towns, big ditches were dug, and from morning to sunset the priests did nothing else but carry the dead bodies and throw them into the ditches without any of the solemnity usually reserved for the dead, because the time did not allow otherwise. At night they covered the ditches with dirt. . . . It lasted for one and a half years, and with great excess in the number of deaths. After the murderous epidemic, the Viceroy Martin Enriquez wanted to know the number of missing people in New Spain. After searching in towns and neighborhoods it was found that the number of deaths was more than two millions. . . .

The medical aspects of the epidemic were described by Dr. Francisco Hernández, the Proto-medico (Physician-in-chief) of New Spain and former physician of King Philip II of Spain,⁴³ Dr. Alfonso de Hinojoso, a physician of the Hospital Real de Indios,^{44,45} and Dr. Agustin Farfan.⁴⁶ Dr. Hernández and Dr. Hinojoso performed autopsies together and wrote reports independently. Their descriptions are similar. Dr. Hernández wrote:

The fevers were contagious, burning, and continuous, all of them pestilential, in most part lethal. The tongue was dry and black. Enormous thirst. Urine of the colors sea-green, vegetal-green, and black, sometimes passing from the greenish color to the pale. Pulse was frequent, fast, small, and weak—sometimes even null. The eyes and the whole body were yellow. This stage was followed by delirium and seizures. Then, hard and painful nodules appeared behind one or both ears along with heartache, chest pain, abdominal pain, tremor, great anxiety, and dysentery. The blood that flowed when cutting a vein had a green color or was very pale, dry, and without serosity. In some cases gangrene and sphacelus invaded their lips, pudendal regions, and other regions of the

body with putrefact members. Blood flowed from the ears and in many cases blood truly gushed from the nose. Of those with recurring disease, almost none was saved. Many were saved if the flux of blood through the nose was stopped in time; the rest died. Those attacked by dysentery were usually saved if they complied with the medication. The abscesses behind the ears were not lethal. If somehow their size was reduced either by spontaneous maturation or given exit by perforation with cauteries, the liquid part of the blood flowed or the pus was eliminated; and with it, the cause of the disease was also eliminated, as was the case of those with abundant and pale urine. At autopsy, the liver was greatly enlarged. The heart was black, first draining a yellowish liquid and then black blood. The spleen and lungs were black and semi-putrefacted. The bile was observed in its container. The abdomen dry. The rest of the body, anywhere it was cut, was extremely pale. This epidemic attacked mainly young people and seldom the elder ones. Even if old people were affected they were able to overcome the disease and save their lives. The epidemic started in June 1576 and is not over in December, when I am writing these lines. Of all New Spain, the disease invaded cold lands (highlands) in a perimeter of 400 miles, and had a lesser effect in lowlands. The disease attacked primarily regions populated by Indians here and there, then regions of mixed population of Indians and Spaniards, later the Ethiopians, and now, finally the Spaniards. The weather was dry and quiet, and disturbed by earthquakes, the air was impure, filled with clouds but without resolving into rain. . . . Very few with abdominal distention were saved. At the beginning, the blood was expelled by some without severe disease, then by very few. Vital energy was consumed quickly.

Dr. Hinojoso made additional observations. He reported that from onset to death, the disease lasted three to four days, and that on the second or third day, patients became insane and restless and were unable to stay in bed. He also mentioned that the eyes of the sick were red, and emphasized that their thirst was insatiable and that the nodules behind the ears were sometimes so large that they occupied the entire neck and half of the face. He also indicated that the fever was very high. Commenting on the autopsy findings, he described the liver as extremely enlarged and hard; he also identified splenomegaly.^{44,45}

Dr. Farfan's description of *cocoliztli* agrees with the others. He considered the disease so dangerous that he recommended that his patients prepare their wills and confess themselves as soon as possible.⁴⁶ Other reports point out that the jaundice was so intense that patients took on a greenish hue,⁴⁵ that the abdominal pain was very intense,¹⁵ and that survivors were left extremely thin and weak.^{26,40}

All witnesses mentioned that a striking aspect of this epidemic was its marked selectivity for the Indian population. Everywhere the disease was reported the Spanish remained almost untouched.^{4-16,32-35,37,47} This pattern of preference for the Indian population recalls the behavior of imported diseases such as smallpox, chickenpox, measles, and mumps, which induce protective immunity that is generally acquired at a young age. All Spaniards were newcomers to the country and had acquired immunity to those diseases back in Spain. Therefore, immune protection was effective only for the first generation of immigrants. Approximately 20 years after the conquest, the native populations had also developed some degree of immunity to those diseases that were then endemic-epidemic in Mexico.^{7,8} By 1576, the time of the second epidemic of *cocoliztli*, many of the children of the

first Spanish settlers, who were then between 0 and 54 years-old, helped the sick Indians,³⁸ but reportedly none of them died of the disease.⁴¹ It is unlikely that fifty-five years after the conquest the immune status of the Spanish immigrants could explain the selectivity of the disease for the Indians. A possible explanation for the increased susceptibility of the native populations may reside in the great socioeconomic differences between the Indians and the Spanish and their descendants. The vast majority of the Indian population lived in poverty and were undernourished.^{8,52}

