Essay

Outbreaks and epidemics investigations: changes in theories, concepts, and practices from the 18th to the 21st century

Investigação de surtos e epidemias: transformações na teoria, nos conceitos e nas práticas do século XVIII ao século XXI

Rita Barradas Barata[a]
https://orcid.org/0000-0002-7215-9788
E-mail: rita.barata@fcmsantacasasp.edu.br

[a] Faculdade de Ciências Médicas da Santa Casa de São Paulo. Departamento de Saúde Coletiva. São Paulo, SP, Brasil.

Abstract

This essay aims to discuss the investigation of outbreaks and epidemics, from the first reports available in scientific literature from the 18th century to the present time, using scientific articles and books on the subject for its construction. The main argument developed is the transition from qualitative approaches of epidemiology, which predominated in the early periods, to the quantitative approach, which initially coexists with the qualitative one but became dominant from the second half of the 19th century. It concludes with a brief reflection on the current moment of confronting the COVID-19 epidemic.
Keywords: Epidemiological Investigations; Outbreaks; Epidemics; Methodological Approaches; Historical Perspectives.

Correspondence
Rua Dr. Cesario Mota Jr 61. São Paulo, SP, Brasil. CEP 01221-020.

Resumo

Este ensaio objetiva discutir as investigações de surtos e epidemias, desde os primeiros relatos disponíveis na literatura científica do século XVIII até o momento atual, utilizando para sua construção artigos científicos e livros sobre a temática. O principal argumento desenvolvido é a passagem de abordagens qualitativas da epidemiologia, predominantes nos períodos iniciais, para a abordagem quantitativa, que inicialmente convive com a qualitativa, mas se torna dominante a partir da segunda metade do século XIX. Conclui-se com uma breve reflexão sobre o momento atual de enfrentamento da epidemia da covid-19.

Palavras-chave: Investigação Epidemiológica; Surtos; Epidemias; Abordagens Metodológicas; Perspectiva Histórica.

Background

The transition from feudalism to capitalism was marked by the resurgence of major epidemics, the main factors being maritime trade routes, population growth, urban density, the African slave trade, among others.

During the Renaissance period, the theory of contagion predominated as an explanation for these occurrences. Contagion was conceived as the direct passage of some physical or chemical influence from a sick person to a susceptible one, by contact or the atmosphere, via fomites. Epidemics were seen as the result of importation, that is, the sick arrived from elsewhere, introducing the disease into areas where it did not occur or did not present the epidemic form. Control measures were based on the establishment of cordons sanitaires intended to isolate affected areas of quarantines, usually in ports, to prevent the passage of the sick (Ackerknecht, 2009).

From the Enlightenment onwards, the miasma theory took hold among engineers and doctors, based on the opposite idea: that diseases were produced locally and resulted from climatic, meteorological, and topographical factors, as well as from chemical transformations from the putrefaction and deterioration of dead plants and animal tissues, which altered the quality of the air and thus affected the population. Epidemic periods were then triggered by abrupt changes in these constituents. In general, throughout the 17th, 18th, and 19th centuries, the miasma theory associated diseases with the dirt and filth that dominated large urban agglomerations and major port cities in Europe and the Americas (Ackerknecht, 2009).

Epidemic investigations took place even before epidemiology was established as a scientific discipline, relying exclusively on qualitative descriptions of the various environmental conditions and the inhabitants of the affected places, occasionally counting the deaths that the physicians were aware of.

Both contagionists and anti-contagionists strove to gather data and facts that confirmed their theories, often analyzing the same data in different light. Normally, the contagionists were in the majority among the military doctors and the state bureaucracy, whereas the anti-contagionists had liberal physicians in their ranks, advocates of free trade and movement of people, opposing quarantines and cordons sanitaires as useless and misguided measures. The main argument against the contagionists was that there were sufficient reasons in the affected places for epidemics to develop there, and there was no need to look for an explanation in the importation of the sick. Consequently, control measures should be based on improving urbanization conditions, basic sanitation, personal hygiene, isolating the sick, and disinfecting homes.

This essay aims to highlight the characteristics that prevailed before epidemiology was established as a scientific discipline and the transformations that took place at the end of the 19th century, with the contributions of microbiology, which led to the developments that came to constitute the epidemiology of communicable diseases throughout the 20th century. As the literature on the subject is very vast, the selection of texts for this investigation was based on the author's choices in order to typify the different moments and the main changes in epidemiological practices, within the limits of the article's length.

