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Protection against severe infectious disease in the past

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ABSTRACT

Before the 20th century many deaths in England, and most likely a majority, were caused by infectious diseases. The focus here is on the biggest killers, plague, typhus, smallpox, tuberculosis, cholera, typhoid, dysentery, childhood infections, pneumonia, and influenza. Many other infectious diseases including puerperal fever, relapsing fever, malaria, syphilis, meningitis, tetanus and gangrene caused thousands of deaths. This review of preventive measures, public health interventions and changes in behavior that reduced the risk of severe infections puts the response to recent epidemic challenges in historical perspective. Two new respiratory viruses have recently caused pandemics: an H1N1 influenza virus genetically related to pig viruses, and a bat-derived coronavirus causing COVID-19. Studies of infectious diseases emerging in human populations in recent decades indicate that the majority were zoonotic, and many of the causal pathogens had a wildlife origin. As hunter-gatherers, humans contracted pathogens from other species, and then from domesticated animals and rodents when they began to live in settled communities based on agriculture. In the modern world of large inter-connected urban populations and rapid transport, the risk of global transmission of new infectious diseases is high. Past and recent experience indicates that surveillance, prevention and control of infectious diseases are critical for global health. Effective interventions are required to control activities that risk dangerous pathogens transferring to humans from wild animals and those reared for food.

KEYWORDS

Pandemic; infectious disease; zoonotic; emerging disease; prevention; public health

Introduction

Changes in the way of life of our human ancestors and their encroachment into new environments exposed them to new infections. Survival and the capacity to raise offspring depended on immune defenses as well as food, water and shelter. Living and hunting in the tropical rain forest, humans were exposed to a variety of parasites and pathogens carried by insect vectors, birds, fish and animals. Seeking food and hunting in more open grasslands and eventually moving into more temperate zones, groups of humans would have contracted different parasites and zoonoses [1:34 – 39]. When nomadic tribes began to live in settlements and develop crop cultivation, horticulture and animal husbandry in Mesopotamia about 11,000 years ago, this transition created a new infectious disease environment [2:38 – 47]. Living near animal and human waste and contamination of stored grain by rodent feces increased the risk of gastro-intestinal infections. Other pathogens could transfer from domesticated animals such as cows, pigs and birds, with some adapting to humans as hosts [1:46 – 55].

Towns, cities and civilizations developed in Mesopotamia and other parts of the world, and interaction with rural areas, rural-urban migration, trade, transport by ship, exploration and conquest facilitated the spread of infectious diseases. When centers of population increased in size and density, various bacterial and viral infections were sustainable through human-to-human transmission without intermediate hosts or vectors [1:52]. In larger more dense populations, waterborne, foodborne, and airborne pathogens would transmit more easily, and more rapid spread and higher dosage could result in more severe sickness [2:48]. While changes in land use in England in the 18th century may have reduced the transmission of some infectious diseases in rural areas [1:227], the rapid expansion of economic activity in the *Industrial Revolution* began to radically change the infectious disease environment for those living in increasingly crowded towns and cities. In the modern world, urbanization, large inter-connected populations and rapid transport have increased the potential for global transmission, and emerging infectious diseases have brought new challenges.

In recent decades there has been a growing recognition that multidisciplinary research inputs are required for a greater understanding of infectious diseases and the development of measures for prevention and control. In the past, knowledge about these diseases developed through observation of the environmental and social context in which they occurred. Systematic local records of deaths from the plague years of the 16th century into the 19th century indicate

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the acute infectious diseases that contributed to high mortality in England. National registration records from the 1840s onwards provide evidence of changes in disease patterns and differentials in mortality. The limitations of historical disease-specific mortality data are well-recognized, not least because changes in medical knowledge have affected identification and recording of cause of death [3]. Even today, when the causal pathogen is confirmed or identification is technically possible, it is problematic to assign the primary cause of death among comorbidities [4]. From the end of the 19th century, scientific advances and research in many disciplines contributed to a greater understanding of etiology, transmission and epidemics. In recent years, paleogenomic research has provided further evidence of the specific pathogens involved in historically documented epidemics. The aim here is to review infectious diseases which in the light of current knowledge and historical records were major causes of death in England between the 17th and the 21st century. A heuristic contemporary definition of infectious diseases is used — diseases caused by specific pathogenic micro-organisms or parasites that are necessary for them to occur and be transmitted. The review summarizes public health and preventive interventions, improvements in living conditions, and changes in human behavior that reduced the risk of severe infectious disease. This historical perspective emphasizes the importance of similar responses today, given the threat from emerging zoonotic diseases.

The decline of severe infectious disease in England

Plague

The first historically documented plague pandemic, the Justinian Plague of AD 541 – 544, is thought to have originated in Egypt and lasted 200 years. Recent studies of DNA extracted from human remains dating from that period found at burial sites in Western Europe, identified *Yersinia pestis* the causal agent of plague [5]. Further studies found a different lineage of the pathogen in DNA extracted from human skeletons in mass graves in Europe linked archeologically with the Black Death of 1347 – 52 [6]. This second pandemic which lasted 500 years is thought to have reached Europe from the area to the north-east of the Caspian Sea in Central Asia [7:20]. Various burrowing rodents in the steppe have been a focus of infection, which may have transferred to other animals and humans as trading caravans and Mongol armies passed through new territory [1:143,155; 8:225]. In 1346, a plague outbreak ended a siege by Mongols of Caffa in Crimea [9;10]. Ships from there and other Black Sea ports most likely carried infected insect vectors on humans and black rats to Constantinople and Mediterranean trading ports. Plague broke out in Messina, Marseilles, Genoa, Venice and other ports in 1347 and 1348, and the disease spread throughout Europe by ship and along river and land routes used for trade and travel [7:20; 11:87].

In Italy, it was recognized early on that plague was in some way 'infective', and city authorities reacted quickly to organize a medical response and regulate behavior [1:174]. Protective measures were taken including surveillance, restrictions on public assembly, and isolation of the sick for 40 days (quarantine). These preventive interventions were gradually introduced throughout Europe, and local authorities had powers to deny entry to towns and isolate sick people in 'pest houses' [12:71 – 79]. In 1377, 30-day quarantine was imposed on travelers arriving in Ragusa (now Dubrovnik), and port authorities began to target ships arriving from places where plague had been reported. The draconian measure of compulsory isolation of households was widely enforced, arousing hostility among the poor who were most affected. Despite these measures and enforcement of 'cordon sanitaire' around plague-affected towns and along the border with the Ottoman Empire in the 18th century, outbreaks continued to cause high mortality in Europe [12:28].

Infection of humans with *Y. pestis* usually manifests in the distinctive bubonic form of plague, although a subsequent septicemic form can occur. In up to 20% of bubonic cases, infection can reach the lungs and pneumonic plague is spread more rapidly by airborne droplets causing localized outbreaks. Without antibiotics pneumonic plague is almost always fatal, while case fatality in bubonic plague is usually about 50 – 60% without treatment [13:463]. The rapid spread of plague throughout Europe despite high case fatality and relatively slow means of transport has raised some doubt about the exclusive role of *Y. pestis*. Coterminous epidemics of some other rapidly transmitting infectious disease such as viral hemorrhagic fever might have caused symptoms mistakenly attributed to plague [14]. The role of rats and their fleas in the spread and eventual decline of plague in Europe has also been contentious among historians and other researchers. Recent analysis of experimental data on human fleas and body lice suggests these vectors could have driven the rapid spread of plague [15]. Infected people might travel more than 30 kilometers a day over land, and ships could sail 600 kilometers in two weeks [7:21; 9].