The historian Juan Bautista Pomar observed that the separation line for the disease was marked by living conditions and that those “rich, well dressed, and with a comfortable living were not affected by the disease.”⁴ Cristobal Godinez, a government official reporting on the epidemic wrote: “. . . the reason why so many Indians die of pestilence is a God secret. I do not find any better answer than that in the past the Indians were not as badly mistreated and oppressed as they are today with heavy work loads. They are skinny and delicate, the disease finds them overworked and without resistance, so they are finished.”³² Under those conditions, the presence of an infectious agent favored by poor living conditions or nutritional deficiencies may well explain the pattern of the cocoliztli epidemic. It is important to remember that all epidemics of hemorrhagic fevers during the entire colonial period had a marked preference for the Indian population.^{1-5,12-16,32-47}

The dissimilar occurrence rate of cocoliztli among Indians and Spaniards could be explained by two possible processes. The first is that the transmission mechanism was unique to Indians. The second is that the Spaniards were truly immune to the disease, resisting it even when they were repeatedly exposed to the infection. A third possibility is that both circumstances coexisted during the epidemic. It seems that the Spanish population was indeed resistant to the disease. Members of several religious orders, particularly Franciscans and Jesuits, worked in opening new hospitals, assisting the ill, treating, feeding, bleeding and transporting the diseased, confessing the moribund, and organizing mass burials for the dead. Autopsies were performed without gloves or other protective gear. Only a few of the priests and none of the doctors acquired the disease and died even though they were constantly exposed to infection in many ways.^{14,38,39,43-46} The fact that attending personnel were not affected by cocoliztli strongly suggests that the disease was not transmitted by aerosols, fleas, casual contact, or even contact with blood and secretions. Living in the proximity of the epidemic was not a risk factor; even if the disease were waterborne or transmitted by mosquitos, the Spanish were still resistant to it. Spaniards lived in blocks contiguous to the Indians and had extensive social contact with them.^{8,52} Mexico City was surrounded by a lake and numerous water channels that criss-crossed Indian and Spanish neighborhoods. The origin and distribution of fresh water in the city was the same for both populations as was the case in most human settlements around the country.⁸

The dissemination of the epidemic of cocoliztli throughout the Indian population resembles that of the then-recent epidemics of smallpox, chickenpox, and measles—diseases with a person-to-person transmission mechanism. However, the existence of a vector or a reservoir for cocoliztli cannot

be excluded. The geographical distribution of the epidemic is interesting. All authors refer to the fact that the coastal regions were less affected.³²⁻⁴⁷ This means that if the disease were present, it probably had a defective transmission, or alternatively, that it was equally contagious but less lethal in those regions. This last possibility assumes the existence of more benign forms of the disease, which was probably true. Several reports indicate the existence of variants of the disease. Andrés Cavo, an historian, noted that the few Spanish priests who died during the epidemic “did not die of pest but by another disease similar to it. . .”⁴⁰ An interesting report from the town of Tenamaztlan (today Tenamaxtlán), located in a tropical valley approximately 600 km east of Mexico City, notes “This past epidemic of the year seventy-seven caused more damage in the cold (high) lands than in the hot (low) lands. In this place almost nobody died, although everybody got the pest, all of them reached the end of the disease and with little care they all convalesced.”³² It seems that depending on the geographic location and the social conditions, the causal agent of cocoliztli was capable of producing several forms of disease, ranging from mild to highly lethal.

Many diseases must be considered for the differential diagnosis of cocoliztli: primarily hemorrhagic fevers caused by flaviviruses (yellow fever and dengue), Bunyaviridae (hantaviruses, Rift Valley hemorrhagic fever, and Crimean-Congo hemorrhagic fever), arenaviruses (Lassa, Argentine hemorrhagic fever [Junin], Bolivian hemorrhagic fever [Machupo], Venezuelan hemorrhagic fever [Guanarito], and Brazilian hemorrhagic fever [Sabiá]), and filoviruses (Ebola and Marburg). Other diseases that can be included because they cause highly lethal outbreaks are epidemic typhus, plague, anthrax, leptospirosis, malaria, diphtheria, pertussis, louse-borne relapsing fever, and influenza.

Dr. Hinojoso and Dr. Farfan made a clear distinction between epidemic typhus (tabardete) and cocoliztli. One difference, in both descriptions, is that tabardete included a rash while cocoliztli did not,⁴⁴⁻⁴⁶ refuting the possibility that cocoliztli is epidemic typhus. The absence of a rash in cocoliztli makes infections by filoviruses such as Ebola and Marburg unlikely. The notorious lack of respiratory symptoms in cocoliztli leads to the dismissal of influenza, pertussis, and diphtheria. Malaria, known in Mexico at the time of the epidemic as tertian fevers, was caused by *Plasmodium vivax*.^{32,33} Fever due to *Plasmodium falciparum* in a non-immune person manifests intermittent irregular spikes, whereas in cocoliztli, fever ran continuously high. Besides, none of the reports written during the epidemic or afterwards mentioned cyclical fevers. The geographical distribution of malaria and cocoliztli also differs. In Mexico, malaria is more prevalent in coastal areas, while cocoliztli affected preferentially the highlands and was much less aggressive on the coasts. Thus, malaria can also be discarded as a possible cause of the epidemic. Anthrax is another disease that can be excluded because in intestinal anthrax, the clinical manifestations are centered in the gastrointestinal tract, while in cocoliztli they were not. In the case of respiratory anthrax, the severe hemorrhagic and neurological manifestations of cocoliztli are absent. Plague is also a disease that may cause large epidemics with high mortality. It shares some characteristics with cocoliztli such as high fever, restlessness, agitation, low blood