18th century: some examples

During the yellow fever epidemic in Philadelphia in 1793, there was a major dispute over narratives, with both sides accumulating various pieces of evidence in favor of their respective points of view. From the contagionists' point of view, the epidemic was attributed to various factors, all of them external: the arrival in large numbers of white farmers who fled Haiti as a result of the revolt of the slaves, the arrival of sick people from the crew of ships coming from Jamaica, a significant increase in the density of mosquitoes in a very hot summer with few torrential rains, etc. (Middleton, 1928).

On the anti-contagionist side, various physicians in private practice advocated that the epidemic held local causes, resulting both from the rotting of a cargo of coffee in the port district and from plant rotting processes in the swamps, lakes, and backwaters of the Delaware River during the intense summer, as well as the passage of a comet months before the first community cases appeared (Middleton, 1928).

The investigations gathered qualitative data related to environmental aspects or population displacement, and there was no systematic way of synthesizing data or concern with describing the distribution of cases and deaths. There was no systematic recording of health events, and each physician tried to obtain information from their peers to decide whether or not there was an ongoing epidemic. It was not uncommon for professionals to doubt the presence of epidemics, attributing cases of disease to habitual occurrences and seasonal variations. Middleton (1928) refers to the occurrence of around 4,000 deaths and the decline of the epidemic after sanitation measures, such as draining the swamps, planting trees, and cleaning the port and the city streets.

The report of a French military physician on the yellow fever epidemic in Gibraltar in 1828 presents both arguments in favor of the contagion theory and arguments against the anti-contagion hypothesis. The report is written objectively, arguing that the areas in which the division was quartered shared the same climatic conditions as those prevailing in Gibraltar, without the French soldiers having been affected. The city of Gibraltar was quite clean, situated on an elevated terrain, and well ventilated, without the dirt and filth usually claimed by anti-contagionists as a trigger for epidemics. On the other hand, there were many ships from the West Indies (Caribbean) that crossed the strait, disembarking sick crew members who then introduced the disease, not only to Gibraltar, but from there to other locations on the Iberian Peninsula. This report exemplified a more objective form of epidemiological analysis, based on comparisons to draw conclusions and not just a one-sided piece of argumentation (Guyon, 1830).

The accounts by Middleton (1928) and Guyon (1830), chosen for the contrast in the form of argumentation they present, are exemplary of the countless reports produced about epidemics in the 18th and early 19th centuries. All of them use detailed accounts, with no concern for quantifying the phenomenon or its population distribution.

What differentiates the various narratives is the greater or lesser use of logical and comparative arguments that go beyond simple description.

19th century

At the turn of the 18th to the 19th century, Charles Maclean, a Scottish physician who had been to India and other parts of Asia, upon his return to England, began to actively shift the locus of epidemiological discussion from the medical colleges and specialist societies to the public arena, in the form of a newspaper debate for the lay population. At the same time, he began to pressure Parliament to set up commissions of inquiry to discuss the causes of epidemics and review the adoption of quarantines and cordons sanitaires (Kelly, 2008).

Although the popularity of Maclean's theses in the press was enough for parliamentary committees to be convened, their outcome was not what was hoped for. In the first commission, set up in 1819, Parliament concluded that there was not enough evidence to definitively abandon the theory of contagion. However, the commission established in 1824 concluded that quarantines were in fact very costly for England and that they should be used more sparingly, with a shorter duration, and reduced penalties for non-compliance.

Maclean's actions clearly shows the politicization of epidemics and outbreaks, as well as the concern with the economic consequences of control measures. The disputes between contagionists and anti-contagionists not only took place in the scientific field, but were "contaminated" in real life with their economic and political interests.

In the period from 1820 to 1867, the miasma theory became dominant in America and Europe, with fewer and fewer defenders of the contagion theory. The investigation of the typhus epidemic in Silesia, conducted by Rudolf Virchow in 1848, is an example of the investigations proposed by supporters of the miasma theory who aligned themselves with social medicine.