Historical accounts suggest that plague arrived on the south coast of England in 1348, possibly on a ship from France [16:62]. Studies of DNA in human remains from burial pits support historical accounts of plague in the west-country town of Hereford in 1349 [6]. Plague spread throughout England and demographic estimates suggest it had killed at least 30% of the population by the end of that year [17:25], and possibly half the population of London [12:58]. Despite preventive measures, outbreaks with high mortality

continued to occur until the 'Great Plague' of the 1660s when the population of London was devastated again. The Bills of Mortality for 1665 record 97,306 deaths, with 68,596 of them directly attributed to plague [18]. Possibly one in five of the population died [19:9], and the proportion was much higher in some smaller towns [12:59]. People in the village of Eyam in Derbyshire volunteered to quarantine during a plague outbreak in 1665. The parish records indicate that in a population of about 700, 257 (36.7%) died from plague and 11 (1.6%) from other causes. Statistical modeling of the mortality data suggests human-to-human transmission, particularly through contact with people from other households, accounted for more deaths than rodent-to-human transmission [20]. After 1667, there were only a few sporadic cases of plague in England, although epidemics continued to occur elsewhere in Europe causing concern that infection would be reintroduced through frequent trade and shipping contacts [21:313]. In an outbreak of plague in the port city of Marseilles in 1720 – 21, possibly half of the population died [12:28].

Port sanitary authorities in England established under the Public Health Act of 1872 conducted surveillance to warn of outbreaks abroad. They had powers to take infected people to a hospital and order ships not to dock [22:127]. Quarantine for ships was particularly important because of trade links with countries where it was not imposed. When the third pandemic of bubonic plague began in Yunnan, south-west China, and killed an estimated 90,000 people in Canton and Hong Kong in 1894 [16:71], infection spread to Europe. The first known deaths in England were two sailors on a ship that arrived in London from Bombay in 1896 [23], and cases were reported in the ports of Glasgow, Cardiff and Liverpool in 1900 – 01 [16:71]. Between 1899 – 1947, 1,692 cases of plague and 457 deaths were recorded in Europe, mostly in towns with coastal or inland ports where ships arrived from abroad [23]. Port authorities in England were more active in the control of infectious diseases by that time, with environmental sanitation measures including rat control.

The brown rat, *Rattus norvegicus*, which is less inclined than the black rat to live close to humans, is thought to have arrived in England in the 1720s and become predominant. However, a decline in the black rat population may not explain the absence of plague after the 1670s [16:72; 24; 25]. In the 1894 epidemic in Hong Kong, Yersin noted the presence of many dead black rats in the streets [7:9]. The lack of reported die-off before outbreaks in England in the 1660s is consistent with the evidence that the rapid spread was more likely to have been due to human-to-human transmission via fleas and body lice than rodent-to-human transmission via fleas carried by black rats [15]. As discussed below, domestic living conditions, hygiene and facilities to wash clothes are not likely to have improved much in the poorest areas of English towns before the 1870s. The fact that plague was largely absent from the country after the 1670s probably owes much to public health interventions, including surveillance, quarantine, controls on the movement of people, *cordon sanitaire* around towns, and measures taken to prevent infection being introduced on ships arriving from abroad. As yet, there is no convincing evidence that herd immunity can account for the recession of plague in Europe, although those surviving infection with *Yersinia pestis* and related bacilli may have acquired some immunity [1:162; 26].

Typhus

Epidemics of 'fever' were common in Europe in the 16th century, associated with the prolonged wars. Descriptions from that time indicate that louse-borne typhus fever was often the cause [27:217]. By the 18th century, medical personnel in England with experience in army camps were familiar with the symptoms and the conditions in which the disease flourished [28:82]. The first unmistakable outbreaks of typhus in the country were in gaols, and infection spread from there to the most crowded parts of town. Epidemics were associated with war and famine and the related hardship and dislocation of life [8:147]. Thousands of 'fevers' deaths were recorded in times of food shortage, and the proportion of all deaths in this category in the London Bills of Mortality peaked at 16.6% in the 1740s when total mortality peaked [18; 29:44]. Accounts from that time suggest there was a major epidemic of typhus in London in 1741 – 42, and also in the south-west of the country [28:82 – 84]. Typhus and typhoid are likely to have been the main epidemic infections causing 'fevers' deaths in the mid-18th century [29:78 – 89]. From the 1740s, many municipal authorities in England implemented environmental sanitary schemes [30:102 – 120], and after food riots in the 1750s measures were taken to control the grain market to avoid high bread prices [31:66]. Local food shortages could trigger epidemics when vagrants, the homeless, and unemployed people went in search of food [32; 33:416]. Humans are the main reservoir of the causal agent of typhus, *Rickettsia prowazekii*, which is transmitted by the body louse [13:671]. Infection could also have been caused by insect feces entering the skin through lesions or being inhaled off clothes and bedding [34:37]. Murine typhus, transmitted by infected fleas carried by rats and mice in human dwellings was probably not distinguishable from louse-borne typhus, although case fatality is much lower [13: 674].

Physicians who made home visits in impoverished areas would have been familiar with the squalor, poor sanitation and lack of facilities for people to wash clothes, bedding and themselves [35:37]. Wealthier citizens could pass on new knowledge about hygiene

to their servants [36:173], and dispensaries for the poor opened in London from the 1770s providing advice about hygiene, care of the sick, and care of children [37:73]. By the end of the 18th century, it was widely known that typhus was associated with poor personal hygiene, filthy overcrowded dwellings, gaols, meeting halls and ships [28:82]. Despite increased knowledge about the conditions in which the disease occurred, typhus remained endemic in the poorest areas of towns and cities in the 19th century. Large towns became increasingly crowded with many people having to share one room in vermin-infested houses and tenements [38:162]. Only a minority of people could afford to move to the suburbs away from the filthy and neglected areas where most people worked and lived [39:216].

In a resurgence of typhus in London in the 1860s [40:106], infection spread from groups of people living in extreme deprivation – the destitute, vagrants, the unemployed, and those in crowded lodging houses. Certain areas were affected by railway projects, street building and construction which may have become less disruptive in the last three decades of the 19th century, and the death rate from typhus declined [41:209]. Case fatality reportedly remained consistently high at 20–45% [40:115], suggesting there was no decline in virulence of the pathogen. The decline in the death rate from all fevers suggests the decline in the death rate from typhus is unlikely to be explained by transfer of diagnosis. Slum clearance aimed at eliminating 'fever-nests' [41:206], and new housing for the poor [38], probably enabled many low-income city dwellers to keep away from foci of infection, while improved water supply from the 1870s enabled improvements in cleanliness. Isolation of infected people in fever hospitals and placing the destitute in workhouses could also have reduced transmission in inner-city areas. The annual death rate from typhus in the country as a whole declined from 609 per million in 1869 – 73 to 1 per million by the end of the 19th century, long before any effective treatment was available [42]. The disease had ceased to be a major killer in most towns, with the notable exception of Liverpool whose port had sea links with Dublin and Belfast where death rates remained relatively high [29:81; 40].