pressure, and the presence of subcutaneous masses (buboes). However, patients with cocoliztli had marked jaundice, severe bleeding manifestations, and injected eyes which are not part of the classical description of plague. Several times in history, mixed epidemics of typhus and louse-borne relapsing fever produced large outbreaks with high mortality.⁵³ When considering the possibility of a mixed epidemic of typhus and louse-borne relapsing fever, we saw that the manifestations of cocoliztli were more severe, in particular the bleeding and the acute neurologic manifestations.

The acute and lethal course of cocoliztli is reminiscent of hemorrhagic fevers caused by flaviviruses, Bunyaviridae, arenaviruses, and leptospirosis, all of which have overlapping clinical manifestations.⁵⁴ Today, making a precise diagnosis based exclusively on clinical manifestations without geographical or laboratory data in a patient with severe hemorrhagic fever carries a high probability of error. There are, however, interesting similarities between cocoliztli and specific forms of hemorrhagic fevers. Leptospirosis is a highly polymorphic disease that matches many aspects of cocoliztli, with the exception of the large retroauricular and neck nodules. Most of the cited signs and symptoms of cocoliztli resemble classic yellow fever. Even the prominent retroauricular nodes might be interpreted as the parotiditis of advanced yellow fever, and Dr. Hernandez's description of the pulse as "becoming null," could indicate Faget's sign. Yellow fever appeared along the coast of the Gulf of Mexico during the Seventeenth Century, producing large outbreaks in surrounding areas, but it was always centered on the coast and affected Indians and Spaniards equally. The primarily coastal distribution is also true for dengue.^{14,20}

Over the years, several authors have proposed that diseases such as yellow fever, plague, influenza, leptospirosis, hepatitis, malaria, or typhus caused the epidemic of 1576.^{12,22,23} However, none of them has a satisfactory counterpart to the course and manifestations of cocoliztli. Despite some similarities, there is not a perfect match between cocoliztli and any other specific form of hemorrhagic fever. In fact, cocoliztli's particular selectivity for the Indian population makes it different from the rest of hemorrhagic fevers. Similarities are perhaps related to common physiopathologic mechanisms such as severe liver damage, capillary leak syndrome, and metabolic disturbances.

Cocoliztli was described concordantly by numerous witnesses in multiple locations and for a long period of time, meaning that it was not the result of sporadic or exaggerated descriptions nor a casual mix of different diseases, but a disease within its own right. The clinical, geographical, and social variability of the disease is intriguing. At this time we do not know if the disease was caused by one or by several related microorganisms. In any case, whatever microorganism caused cocoliztli, the resulting disease was highly infectious and deadly. Today, the etiologic agent(s) would be classified as extremely dangerous. In the last decades, several geographically-restricted arenaviruses and hantaviruses have been isolated on the American Continent. These are rodent-borne viruses that produce hemorrhagic fevers which cause high mortality. Their presence is probably ancient and perhaps more agents remain to be discovered.^{55,56} It is not unlikely that the virus that caused cocoliztli remains hidden in the highlands of Mexico. The constant outbreaks of cocol-

iztli in the same area for a period of at least one hundred years indicate the existence of an endemic life cycle of a hypothetical etiologic agent.^{6,17,47} The last epidemic of hemorrhagic fever ended 185 years ago, a very short period of time in terms of a historical time-line. For more than two thousand years before the conquest and at intervals of hundreds of years, entire civilizations in Mexico collapsed in the midst of their splendor, perhaps victims of devastating epidemics,^{57,58} possibly caused by hemorrhagic fevers. The high mortality ranging up to 80% of the entire population⁹ observed during the epidemics of the colonial period may explain the sudden perplexing changes in the pre-Hispanic population.

Cocoliztli was an emerging disease of its time and it appeared at a time of intense social and ecologic change. The illness ran without control and caused catastrophic damage to the Indian population for at least a century. Today, there are no reported human or animal diseases resembling cocoliztli in the area. The disease has not been reported for a long time and the probability of an epidemic reemergence remains unknown. As for potential risk factors, it is important to remember that poverty, a key element in the epidemic, remains prevalent in some areas formerly affected by the disease. In the small towns around the city of Tehuacán, in the state of Puebla where cocoliztli once flourished, the word cocoliztli is still used as synonymous with lethal disease. Perhaps it is only representative of a historical vestige, but if the word and the concept remain active, we may well wonder if the etiologic agent is also alive and waiting to emerge again.

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