With only 15 days in the area, Virchow's report (2006) analyzes the historical, cultural, socioeconomic, and political conditions of the inhabitants of Upper Silesia, describing the history of the region, the wars, and changes of dominion until subordination to Prussia. The geographical and geological conditions of the territory are described, as well as the composition of the population, which includes Poles, Germans, and Serbs. Virchow (2006) characterizes typhus victims as a poor population, with no real alternatives for obtaining economic sustenance, subject to constant famines, subjugated by the Catholic religion, with poor hygiene habits, precarious housing, and a high frequency of alcoholism.

Virchow (2006) concludes that the typhus epidemic was caused by extreme poverty, agglomeration in enclosed spaces, exhalation of excrement from animals sheltered in the same places, and the putrefaction of animal meat, giving rise to the pestilential miasma, which, according to him, differentiated epidemic cases from those observed in the endemic form.

An important change in the way epidemic investigations were conducted occurred in England, with the appointment of William Farr to the General Register. England had a system for reporting epidemic diseases, created by royal decree in 1603. During the 17th and 18th centuries, these records were used only to count cases or deaths, and did not produce analyses, other than trend analyses, of the impact of epidemics on mortality statistics.

William Farr introduced the systematic use of calculating death rates and, in the 1831 cholera epidemic in London, analyzed the spatial distribution of deaths, identifying nine areas with the highest concentration of cases, most of them in neighborhoods located along the banks of the River Thames. Farr believed that epidemics, like disease in general, were social phenomena that could be prevented and controlled by improving the urban environment. He carried out an ecological analysis, demonstrating that there was an inverse proportionality between cholera mortality and the altitude of London neighborhoods, a fact that he interpreted as confirming the miasma theory, since the neighborhoods located on the banks of the river were more subject to miasmas, which remained more stagnant in these locations (Eyler, 1973).

With the publication of John Snow's work on the 1848-1849 epidemic, which suggested that cholera was a contagious disease and that the "poison" responsible for its production was ingested from food and water contaminated by the waste of the sick, Farr decided to analyze the areas most at risk in relation to the source of water supply, since various private companies operated in this sector in the city of London. He analyzed mortality in neighborhoods in which only one company was responsible for supplying all households, excluding areas in which more than one entity was involved in water supply. In this analysis, Farr found no differences in mortality rates among neighborhoods supplied by different companies (Eyler, 1973).

In his work, Snow presented descriptive data showing that the time intervals between the arrival of cholera on the European continent, its movement to England, and its spread inland from the port cities were never shorter than the time of human movement, suggesting that the sick were responsible for introducing the disease. Finally, he reported some investigations into clusters of cases, in which the contamination of water by the contents of the cesspools was evident (Underwood, 1948; Eyler, 2001).

The evidence gathered by Snow was not considered sufficient by the members of the Royal Society of Medicine, nor did it convince the local health authorities. In the next epidemic, that of 1853-1854, influenced by the data produced by William Farr—which showed a greater risk of infection in the area of the South district, supplied by two companies, one of which had changed the collection site to a less polluted area—Snow conducted a house-to-house survey, thus showing a greater risk in the houses served by the company that collected water in the most polluted area. In addition, the data collected in the Broad Street outbreak in Soho was also more robust than that previously presented. This new publication by Snow practically turned the tables, and many anti-contagionists began supporting the contagion theory in the case of cholera (Eyler, 1973; Underwood, 1948; Snow, 1990).

Both Farr's and Snow's work show that epidemiology provided investigations into outbreaks and epidemics with a methodology for analysis and tools for quantifying risks that had not been used before. Farr, in his initial works, used the tools of descriptive epidemiology to analyze the distribution of deaths over time, space, and according to population characteristics, whereas Snow sought to characterize each outbreak by analyzing individualized information, mapping the residences of cases and deaths, investigating the source of the water supply in each case, and analyzing situations that deviated from the expected, such as the brewery and workhouse not affected during the Broad Street outbreak, both supplied by artesian wells (Underwood, 1948; Snow, 1990).

Epidemiological observation in 1831, 1848, and 1853 allowed English sanitarians to realize that epidemics moved in successive stages, following trade routes and lines of communication, always arriving in England a year after reaching the European continent. From 1857 to 1866, there was a considerable improvement in English sanitary organization, with control of the quality of the water supply and control of ports to prevent the disembarkation of the sick. Health surveillance, isolation of the sick, and disinfection measures were adopted (Underwood, 1948; Hardy, 1993).