Smallpox

By the end of the 17th century smallpox had become a more regular cause of high mortality in England than plague or typhus. In most decades between the 1670s and the 1800s, 7–10% of all deaths recorded in the London Bills of Mortality were attributed to smallpox [18], and this would not include many deaths among infants who were less likely to show the distinctive signs and symptoms [43:105]. Death registers for other towns and some national populations in Europe, indicate that smallpox was the main cause of spikes in the annual number of deaths in the 18th century, and 8 – 20% of all deaths were attributed to the disease [44]. Other infectious diseases frequently recorded as the cause of death included 'consumption' (mostly tuberculosis and some other lung diseases), various fevers, dysentery, measles, whooping cough, and jaundice [45]. As the population of towns in England increased, smallpox became endemic, and epidemics occurred when the number of new susceptibles was large enough to sustain transmission. Immunity among survivors led to smallpox becoming mainly a disease among young children in the towns, and among older children and young adults in rural areas as epidemics were less frequent [28:525].

The causal agent in severe forms of smallpox, *Variola major*, may have evolved from a pathogen infecting African rodents which spread to Asia and Europe [46; 47]. Recent genetic research on human remains from burial sites in northern Europe in the Viking-era identified strains of smallpox virus that were genetically closer to animal poxviruses and different from those causing smallpox in more recent times [48]. An unmistakable description of smallpox comes from China in the 4th century AD [49:210], although medical texts from India and China 3,000 years ago describe a smallpox-like disease [46; 47]. Inoculation was practised in Tibet as early as the 11th century [50]. Although crude by today's standards, a small dose of a mild strain of the virus could have been less harmful than natural infection with a more virulent strain. Knowledge of this potentially dangerous practice of injecting people with matter from smallpox sores was brought to England from Turkey by a member of the aristocracy in 1721, following reports to the Royal Society in London [51:254]. After experiments on prisoners, two royal children were safely inoculated and it became widely used among the general population. Surveys in the 1720s and other records suggest case fatality was much lower than for natural infection, which was estimated at 17% [28:513 – 518]. The method was not always effective [16:82], and there was much religious opposition [52], but inoculation became a common medical practice in England. In East Anglia, a surgeon (Sutton) inoculated thousands of people reportedly with very few deaths [53], and mass inoculations were common in many parts of the country [28:508; 43:188]. Use of inoculation probably reached its peak in the 1790s, after which it was rapidly replaced by vaccination.

Vaccination was developed as a preventive measure against smallpox in rural communities in the southwest of England in the second half of the 18th century. The method was based on the observation that cowpox sores developed on the hands of farm workers and milkmaids who seemed to be protected against

smallpox [54:2]. Deliberate infection with matter from cowpox sores was practised for many years before a more scientific investigation by Edward Jenner a country doctor in Gloucestershire. Hearing stories of the protective measure, he deliberately infected a young boy with cowpox in 1796 and observed no ill-effects when he later infected him with matter from smallpox sores [16:85; 34:128]. Jenner published his evidence of the effectiveness of vaccination long before any knowledge of microbes and immunity. Within weeks vaccination was practised throughout England and records from several towns indicate a dramatic reduction in smallpox deaths after 1800 [44].

Vaccination was widely used in many European countries within a decade which resulted in a rapid decline in smallpox mortality [44]. It quickly became compulsory in some countries, while in England there was reliance on infant vaccination which only became compulsory in 1853 [55:282 – 295]. Possibly half of the children in British towns were vaccinated between 1800 – 1870 [16:90], but coverage may have declined when fewer children were dying from the disease, leading to resurgence of infections and deaths [22:125; 56]. There was no effective system of enforcement and it was recognized that eradication through universal vaccination was unlikely to be achieved [22:115]. Local sanitary authorities focused more on identifying cases, isolation at home or in hospital, tracing contacts and vaccinating them. Isolation was introduced in the 1860s, which along with vaccination was central to the "stamping out" strategy after the arrival of a pandemic in 1870 [41:124]. Cases were severe and with vaccination coverage inadequate, 42,220 deaths from smallpox were recorded in England in 1871 – 72 [42]. The Vaccination Act of 1871 established a national framework for vaccination or revaccination of contacts and strengthened the system for enforcing infant vaccination [41:126; 57:57]. Vaccination Officers were appointed who were paid to ensure that all infants under the age of 3 months in their district were vaccinated, and initially coverage was high [16:90].

From the 1870s, growing opposition to compulsory vaccination and isolation led to organized protest [58]. Cases were concealed by the poor because of the financial consequences of isolation, but also by wealthier households [41:131]. Local control strategies were developed such as that in Leicester based on a notification system, hospital isolation of cases, and financial compensation for quarantined contacts [59]. In London, opposition to the smallpox hospitals from local residents who feared infection would spread from them led to the use of hospital ships [22:123; 60]. After an epidemic in 1884 – 85, a decline in smallpox deaths coincided with the use of hospital ships for isolation, compulsory notification of cases in the Port of London, and tighter controls on incoming ships [22:133]. When the Europe-wide pandemic of 1901 – 03 affected London, isolation measures were well-organized, cases were largely confined to certain areas, and smallpox was virtually eliminated from the city [22:137]. The outbreak in Liverpool in 1902 – 03 was controlled locally without a national vaccination campaign. The first known case was a seaman, and most of the 2,032 cases and 161 deaths (7.9%) occurred in the densely populated port area. Control was achieved through active surveillance, contact tracing, hospital isolation of cases and vaccination of contacts [61].

Along with vaccination and isolation, the port sanitary authorities made a significant contribution in the final phase of smallpox eradication by monitoring outbreaks abroad and inspecting ships to identify cases [22:125 – 127]. The smallpox death rate was 584 per million in 1838 – 42, but after 1903 there were no further epidemics in England [42]. The last case in the country in 1978 resulted in the last known death from smallpox, and global eradication was declared by the World Health Assembly in 1980 [49:1137].

Tuberculosis

In England in the 19th century, poorly ventilated crowded dwellings and inadequate diet contributed to high death rates from respiratory tuberculosis. When people got sick some would return to their home village, and infection is likely to have been universal [62]. In 1848 – 54, 12.4% of all deaths in England and Wales were attributed to respiratory tuberculosis and 3.7% to non-respiratory forms of the disease [29:234]. *Mycobacterium bovis* is usually transmitted to humans in cow's milk, mostly causing non-respiratory tuberculosis. The causal agent in respiratory tuberculosis, *Mycobacterium tuberculosis*, is usually transmitted in droplets coughed out or exhaled by those infected. Most children living in towns in England in the 19th century would have contracted a primary infection early in life. When inhaled, bacilli multiply relatively slowly in the lung causing inflammation and an immune response which conveys a degree of immunity to the antigens. In the process, chemicals can be released which damage cells and cause a type of allergy with sensitivity to the toxic product tuberculin. The body rapidly produces new cells to maintain tissues, which usually results in bacilli being 'walled off' in nodules (tubercles) that calcify [63:116]. Bacilli can remain virulent for weeks or years and cause reinfection if the nodule is disrupted. Many cases of clinical tuberculosis were probably due to reactivation of latent infections as a result of coughing and physical disruption of the lungs [64; 65:737]. Children in large families and overcrowded dwellings would experience frequent respiratory infections, and

also respiratory complications of smallpox, measles and whooping cough [29:121].