In 1851, the First International Sanitary Conference was held in Paris to examine the European position against cholera. On the continent, the defense of quarantine and cordons sanitaires predominated, which England opposed head-on.

Gradually, the English experience, based on surveillance and monitoring of notifications, isolation of the sick, home disinfection, and urban improvements, prevailed and became widely accepted on the continent. At the Seventh International Sanitary Conference, held in Venice in 1892, the English position of abandoning quarantines and adopting sanitary surveillance measures, improving water supply systems and epidemiological surveillance measures, such as isolation of symptomatic cases and disinfecting homes, prevailed (Hardy, 1993).

In the last decades of the 19th century, the discoveries of Louis Pasteur and Robert Koch, which gave rise to microbiology, changed the meaning of outbreaks and epidemics of contagious diseases, speeding up the identification of specific etiologies and putting aside the previous concern with characterizing the local context.

Therefore, the emergence of epidemiology as a scientific discipline in the field of public health changed the way outbreaks and epidemics were approached, providing a methodology for analysis that made it possible to consider the distributions according to time, space, and people who were affected, which helped identify the modes of transmission and guided the investigation of hypotheses about the process.

20th century

At the beginning of the 20th century, some epidemiologists were concerned not to lose sight of the social determinants of epidemic diseases in the face of the avalanche of microbiological discoveries, which threatened to completely isolate the contextual aspects of both public health knowledge and practice.

In the very first decade of the 20th century, the investigation of pellagra in South Carolina was an example of the preservation of the principles of social medicine in the investigation of diseases. Pellagra cases were considered infectious and attempts were made to find the etiological agent of the disease. Notably, neither vitamins nor the harmful effects of a lack of them were known. Joseph Goldberger soon ruled out the hypothesis of an infectious disease, noting that in orphanages and other long-term institutions, only the inmates were affected, with no cases among professionals or staff in general (Goldbergerg; Wheeler; Sydenstricker, 1920).

To investigate the possible causes of pellagra, Goldberger planned an extensive investigation with the help of Edgar Sydenstricker, an economist and statistician with experience in household surveys. Seven villages dedicated to the cotton industry in South Carolina were studied. The population survey included demographic, social, and economic characteristics, as well as active house-to-house case finding every two weeks. Age- and sex-standardized rates were used to compare results among villages. The analysis of prevalence by income level showed an inversely proportional risk (Goldberger; Wheeler; Sydenstricker, 1920).

Thus, the main conclusion of the investigation was that there was an evident variety of factors of an economic nature which, due to their influence on the population's diet, conditioned the incidence of pellagra in the communities studied (Goldberger; Wheeler; Sydenstricker, 1920).

However, the major event in terms of infectious diseases in the first decades of the 20th century was the influenza pandemic of 1918, known as the "Spanish flu." Everywhere affected by the pandemic, around 25% to 40% of the population was infected and the lethality rate among symptomatic cases was more than 2.5% (Morabia, 2021).

The public health service of the United States of America (USA) carried out a population-based survey to estimate the incidence and mortality rate of the influenza pandemic in 18 cities in the country. The survey was coordinated by Wade Hampton Frost, first professor of epidemiology at the Johns Hopkins University School of Public Health, and Edgar Sydenstricker, from the Office for National Statistics (Morabia, 2021).

Just over 146,000 residents of the cities included in the survey were interviewed. Sydenstricker designed a cluster sample, drawing 10 districts in which all households were investigated. Thus, each city produced a sample of at least 5,000 residents. The age-adjusted rates were 30 cases per 100 inhabitants, 4.3 deaths per 1,000 inhabitants, and 1.7 deaths per 100 clinical cases. The incidence was highest in children aged five to nine and young adults aged 25 to 29. Although there was no difference in incidence between the sexes, lethality was higher in men. There was a clear gradient in incidence, mortality, and lethality, inversely proportional to socioeconomic status (Table 1). The same excess of cases and deaths was observed in the black population (Morabia, 2021).