For older children and adults who contracted *M. tuberculosis*, the reaction is likely to have been more violent when they had already been sensitized by an earlier infection [8:215]. If the containment process failed due to a high dosage of bacilli, poor health, undernutrition or other factors affecting resistance, the infection could destroy the lung or spread to other organs. Men were particularly at risk of contracting a high load of bacilli in crowded public houses, workshops, and dusty factories where ventilation was poor [66]. Engels described factory workers looking like 'hollow-eyed ghosts riddled with scrofula (tuberculosis) and rickets' [67]. Those with tuberculosis had little choice but to continue working in the crowded conditions conducive to the spread of infection to feed themselves and their dependents. The alternatives were the workhouse, begging or stealing. Confinement of the destitute in workhouses probably increased the incidence of clinical tuberculosis there, although it may have reduced transmission in the outside community. By the 1890s, one-third of tuberculosis deaths recorded in London occurred in workhouses [68].

With the population of industrial towns in England growing rapidly due to in-migration from rural areas, private landlords could charge high rents, which forced people to share crowded, poorly ventilated rooms. Common lodging houses and areas where groups of people lived on the street were particular foci of infection. From the 1860s, Local Housing Acts in some towns focused on housing and sanitation, and slum clearance schemes were introduced in London and other cities [41:206]. The Housing Act of 1890 facilitated increased provision of housing for the poor by municipal authorities and philanthropic organizations, which met some of the needs that the 'free market' economy would not address [38; 69:29]. National death registration had provided evidence since the 1840s of the devastation caused by tuberculosis, but there was no national prevention policy before the end of the 19th century. Koch identified *M. tuberculosis* as the cause of respiratory tuberculosis in 1882, and the contagion theory provided a scientific rationale for isolation and other preventive measures. He emphasized the importance of educating the public about transmission [70], recognizing that their participation would be essential for a national programme based on early diagnosis and isolation. Municipal and local authorities were made responsible for implementation supported by a network of diagnostic centers and an increasing number of residential sanatoria and dispensaries in the first three decades of the 20th century [70]. However, there was still no effective medication and case fatality remained extremely high (50%) in the 1920s and 1930s [71].

The decline in the tuberculosis death rate after World War I was due to a decline in the incidence of clinical disease [29:129], although most children in England still tested tuberculin positive in the 1950s as a result of natural infection. The prevalence of infectious cases is estimated to have declined from 600 per 100,000 in 1900 to 200 per 100,000 in 1950 [72]. By that time, tuberculosis accounted for 2.5% of all deaths in England compared with 16% in the mid-19th century [29:234]. Several factors probably contributed to the reduction in mortality — a decline in severity of infections that could reactivate latent tuberculosis, birth spacing and smaller families, reduced household size from the 1890s [73:174], isolation of infected people in sanatoria, improved public hygiene behavior (sneezing, coughing and spitting), laboratory testing and sterilization of milk, improved nutrition after World War I, BCG vaccination from the 1920s, and treatment with streptomycin from 1947 [29:130; 72].

Cholera

The first case of cholera in England was reported in the port town of Sunderland in 1831, after a pandemic began in Asia in 1817 – 18 [16:98]. The cause of the disease, how it spread, and how to treat the sick were largely unknown. The causal bacterium, *Vibrio cholerae*, is highly pathogenic to humans who can be infected by consuming water, milk or food contaminated by fecal matter, or by direct contact with an infected person followed by hand-to-mouth transmission. Infection spreads rapidly where water supplies are contaminated and sanitation is poor, and case fatality in untreated epidemics can be over 50% [74:166].

In London in 1831, 11% of all deaths were directly attributed to cholera and more deaths than usual were recorded as due to 'old age' and 'unknown causes' [18]. The Central Board of Health established in that year accepted the 'contagion theory' and imposed quarantine on ships arriving from the Baltic ports. The measure was suspended in 1832 following pressure from owners of businesses whose profits were affected, and the Board was dissolved [75]. Investigations by Edwin Chadwick a journalist and lawyer, linked cholera with the dreadful living conditions for most people in industrial towns and raised awareness among the middle classes [16:103]. The government established a Royal Commission to review the system of relief under the Poor Law, but this focused on finding a cheaper system not on improving living conditions. Influential advocates of an unregulated 'free market' economy and a *laissez-faire* social policy lobbied the government to dramatically reduce its support for the parish-based system of relief [39:211]. The New Poor Law of 1834 introduced enforced labor in workhouses for those with no work or means of support.

Chadwick initially supported revision of the Poor Law, but recognized infectious disease required urgent attention [39:215]. He proposed environmental

measures to reduce the health hazards of contaminated water and wells, industrial pollution, animal waste, and inadequate drains and sewerage. His report on the sanitary conditions of the poor was published in 1842 [76], and his public health proposals were initially ignored by the government. However, the evidence of higher incidence of infectious disease in overcrowded areas, and other data from the new national registration system on deaths in industrial towns supported the case for new public health legislation. Despite opposition from many property owners and their representatives in parliament, the first national Public Health Act was passed in 1848 establishing a General Board of Health [16:105]. Local authorities were given more responsibility for environmental improvements and water supply, although they lacked political support and resources to implement schemes until the 1870s [39; 77:707 – 711].

Most champions of public health reform were not medical practitioners with the notable exception to John Snow. His scientific investigations during the cholera epidemics in London in 1848 – 49 and 1853 implicated particular water sources. In 1849, he analyzed data on deaths from cholera in the neighborhood of Broad Street in Soho, suspecting that water from a local street-pump had become contaminated. By interviewing families of those who had died in the surrounding sub-districts, he found that most had taken water from the pump for drinking, and the handle was removed. He attributed a decline in the daily number of deaths in the week before that to people fleeing the area [78:39]. Snow's observation in 1849 that districts of London with the highest cholera death rates were those supplied with water from the nearby River Thames, supported his theory of waterborne transmission. The suppliers were the Southwark and Vauxhall Company and the Lambeth Water Company. After the latter relocated its water works upstream where water was not contaminated by London sewage, there was an opportunity to collect comparative data when cholera returned in 1853. Both companies operated in some districts, but Snow found that areas at least partially supplied from the new source had lower cholera death rates [78:68]. He obtained addresses from the Registrar General for people who had died from cholera, and conducted a household survey to identify their supplier. The cholera death rate among people supplied with water from the Thames in town was fourteen times higher than that among people supplied with water from outside London [78:80]. Snow published this evidence of waterborne transmission of cholera providing a scientific rationale for the construction of new water and sewage systems to avoid fecal contamination of drinking water.

Chadwick proposed sewers that could be flushed with water to convey waste matter away from human habitations. Opponents of public health reform viewed sanitation measures as an interference with natural selection and a 'law of nature' by which the fittest survived and the weak died off. However, fear of another cholera epidemic, and the prospect of compensation payments helped to overcome opposition from owners of property where pipes would be laid [79:102 – 110]. When the cholera epidemic of 1853 – 54 ended, parliament voted against the continuation of the General Board of Health led by Chadwick and he was dismissed. Under threat of another cholera epidemic, the Sanitary Act passed in 1866 allowed local authorities to appoint officials, although powers to enforce public health measures were still inadequate [16:111]. Despite continuing non-interventionist *laissez-faire* opposition, influential public health reformers succeeded in passing further legislation after the election of 1868. The franchise had been widened to include those renting property not just owners [66; 77:710]. In the 1870s, municipal authorities in industrial towns and cities such as Birmingham had the political support to overcome opposition from ratepayers and other vested interests, and effective sanitary schemes were implemented with low interest loans [39:219; 80:424]. New local Medical Officers of Health were given powers to control environmental hazards, investigate disease outbreaks, search for infectious disease cases on household visits, and remove sick people from overcrowded tenements [16:106; 35:57].

The cholera epidemic in London in 1866 was the last major outbreak of the disease in England, and sporadic cases after that were linked with infected people arriving from abroad [81:228]. The Public Health Act of 1872 gave port sanitary authorities power to inspect ships to prevent cholera from being introduced from overseas [22]. New legislation gave Local Boards of Health powers to monitor water quality, impose strict standards, and take action against private companies that supplied contaminated water. The Public Health (Water) Act of 1878 allowed municipal authorities to buy private waterworks and ensure clean water was supplied to those less well off. By the end of the 19th century, about two-thirds of urban sanitary authorities in England operated waterworks that supplied the majority of people in their area [69:24]. Although several preventive measures contributed to the control of cholera, evidence from England and other countries suggests improvements in water quality probably had the greatest impact, and also contributed to the reduction in death rates from other infectious diseases [29:86].

Typhoid and gastro-intestinal infections

The enteric fevers, typhoid and paratyphoid caused by *Salmonella typhi* and *Salmonella paratyphi* bacteria, are usually due to consumption of contaminated water, milk and food, or transmission on hands contaminated

with fecal matter. Before antibiotics, case fatality was probably 10 – 20%, although many cases may have been mild as in endemic areas today [13:665]. The decline in deaths recorded as due to 'fevers' in the London Bills of Mortality after the 1740s could in part reflect the growing awareness of a link with environmental conditions and poor hygiene [30:89 – 98]. Improvements in cleanliness reported at that time could have helped to reduce fecal-oral transmission of infection [82]. There was no central government action on environmental hazards, but as mentioned many municipal authorities implemented environmental schemes focused on drainage, sewage disposal, and street cleaning. In London, parish commissioners were authorized to collect taxes for environmental sanitation and private companies were formed to construct sewers [83].

In the 19th century, implementation of environmental schemes varied considerably, and many poorer areas in industrial towns lagged behind. Squalid living conditions and structural poverty persisted in working-class areas of northern towns such as Manchester [84], and in London there was wide variation between districts [41:172 – 181]. Most working-class households had no water closet and many families had to share unhygienic 'privies' which could not be flushed. Poor domestic sanitation, lack of personal hygiene, and consumption of contaminated water, milk and food continued to cause outbreaks of typhoid in urban areas of the country. Better-off households were also affected due to poor plumbing for newly acquired water closets and consumption of contaminated dairy products [85:131]. The risk of typhoid being transmitted in milk, either because of contaminated water used during processing or infected workers with no symptoms, was recognized by the 1870s [86:333]. Milk consumption was increasing and a public health response to contamination was supported by a growing body of scientists in different disciplines. Laboratory services, identification and hospitalization of cases, food inspection and improvements in dairy practice contributed to reduced incidence of typhoid and other infectious diseases transmitted via milk and food.

Following recommendations by the Royal Sanitary Commission of 1869 – 71, national legislation enabled local sanitary authorities to regulate food markets, supply potable water, and implement environmental schemes essential for the prevention of typhoid [69:24 – 26]. In the most deprived East-end areas of London, measures to alleviate poor drainage, soil pollution, and contaminated wells contributed to a dramatic reduction in typhoid mortality from the 1870s [40:106 – 111; 41:172 – 181]. At the national level, separate recording of typhoid deaths from 1869 revealed a steady decline in the death rate from 1,910 per million in 1869 – 73 to 185 per million by the end of the 19th century [42]. The incidence of enteric fevers declined until the 1940s then leveled off with fewer than 100 deaths annually, despite the lack of effective treatment before chloramphenicol was used in 1949 [87; 88:81].

The death rate from dysentery, gastro-intestinal and diarrheal diseases also declined rapidly after the last major cholera epidemic in 1866, reflecting the improvements in environmental sanitation, sewerage, and particularly the supply of potable water [29:81]. However, there were higher death rates at all ages from these diseases in the 1890s when a series of hot dry summers increased the risk of fly-borne fecal contamination of food [29:86 – 99]. The subsequent improvement in hygiene – personal, domestic, and food, helped to prevent related gastro-intestinal infections, along with further environmental improvements such as removal of refuse and human waste from inhabited areas, the introduction of covered dustbins, and less manure in the streets as motor vehicles began to replace horse-drawn carriages [41:190].

Infants were vulnerable to pathogens in contaminated milk, feeding bottles and weaning foods [85], and diarrheal disease deaths and total infant mortality increased in the hotter 1890s [29:94]. It was recognized that the home environment was dangerous for young children, and mothers should breastfeed and practice better hygiene [89:7]. The new scientific understanding of germs and transmission of infectious disease provided a rationale for protective measures such as sterilizing feeding bottles, boiling milk, covering food, isolating sick family members, and washing hands [90]. Health visits were introduced for every home with a mother and young child, and nurseries were opened providing education on infant care and feeding [91:113]. Improvements in hygiene and infant care contributed to the rapid decline in infant deaths from diarrheal diseases from 21.3 per 1,000 births in 1901 to 1.3 in 1951 [29:92 – 100]. The proportion of deaths attributed to these diseases at all ages declined from 7.3% in 1901 to 0.5% in 1951 [29:234,236].

Childhood infectious diseases

In the 19th century, young children in large families with poor living conditions and inadequate nutrition were at high risk of dying in a succession of epidemics of childhood infections, as in developing countries today. Despite the lack of sustained decline in infant mortality until the beginning of the 20th century, child survival improved after the 1860s reflecting declining death rates at ages 1 – 4 years from cholera, typhoid, smallpox, tuberculosis, and the biggest killer at these ages, scarlet fever [29:101].

Scarlet fever

More than one-third of all deaths in England in the second half of the 19th century were children under five

years of age, and the majority were caused by infectious diseases with the highest number attributed to scarlet fever. The causal agent, *Streptococcus pyogenes*, was endemic and could produce repeated subclinical throat infections as no immunity develops. Streptococci which infect a large proportion of the whole population are transmitted through human contact, airborne droplets, or contaminated milk and food. Several types can cause scarlet fever when the bacteria are infected with a bacterial virus which produces a toxin [8:200]. In the past, the severity of infections is likely to have been determined by a child's health and nutritional status, the dosage of streptococcus, the particular strain and the mode of transmission [74:16]. Descriptions of epidemics suggest that severity varied over long periods, and a more virulent strain from abroad was thought to account for the destructiveness of epidemics in England in the mid-19th century.