Table 1 – Influenza incidence, mortality, and lethality according to socioeconomic status, USA, 1918–1919

Social level	Incidence per 100 inhab.	Mortality per 1,000 inhab.	Lethality per 100 cases
Good	25.0	3.8	1.5
Moderate	27.2	3.8	1.5
Poor	32.6	5.2	1.7
Very poor	36.4	10.0	2.8

Source: Data obtained from the article "The US public health service house-to-house canvass survey of the morbidity and mortality of the 1918 influenza," by Alfredo Morabia (2021)

The measures adopted to contain the influenza pandemic were social distancing, the mandatory use of masks, the isolation of all clinical cases, compulsory notification, disinfection, and respiratory hygiene rules (Morabia, 2021). It is interesting to compare the level of organization of the North American public health service with the descriptions made by Lilia Schwarcz and Heloisa Starling (2020) about the occurrence of the pandemic in Brazil. The way the pandemic was dealt with here is reminiscent of the investigations of epidemics described in the 18th century, that is, a set of assumptions without much practical or scientific basis, with attempts by the authorities to deny the evidence, difficulty in implementing control measures, and fatalistic behavior by the authorities and the population.

In the investigation of the North American national public health service, it is possible to identify the methods of analysis of descriptive epidemiology which, in general, remain to this day the main foundations of outbreaks and epidemics investigations. The household survey is designed to assess a representative sample of the country; age-adjusted rates are used to avoid selection bias in the estimates; and the behavior of the disease is described in relation to its population distribution according to time, place, and characteristics of the people affected, emphasizing socioeconomic, demographic, and ethnic inequalities.

During the first half of the 20th century, there was a profusion of research aimed at understanding the process of disease transmission and its population dynamics, which would establish new ways of carrying out investigations. Gradually, essential knowledge was developed about transmission modes, incubation period, transmissibility period, infection sources, and host susceptibility, all of which were necessary for proposing control measures.

In the middle of the last century, with urbanization and the growth of urban populations, cases of poliomyelitis in its paralytic form began to produce epidemics, especially in the summer months. The acute effects on preschool or school children and the permanent sequelae that the disease generated characterized it as a priority problem. Efforts to produce effective vaccines resulted in the production of the Salk vaccine, with inactivated viruses, and the Sabin vaccine, with live attenuated viruses (Oshinsky, 2005).

The licensing of the Salk vaccine in 1958 made large-scale vaccination possible, with a reduction in reported cases, which in the period from 1951 to 1954 had reached 24,000 cases per year, to about 1,000 cases in 1961. Various researchers considered that the Salk vaccine, being an inactivated virus vaccine, would only be able to protect vaccinated children and therefore the incidence would only fall if the coverage achieved was very high. Other researchers, however, expected that, if coverage was high, it could protect the unvaccinated, dampening and eventually suppressing the infection in the population (Stickle, 1964). The concept of herd immunity had already been formulated theoretically based on arithmetic models of exposure and susceptibility, but had not been demonstrated empirically.

In 1961, around 78% of the population aged under 20 had been vaccinated with the three doses of the Salk vaccine, thus allowing the existence or not of herd immunity to be assessed. Gabriel Stickle (1964), a physician and statistician, developed a study capable of answering this question. He calculated the number of expected cases of poliomyelitis, taking into account population growth and efficacy according to the number of doses received, projecting the occurrence of 8,471 cases in 1961. Comparing this number to what had occurred in the pre-vaccine period, he estimated a 65% reduction in the incidence of the disease, which could be attributed to the use of the vaccine. However, the cases notified in 1961 were only 1,000, showing an effective reduction of 96% in the incidence. In this way, the author was able to empirically demonstrate that the vaccine, even with an inactivated virus, was capable of producing herd immunity, that is, indirect protection for the unvaccinated, by reducing the number of susceptible people in the population.

Throughout the 20th century, the investigation of outbreaks and epidemics was an important tool for producing knowledge about the dynamics of communicable diseases and for practical intervention with a view to controlling, eliminating, or eradicating them.

With the creation of the World Health Organization (WHO), various vertical programs aimed at controlling certain diseases had been set up in the member countries, with greater or lesser success, depending on the structure and functioning of the pre-existing health systems. Precisely because of the precarious conditions in most countries, located outside the European continent and Anglo-Saxon North America, vertical programs were proposed, set up with technical assistance and partly financed with funds from international organizations. By the early 1960s, programs had already been set up to eradicate malaria, yellow fever, hookworm, and yaws, all without much success, and vertical programs came to be criticized and seen as detrimental to the development of a network of primary care services (Henderson; Klepac, 2013).