The decline in the scarlet fever death rate after the 1860s has long been attributed to a supposed decline in the virulence of *S. pyogenes* [88:92], although thousands of children continued to die from the disease in the early 20th century. Recent evidence that dysentery, typhoid, and paratyphoid impair the ability to absorb key micro-nutrients, suggests these infections which were common in England in the 19th century would have caused nutritional deficiencies in young children [92; 93]. A decline in incidence of these diseases when water quality improved after the 1860s may have reduced case fatality from scarlet fever. When polluted wells were replaced by piped water in West Bromwich in the Midlands there was a dramatic decline in scarlet fever deaths [91:227]. This association has contemporary relevance as severe forms of scarlet fever began to reemerge in Britain, other parts of Europe and North America in the economic recession of the 1980s [92; 94; 105]. A number of countries in south-east Asia reported increased incidence between 2009 – 15, and in England, incidence increased three-fold in 2014 – 16 resulting in more hospital admissions. Genome sequencing of samples from different parts of England and comparison with historical strains indicated that these were not newly emergent strains of *S. pyogenes* [95].

Diphtheria

Sore throat was a symptom of diphtheria as well as scarlet fever and the disease also occurred with variable severity over the long term. The causal agent, *Corneybacterium diphtheriae*, may have been endemic in England in the first half of the 19th century causing mild throat infections, and diphtheria was not recorded as a cause of death until a pandemic in 1859 resulted in more than 9,000 deaths. Transmission occurs through contagion, inhaled droplets, infected dust and contaminated milk [74:3]. The diphtheria death rate had fallen about 50% by the 1870s before any effective treatment. Antitoxin was introduced in England in 1895, possibly the only effective medication for a major infectious disease before salvarsan was used for syphilis after World War I, and sulfonamides for streptococcal infections in the 1930s [29:15, n65]. The downturn in the diphtheria death rate in England in the mid-1890s is widely regarded as due to treatment with antitoxin, although trends in other countries suggest other factors were involved [29:109; 41:104]. Some children may have experienced less severe sickness being less debilitated by other childhood epidemic diseases and enteric fevers. Immunization developed in 1923 had a major impact on incidence, and mortality declined sharply in the 1940s when national coverage reached 50% [8:198].

Measles and whooping cough

Measles epidemics have an independent cycle linked with demographic factors and patterns of social contact [96]. In relatively large populations, the proportion with immunity (herd immunity) affects the transmission, the interval between epidemics, age at infection and severity [97–98]. Measles virus causes an inflammatory reaction in the respiratory system, and both pneumonia and bronchitis were common complications in fatal cases at the end of the 19th century [99]. Respiratory complications were more likely to occur in children with a large number of siblings, and deaths were associated with large families, poor housing conditions, and high population density [100]. Measles is still an extremely common cause of death in developing countries, and bacterial pathogens such as pneumococci, streptococci, staphylococci, and *Haemophilus influenza* are often found in children who have respiratory complications [101]. Evidence from Africa suggests measles is more severe in large families, and case fatality is higher in households where several children are infected [102; 103]. Children attending school infect younger siblings, frequently exposing them to streptococcal, pneumococcal, and other airborne and respiratory infections.

The bacillus *Bordetella pertussis* produces an acute inflammatory reaction and very young children are susceptible to respiratory complications and pneumonia [104]. In the 19th century, coterminous epidemics of measles and whooping cough were particularly debilitating and reduced children's nutritional status [41:21]. Social and demographic factors, including family size, the birth rate, population size and density, the number of susceptibles, and behavior patterns in the community affect the average number of cases arising from one infected individual (R_o). Duration of the latent period and of infectiousness, the number and frequency of contacts with infected individuals, and susceptibility to infection can also affect transmission [105; 106]. From the end of the 19th century, the decline in family size and less overcrowded living conditions most likely reduced transmission rates, severity and case fatality rates for measles, whooping cough and respiratory infections in

children. After high coverage of immunization against measles and whooping cough was achieved in the 1960s, relatively few cases were hospitalized [107]. By that time, measles, whooping cough, diphtheria, and scarlet fever caused less than 0.2% of all deaths in England, compared with 7.8% in the mid-19th century [29:234].

Respiratory infections

Respiratory diseases, including bronchitis, pneumonia, influenza and asthma, accounted for about 13% of all deaths in England in the mid-19th century, and the proportion is the same today [29:239]. Children attending school appear to be the main source of respiratory infections introduced into households, and older adults are particularly vulnerable if they contract influenza [108; 109]. Severe respiratory infection in infants is associated with the number of siblings in the household and low socio-economic status [110; 111]. In the 19th century, larger families, under-nutrition, damp overcrowded housing, indoor smoke from coal fires, air pollution and poorly ventilated work places contributed to high respiratory disease death rates. The new housing built toward the end of the 19th century alleviated some of the harmful effects of overcrowding, damp, and poor ventilation [38]. Successive generations of children benefitted from smaller family size as infections were less likely to be severe [29:112]. As mentioned, average household size declined from the 1890s [73:174], and death rates from respiratory disease and measles declined from that time [112].

Pneumonia

Many bacterial and viral pathogens cause pneumonia, which can be an extremely severe infectious disease. The most common bacterial form is pneumococcal pneumonia caused by *Streptococcus pneumoniae*. Bacteria multiply in the lungs and eventually kill an infected person unless sufficient antibodies are produced. Without treatment case fatality is up to 35% [13], and no effective treatment was available before sulphapyridine was introduced in 1938 [113:94]. The most common cause of viral pneumonia in adults is influenza, while the respiratory syncytial virus is the most common cause in young children. The death rate for lobar and pneumococcal pneumonia declined for both children and adults from the 1930s along with the decline in the influenza death rate [114]. The extent to which the decline after the 1940s was due to the use of antibiotics is difficult to assess [113:95]. Pneumococcal vaccines (PCV) routinely given to children under two years of age in England from 2006 reduced the incidence of invasive pneumococcal disease at ages under five years. This also contributed indirectly to a decline in incidence at ages over 65 years, while PPV23 vaccine available to those adults from 2005 provided some direct protection [115].

Influenza

Influenza has been a major cause of death in England and continental Europe for centuries, with epidemics every few years. Deaths are usually among infants and older people who are prone to develop pneumonia. Major pandemics have occurred at longer intervals, such as those in 1847 – 48 and 1889 – 93 when thousands of deaths were recorded. Between those outbreaks, very few deaths from influenza were recorded in England, although the disease remained prevalent in Europe [112]. After the 1889 – 93 pandemic, the death rate from respiratory disease as a whole declined [29:132], although 'seasonal influenza' continued to cause significant mortality up to World War I. In the chaotic conditions at the end of the war, one of the most destructive pandemics in history occurred in 1918 – 19 in which an estimated 25 – 50 million people died [8:206]. A new influenza virus caused high case fatality among soldiers at the Western Front in autumn 1918, and secondary infections with bacteria such as *Haemophilus influenzae* were common. Many of the sick were transferred to hospitals and infection spread rapidly in the crowded conditions. Rapid transmission around the world was fostered by massive troop movements and upheavals in civilian life, with under-nutrition contributing to extremely high mortality [116:22]. In the period June 1918 through May 1919, there were three waves of this misnamed 'Spanish Flu' in England with peaks in July, November and February. In that one-year period there were 198,000 excess deaths in England and Wales, with 151,443 of them attributed to influenza [117]. The highest proportion of deaths was among 15 – 44 year olds, while in the 1889 – 93 pandemic it had been among older adults [8:205]. After the 1918 – 19 pandemic, there were epidemic fluctuations in the influenza death rate in England with a downward trend from the 1930s.

Pandemics have occurred about every 10 – 40 years when a major genetic change produced a new strain of virus to which most people had no immunity. The main factors contributing to epidemics are the strain of virus, large numbers of people with no immunity, and climatic conditions. When a virus passing regularly between different geographical regions mutates, it is more likely to spread than an earlier strain to which some people have immunity. This theory of 'antigenic drift' and a competitive advantage for a mutated virus was thought to explain periodic pandemics. The 'Asian Flu' pandemic of 1957 was possibly the most widespread of any kind in history, but far less destructive than that in 1918 – 19. Most people in industrial countries were more prosperous by then and antibiotics

could be used for secondary bacterial infections, whereas in 1918 there were no effective drugs [8:207]. The pandemic in 1957 was caused by a type A virus (A2) with such a marked antigenic difference that it was unlikely to have been due to a simple mutation, and the idea developed that the virus came from an animal reservoir [8:210].

A new influenza A virus genetically related to those found in pigs was detected in the United States in April 2009, and also in samples sent from Mexico. The H1N1 combination of proteins was similar to that in the 1918 influenza virus. The new virus spread rapidly to thirty countries within one month and WHO declared a pandemic in June 2009 [118]. The initial outbreak followed sporadic cases of swine influenza virus affecting people in California, and many of those sick reported direct exposure or close proximity to pigs. The gene segments in the new human H1N1 virus were a mixture of those found in pigs in North America and some that circulate among pigs in Eurasia. Pigs reared for food are susceptible to human strains of influenza and genetic recombination can occur during co-infection, followed by transfer of a new strain from pigs to humans [118–120].

The vaccines developed for the human 'Swine Flu' pandemic in 2009 were effective and the H1N1 virus was less virulent than anticipated. Even though an estimated 250,000 – 500,000 deaths occurred worldwide, this was similar to the annual mortality from seasonal influenza [121; 122]. Vaccines are modified each year because of the constant change in the influenza viruses circulating. The WHO Global Influenza Surveillance and Response System facilitates this through a network of cooperating National Influenza Centers that monitor the strains prevalent. These centers collect virus specimens in their country, perform preliminary analysis, and send clinical specimens and isolated viruses to WHO for advanced antigenic and genetic analysis. Based on the results, WHO recommends the composition of influenza vaccine each year [8:212; 120:99].

A pandemic can occur when a new virulent subtype of an influenza A virus emerges [8:209]. All the known ones have descended from wild-bird viruses, and waterfowl such as ducks are the main natural reservoir. Large-scale poultry farming, transportation of birds, and food markets selling live birds expose human populations to new viruses [123]. Two highly pathogenic avian influenza viruses, H5N1 and H7N9 emerged in China and cases of H7N9 infection were reported in humans in 2013. Closure of live poultry markets and mass vaccination of poultry were effective in controlling the transmission to humans by 2018 [124]. Protection for humans against pandemic influenza in the future is likely to depend on timely development and distribution of effective human vaccines, and prevention of the transfer of new viruses from birds and animals.

New zoonotic diseases

Coronaviruses

When there is no vaccine or specific treatment for a new infectious disease, the only effective public health measures are isolation, quarantine, social distancing, and community containment [125]. In the first two decades of the 21st century several new respiratory infections emerged. A bat-derived coronavirus (SARS-CoV) found in civets was identified in humans in Guangdong Province, China in November 2002. The virus caused the outbreak of severe acute respiratory syndrome (SARS) in 2003 which spread rapidly to 26 countries. Cases were mostly confined to South East Asia – China, Taiwan, Hong Kong, and Singapore. SARS was effectively eradicated within eight months by preventing human-to-human transmission, but not before 774 (9.6%) of the 8,098 reported cases resulted in death [125]. The response to SARS in China was draconian and centrally coordinated. Public health measures included quarantine for whole villages, towns and cities, and the closure of schools, universities and public places. The outbreak was mostly confined to the hospital setting where rigorous protective measures could be implemented. Lessons from the SARS epidemic were applied elsewhere when another bat-derived coronavirus, MERS-CoV found in camels, caused the outbreak of the Middle East respiratory syndrome (MERS) in 2012. In the initial stages in September, the US Centers for Disease Control and Prevention in collaboration with WHO focused on case identification and mitigation [126]. By the end of January 2020, there had only been 2,519 laboratory-confirmed cases, mostly in Saudi Arabia, but 866 (34.3%) of those people died [127].

In December 2019, a new unknown virus was reported among patients with pneumonia in Wuhan, a city of more than ten million people in Hubei Province, Eastern China. The health authorities informed WHO at the end of that month, and reported less than two weeks later that eight of the cases were associated with visits to the Huanan seafood market in the city where live animals were sold. Scientists in China identified the causal agent as a new coronavirus, SARS-CoV-2, and shared the genetic data online on 12 January 2020 [128]. The South East Asian countries that had experienced SARS recognized the seriousness of the new infectious disease, later named COVID-19, were well prepared and responded quickly. In other countries, preparedness, health system capacity, and

political commitment varied enormously. The virus spread rapidly around the world through human-to-human transmission, and cases had been reported in over one hundred countries when WHO declared a pandemic on 11 March 2020 [129].

Analysis of genomic data in the United States revealed that the SARS-CoV-2 virus was not manufactured and most likely jumped species from an animal host [130]. The genetic sequencing in China showed that the virus was closely related to the two bat-derived coronaviruses that caused the SARS and MERS outbreaks [128]. As contact between humans and bats is limited, it seems likely that SARS-CoV-2 transferred to humans who handled an intermediate host, either a wild or domesticated animal. The most closely related coronavirus was identified in the lungs of two dead Malayan pangolins found in Guangdong Province, China [131]. Establishing the source of a new pathogen is clearly important to prevent reintroduction into the human population. Genetic similarities between SARS-CoV-2 and SARS-CoV, and the likely origin of both viruses in markets selling live animals, indicate that another dangerous pathogen could transfer to humans from a similar source in the future.

Other new zoonotic diseases

Recent ecological research has shown that serious zoonotic threats arise when humans encroach into natural habitats, or transform them for commercial, agricultural or habitation purposes. As in the past, this causes a decline in many large species, but also increases the population of smaller species, including rodents, bats and some birds that host pathogens capable of transferring to humans [132; 133]. Unregulated commercial logging and other human activities have opened up previously inaccessible forest areas for hunting [134]. Sought-after animals and bush meat sold in markets are a vital source of income for many people in parts of Africa and Asia, but the trade risks new infectious diseases emerging in human populations. Analysis of a database of 335 new diseases recorded in the global human population between 1940 and 2004, found that 202 (60.3%) were zoonotic and 145 (43.3%) had a wildlife origin [135]. For example, Nipah virus with its origin in fruit bats transferred to humans from infected pigs, causing an outbreak in Perak, Malaysia in 1998 – 99 with a case fatality of almost 40% [136]. Fruit bats also carry Ebola virus, although humans are more likely to contract the virus from other primates and forest animals. Subsequent human-to-human transmission by direct contact has resulted in outbreaks with case fatality between 25 – 90% [13; 137]. By far the biggest new killer has been human immunodeficiency virus (HIV). An estimated 23–44 million people worldwide died from AIDS-related conditions between 1980 – 2018 [138]. HIV is likely to have originally transferred to humans from animals. Both HIV-1 and HIV-2 are closely related to simian viruses to which many people in Africa are exposed, particularly through hunting and butchering primates for food [134].