Despite this, the Union of Soviet Socialist Republics (USSR), in 1958, and the United States government, in 1965, asked the WHO for the General Assembly to discuss a proposal for the eradication of smallpox. According to the proponents, smallpox had some characteristics that would favor eradication initiatives: an exclusively human disease, a virus that did not show important variations, a clear clinical picture, an incubation period with little variation, and an effective vaccine, applicable in a single dose, stable, and not requiring refrigeration in the field, capable of being applied with the so-called bifurcated needle, which required no practice in use. Each vaccinator could administer up to 500 doses of vaccine a day and the immunity conferred was long-lasting, and produced a scar that made it possible to verify who had been vaccinated (Henderson; Klepac, 2013).

In 1966, the General Assembly approved the proposal for an eradication campaign, estimated to last 10 years, based on two main components: systematic vaccination of the entire population and active epidemiological surveillance. The identification of new cases promoted the isolation of the sick and containment vaccinations in the area of residence, aiming to interrupt the chain of transmission. There were 31 countries with endemic occurrence of smallpox when the program was approved (Henderson; Klepac, 2013).

By 1973, there were only five smallpox-endemic countries left in the world: India, Pakistan, Bangladesh, Nepal, and Ethiopia. In these countries, more intensive activities were instituted, including active case finding and house-to-house vaccination, until the last case of smallpox was recorded in Somalia in 1977 (Henderson; Klepac, 2013). All the knowledge that had been accumulated in the investigation of outbreaks and epidemics could be put at the disposal of this worldwide effort to eradicate smallpox, the only case of eradication of a disease, resulting from human intervention.

The expertise accumulated in the first half of the 20th century was of great help in investigating the emerging diseases that followed in the second half of the century. The profound and constant social transformations have been accompanied by the emergence of new communicable diseases, challenging epidemiological knowledge and the assumption that humanity could live without them. In the second half of the 20th century, the world's population experienced the emergence of AIDS as the most lethal of sexually transmitted diseases, in addition to various hemorrhagic fevers originating on different continents (Barata, 1997).

The AIDS epidemic is emblematic of the importance of epidemiological research, which is capable of guiding health services even before the etiological agent is identified, allowing us to learn about forms of transmission, progression, and dissemination of cases and the groups most affected by the disease. The suspicion of the presence of a new disease arose from the observation of clusters of cases of acute immunodeficiency in young people who had no previous immunological problems or the occurrence of Kaposi's sarcoma in a different age and ethnic group from usual.

Once it became apparent that something unusual was happening, the Centers for Disease Control and Prevention (CDC) began to investigate suspected cases to identify the epidemiological behavior of the disease and formulate hypotheses about causes, modes of exposure, dissemination, and groups at greater risk. Observation of the first thousand reported cases identified important characteristics: it really was a new disease, with an accelerated increase in incidence since the first case was recorded in 1981, affecting individuals aged from 10 to 73, with a concentration in the 30 to 39 age group, predominantly male (99.9%). Cases had already been detected in 32 USA states, with the highest concentration of notifications in the metropolitan areas of San Francisco, Los Angeles, Houston, Miami, Chicago, Newark, Boston, and New York. Almost half of the cases had *Pneumocystis carinii* pneumonia, around 25% had Kaposi's sarcoma, 10% had both manifestations, and the rest had different opportunistic diseases. Of the first 269 known cases, 73% had already died by the time the data was analyzed, demonstrating high lethality (Jaffe; Bregman; Selik, 1983).

There were various hypotheses about the causes of the new disease, predominantly suspicions of chemical intoxication or infectious disease. The first interviews with patients and their closest contacts seemed to suggest the possibility of a sexually transmitted disease, which was confirmed by analyzing the contact network between dozens of patients and a flight attendant, called patient zero to indicate the main node in the network (Auerbach et al., 1984). There were many misunderstandings about this designation, although at no time did CDC professionals consider this to be the index case of the epidemic.

The groups most at risk were male homosexuals, bisexuals, hemophiliacs, drug users, and Haitians, according to the classification created by the CDC at the time. The presence of hemophiliacs and drug users among the most affected groups raised the suspicion that there could be transmission by blood and blood products. There was a lot of resistance to accepting this possibility, before it was identified that the disease was in fact caused by an infectious agent, capable of being transmitted by contaminated blood transfusions or needles, although the CDC considered that there was sufficient evidence of contamination of drug users by sharing needles and of hemophiliacs by the use of coagulation factors obtained from donor pools that included people who had developed AIDS (Curran et al., 1984).