Conclusions

Recent epidemics and pandemics have shown how destructive of life new infectious diseases can be, even in well-nourished populations. Despite widespread under-nutrition and poverty, average life expectancy in England gradually improved over the period 1741 – 1901, from about 32 to 50 years [33:527; 139]. As there were no effective treatments for infectious diseases, some researchers have concluded that mortality decline was largely due to improvements in nutrition [31; 113]. However, the studies did not take into account the inconsistent temporal association with nutritional and economic indicators, differences in disease-specific mortality trends, or the adverse effects of infectious disease on nutritional status [29:48 – 57]. Much of the increase in life expectancy was due to public health interventions, preventive measures and changes in human behavior, without which further improvement may not have occurred. Threatened by devastating epidemics people experimented with ways to protect themselves based on observation of the incidence of disease in different situations and environments. The most beneficial interventions in this period were smallpox vaccination, provision of clean drinking water, sewerage, and improved environmental sanitation [29]. Without the development of public health and preventive measures, plague, smallpox, tuberculosis, typhus, typhoid, dysentery and cholera are unlikely to have become less destructive of life.

Toward the end of the 19th century, the decline in family size and new housing reduced average household size [38; 73:174], which probably reduced the severity of the infectious diseases of childhood. New scientific discoveries about microbial causal agents provided a rationale for measures to control the transmission of infectious diseases, such as personal, domestic and food hygiene, isolation of cases and institutional care for the sick. Improved knowledge about infant care contributed to a decline in mortality, which along with declining death rates at ages over 35 led to a more rapid improvement in life expectancy from 50 to 69 years between 1901 – 1951 [29:238]. This occurred despite the continuing lack of effective treatment for most infectious diseases before the use of antibiotics for cases in the civilian population after World War II [113:91 – 109]. Diseases that probably

killed the majority of people in earlier times had been controlled through prevention, changes in health-related behavior, and social organization. After the 1950s, severe cases of acute infectious disease became relatively rare in England. The decline in infectious disease mortality gave rise to the concept of epidemiological transition from acute infectious disease to chronic conditions associated with age. However, emerging diseases and the pandemics of influenza and HIV/AIDS led to the modification of transition models based on linear progression through distinct phases characterized by predominant diseases [4].

Many emerging infectious diseases have threatened human populations in the past when human activities changed the environment or created ecological conditions favoring a new pathogen. This can disrupt the ecological balance of the interacting infectious disease agents prevalent in the human population [140]. Clinical manifestation will vary with the characteristics of the pathogen including virulence and infectivity, and with characteristics of the host such as age and gender. Other demographic factors including population growth, movement of people, and crowding are major determinants of the spread of infectious disease. The majority of the important emerging infectious diseases of the 20th century and recent years have been viruses, particularly RNA viruses such as influenza, coronaviruses and Ebola, and arboviruses including dengue and Zika. Their emergence reflects changes in the dynamic balance within complex global ecosystems of humans, animals, pathogens and the environment [141]. As in the past, vaccination has a key role in protecting individuals and populations. Since it was used successfully for the prevention of smallpox, vaccination has become a highly effective population-level strategy for the control of infectious disease globally. Vaccines against influenza, whooping cough, measles, diphtheria, poliomyelitis, meningitis, hepatitis and tetanus have reduced incidence and prevented millions of deaths worldwide. Vaccines with various levels of effectiveness have also been developed for the prevention of plague, typhus, typhoid, cholera, Ebola and other warm-climate diseases [13; 142]. Recent trials have shown that vaccines are effective for the prevention of severe sickness in people infected with SARS-CoV-2 [143]. Other factors will determine the contribution they make at the population level, including coverage, duration of immunity, the extent to which viral transmission is prevented, and the stability of the virus [144].

Scientific and technological advances alone will not be sufficient to prevent the emergence and spread of other new infectious diseases, while many well-known pathogens still cause much acute infectious disease and many deaths in low-income countries. The causal role of specific microorganisms in some chronic diseases has also been confirmed, and there is considerable ongoing research into the role of infections in most of the other morbid conditions and chronic diseases frequently recorded as causes of death in high- and low-income countries [4]. The complex interactions and synergies between diseases add to the difficulty of classification, the basis for monitoring changing disease patterns and developing public health policy. The disease and demographic profile of particular countries and sub-populations is likely to be a key determinant of the overall health impact of SARS-CoV-2, given preliminary findings from several studies that comorbidities are associated with severe infection and related mortality [145; 146]. Further research is needed to confirm independent risk factors, although preliminary analysis of large health databases in England indicates that older adults, certain minority groups based on ethnic-origin, people living in deprived areas, and those with less formal education are much more at risk [147; 148]. SARS-CoV-2 infection is more likely to occur among people living in large households, particularly the economically insecure and those less able to protect themselves when working [149]. The clustering of morbidities in certain communities has been a focus of attention for researchers since the HIV/AIDS pandemic, and perpetuation of vulnerabilities is likely to be influenced by the wider societal context [150–152].

Differences in political systems, leadership, health service organization, and people's attitudes to science and health advice are likely to contribute to a differential impact of SARS-CoV-2 within and between countries. National strategies and capacities for controlling infectious disease vary enormously, and support is required to develop public health systems, particularly in countries where pathogens first transfer to humans. Stricter controls on the trade in wild animals killed for food or other purposes are urgently needed, enforced in collaboration with local populations supported by poverty reduction initiatives. Further regulation and enforcement is also required to prevent epidemics linked with intensive rearing and mass transportation of birds, pigs and other animals. In addition, radical internationally coordinated action beyond the scope of traditional public health policy is needed to mitigate damage to the environment and to human health caused by poorly regulated large-scale economic activities, exploitation of natural resources, deforestation, expansion of agriculture and human settlements, and many forms of pollution. A healthy planet is fundamental to the health of all human beings and the survival of other species.

In the modern world of large inter-connected populations and rapid transport, the risk of global transmission of infectious diseases is high, and international collaboration on surveillance, prevention and control is critical. The experience with new coronaviruses and the devastating pandemics of influenza

and AIDS in the last century highlight the serious threat posed by pathogens that are new within the human population. SARS-Cov-2 has already caused much severe sickness, high mortality, and massive social, cultural and economic upheaval. Political, educational, media and public attention will need to focus on reducing the threats to health from acute infectious diseases as well as the chronic diseases that are an increasing burden on health services. Prevention of outbreaks and related pandemics is a global challenge that requires political will, coordinated action and resources for the development of scientific knowledge, public health systems, and health education. In the past, public health and preventive interventions, together with regulation of human activities and changes in behavior, reduced the incidence of severe infectious disease. Effective preventive measures were often introduced in the face of public mistrust and strong opposition from commercial, industrial and other vested interests. Future interventions based on historical experience, scientific understanding and public support are likely to be less costly in the long-run than dealing with the economic and social consequences of destructive infectious disease epidemics.

Disclosure statement

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