All these investigations conducted by the CDC made it possible to advance knowledge about the new disease even before its causal agent was identified, which only happened at the end of 1984, by the team from the Pasteur Institute in Paris. The isolation of the human immunodeficiency virus (HIV) enabled the development of diagnostic tests, thus providing new techniques for investigating the infection.

In the investigation of the AIDS epidemic, in addition to the traditional resources of descriptive epidemiology, sociological survey methods were used, such as social networking and laboratory resources which, after identifying the virus, were able to extend the scope to asymptomatic infected individuals. Similar resources have been used in the investigation of numerous other emerging diseases, such as the Ebola virus and other viruses.

The emergence of new epidemic infectious diseases with significant consequences for society, the economy, and the safety of the world's population has renewed interest in the epidemiology of communicable diseases, which had been obscured for much of the second half of the 20th century, when many believed that epidemics and outbreaks were a thing of the past, largely supplanted by chronic diseases in the epidemiological profile worldwide. Emerging diseases in the last decades of the 20th century produced an intellectual renaissance of this theme (Reingold, 1998).

Throughout most of the 20th century, investigations into outbreaks and epidemics were conducted based on a quantitative approach to the occurrence and distribution of events, defining their own methodology and combining concepts related to the chain of the infectious process, descriptive epidemiology, and population surveys, to the public health laboratory and the practical aspects of the interventions available to interrupt the transmission process.

21st century

The processes of globalization that intensified in the last decades of the 20th century remained active at the beginning of the 21st century, maintaining the conditions conducive to the emergence of new diseases which, with the potential to mobilize populations worldwide and the relative shortening of distances—resulting in the intensification of international air traffic—represent a constant challenge for global health.

An episode in which Brazil played a leading role, the emergence of major Zika virus epidemics in Latin American countries, marked a new stage in the investigation of outbreaks and epidemics, in which, in addition to the resources normally mobilized by epidemiology, networks of researchers from different disciplines in the biological and health fields were quickly mobilized.

The Zika virus had been identified in 1947 in the forests of Uganda, producing sporadic oligosymptomatic cases without demonstrating epidemic potential. The first epidemic manifestation was observed in Micronesia in 2007, followed by an epidemic in French Polynesia in 2013, in which there was a high rate of viral attack and cases of Guillain-Barré (reversible involvement of the peripheral nervous system) later associated with the disease. Apparently, that same year the virus arrived in Brazil, brought by a team of soccer players from Tahiti who took part in the Confederations Cup in Recife, as well as other travelers from areas where the virus circulates (Vogel, 2016).

About a year later, in November 2014, there was an epidemic of exanthematous disease in the Northeast of Brazil, characterized by rash, arthralgia, joint edema, and conjunctivitis, without high fever and with negative tests for dengue and chikungunya. Some physicians in Rio Grande do Norte suspect the Zika virus and, in February 2015, an epidemic of the disease was officially recognized in the country (Zanluca et al., 2015). In Pernambuco, cases of nervous system involvement began to be noticed in some patients (Guillain-Barré, meningoencephalitis, and encephalomyelitis). In August 2015, two neuropediatricians from public hospitals in Recife observed an increase in cases of microcephaly of unknown cause in newborns.

The epidemiological investigation teams of the Pernambuco State Health Department began an active search for cases of microcephaly in reference maternity hospitals for high-risk pregnancies, detecting 29 cases. At this point, the hypothesis of an association between microcephaly and maternal Zika virus infection was formulated, based on the observation of the spatiotemporal cluster, the neurological alterations common to the cases, the reports of symptoms compatible with Zika virus infection in the first trimester of pregnancy, and the laboratory demonstration of viral tropism by central nervous system cells. The confirmation of viral RNA in the amniotic fluid of two parturients whose fetuses were found to have microcephaly further strengthened clinical and epidemiological suspicions (Calvet et al., 2016).

As a result, the Brazilian Ministry of Health declared a public health emergency, setting up a microcephaly notification system and a task force to investigate the association. Controversies among specialists began to emerge regarding the definition of suspected cases based on cranial circumference, with disagreements between groups that intended to define a single measure and those who defended the use of growth curves to differentiate situations, in addition to the debate around the cut-off points to be adopted.

Another important controversy arose between the *Sociedade Brasileira de Genética Médica* (SBGM – Brazilian Society of Medical Genetics) and the members of the *Estudo Colaborativo Latino-Americano de Malformações Congênitas* (ECLAMC – Latin American Collaborative Study of Congenital Malformations). The SBGM defended the association between Zika virus infection and the occurrence of microcephaly, listing the evidence available in January 2016: the two cases mentioned of identification of the virus in amniotic fluid, 35 cases in which the mothers had lived or been in epidemic areas during early pregnancy, and 74% of mothers with compatible symptoms in the first two trimesters of pregnancy, according to a case-control study conducted in the process of investigating the epidemic (Schuler-Faccini et al., 2016). The ECLAMC members, on the other hand, claimed that the increase in microcephaly cases could only have been the result of an improvement in the recording of events, without any connection to the epidemic, since, until then, there had been no record of this occurrence in previous epidemics. In this episode, the difference between population-based epidemiological reasoning and clinical reasoning based on individual observations is clear. The members of the ECLAMC had not taken into account the fact that, until then, the epidemics occurring on islands and archipelagos with small populations had not reached proportions that made it possible to record relatively rare events such as microcephaly.

To investigate the causal relationship between exposure to the Zika virus during pregnancy and the occurrence of microcephaly, researchers from various research institutions in Pernambuco carried out a case-control study, which showed a higher risk among black or brown mothers (OR=3.5), smokers (OR=3.2), and those exposed to the virus. All cases and none of the controls had laboratory confirmation of Zika virus infection. There was no association between microcephaly and the vaccines received by mothers during pregnancy, exposure to larvicides used in vector control (in the water supply or elsewhere in the household), daily use of repellents, or occupational exposure to pesticides (Araujo et al., 2016).

Zika can be considered the first pandemic of congenital malformations produced by a vector-borne infectious agent. In addition, its occurrence constitutes the first report of congenital transmission of an arbovirus in humans, and also the first finding of sexual transmission of an arbovirus (Paixão et al., 2016).

However, the 21st century has only just begun, and it seems that we will not stop being amazed by the surprises it holds in store for us. We have just been through the COVID-19 pandemic, which has altered life on every continent in an unexpected and overwhelming way.

What was most striking about the episode we experienced was an apparent return to the end of the 19th century, when the rapid and ready identification of the etiological agent replaced epidemiological research efforts capable of answering questions about the population behavior of the disease. The arguments put forth revolved around the impossibility of identifying the processes of dissemination, given that this was not a restricted outbreak, but a broad pandemic with community transmission. Fortunately, this has never prevented epidemiology from making its contribution to understanding the phenomena in previous epidemics and from expanding knowledge and the capacity for intervention.

It is not very clear at what point it began to be thought that imperfect mathematical models, based on scarce data and a great deal of ignorance, could replace the investigation of epidemics in their real occurrence, with all the imperfections that have always marked this task over the centuries.

More recently, some descriptive epidemiology studies have been produced on the COVID-19 pandemic, which have helped us understand its population dynamics and distribution. In the city of São Paulo, a group of researchers analyzed deaths from COVID-19 recorded from March to September 2020, during the first wave of the pandemic, pointing to a higher risk for men (RR=1.84), Blacks (RR=1.77), mixed race (RR=1.42), residents of areas with a lower proportion of people with higher education, greater intra-household agglomeration, lower household income, and a higher concentration of *favelas* (Ribeiro et al., 2021). As is common in all epidemics, incidence and mortality were not the same for all social groups, disproportionately affecting those groups at a greater social disadvantage or belonging to the social classes with the worst integration into society.

In this brief historical review, we sought to portray how investigations into outbreaks and epidemics have changed over the centuries, incorporating different disciplinary knowledge from the field of health—especially public health and collective health—and always seeking to identify etiological agents, sources of infection, modes of transmission, and the groups most affected, in order to propose and institute measures to control and contain the spread of cases.

I conclude this essay with a quote from Michel Foucault (1975, p. 25), which portrays the challenge of investigating outbreaks and epidemics:

> [...] an epidemic has a sort of historical individuality, hence the need to employ a complex method of observation when dealing with it. Being a collective phenomenon, it requires a multiple gaze; a unique process, it must be described in terms of its special, accidental, unexpected qualities.

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Authors' contributions

Barata conceived the article, selected the texts for elaborating the essay, wrote, and revised the text.

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