The next epidemic – is it inevitable?

Introduction

An epidemic can be defined as a temporal increase in a disease's frequency above what is normally expected in a population[1]. This loose definition includes both communicable and non-communicable diseases and the time-frame of epidemics can stretch from days to decades. Due to their inherent ability to spread throughout a population, communicable diseases readily cause epidemics faster and more frequently than non-communicable diseases and are thus more likely to cause the next epidemic. Therefore, this essay will discuss communicable disease epidemics with a particular focus on the measures that can be put in place to prevent them.

A World in Motion

A susceptible individual is a member of a population that is at risk of being infected with a disease. Changes in genetic composition, immunological and nutritional status, among other factors, alter the proportion of susceptible individuals in a population[1]. The greater the proportion of susceptible individuals in a population the more likely an epidemic will occur in that population. Environmental determinants, such as sanitation, access to healthcare, agricultural practices, over-crowding and climate, are important factors affecting disease type and exposure opportunity[1]. In addition, pathogens are forever evolving to overcome host immune defence in order to infect susceptible individuals and reproduce. This eternal aim of pathogens and the constant flux of populations and environments results in frequent pathogen exposure to susceptible hosts, such events give footholds for epidemics to occur. Thus as the epidemiological triad of populations, pathogens and environments are destined to remain dynamic, epidemics will inevitably occur.

Whilst epidemics are inevitable, they are also preventable. Edward Jenner's observation that inoculation of cowpox conferred immune protection against smallpox lead to the development of a key weapon in the war against infection – the vaccine. This discovery subsequently prompted a public health revolution culminating in the official global eradication of smallpox in 1980[2].

Prior to the introduction of widespread vaccination, measles epidemics occurred in limited cycles[3]. Birth and migration drive an increase in the proportion of susceptible individuals in a population ultimately pre-disposing the population to a future epidemic. Modelling such epidemics mathematically can inform us about the processes that underlie characteristic epidemic patterns[4]. A greater understanding of these processes may improve epidemic forecasting and the effectiveness of public health interventions, including vaccination and quarantine.

Whilst vaccines have been successful in breaking endemic transmission of childhood diseases such as measles, mumps and rubella, as evident by recent measles outbreaks[5, 6], achieving sufficient vaccination levels to prevent epidemics is difficult - especially when working against negative public perception and variable vaccine efficacy[7]. In addition, the development time and cost of vaccines limit them in a particular epidemic prevention scenario: emerging infectious diseases.

Ebola: Sparking an R&D Revolution

Emerging infectious diseases (EIDs) are a major public health risk due to their epidemic potential and the unique problems they pose. Firstly, due to a lack of exposure most individuals have little, if any, pre-existing immunity allowing the disease to easily disseminate throughout populations. The historical medical insignificance of an EID can make correct diagnosis and appropriate management of the disease challenging[8]. Finally, there are often no therapeutics or vaccines available during the time of outbreak due to a historic lack of investment in research and development due to inadequate financial incentives[8].

The 2014 West Africa Ebola Epidemic illustrates the potent damage EID epidemics can cause and the cost of being unprepared. The 2014 Ebola epidemic was the largest ever Ebola outbreak with 28,646 cases resulting in 11,323 deaths across 10 countries - the majority in Sierra Leone, Liberia and Guinea[9].The epidemic outlined significant shortcomings in in global epidemic preparedness and management. As a result of the Ebola outbreak, multiple organisations and initiatives were set up in to improve epidemic preparedness and mitigate the damage outbreaks.

At the advent of the Ebola outbreak there were no diagnostic kits, therapeutics or vaccine[10]. As a result, the WHO Ebola R&D initiative was set up to encourage collaborations that could develop products for use in the ongoing epidemic. The success of the WHO Ebola R&D initiative in mobilising sufficient resources to produce diagnostic kits, an effective vaccine and launch multiple clinical trials in a narrow time-frame prompted the WHO to launch the R&D Blueprint for emerging diseases in 2015[11]. This initiative uses expert opinion to annually evaluate which emerging diseases are the most likely to cause an epidemic for which there is insufficient countermeasures[12]. This disease prioritisation process is followed by the formation of target product profiles with the aim of developing effective countermeasures before an epidemic occurs. Developing therapeutics between epidemics is challenging due to the lack of cases and so inability to perform clinical trials yet despite this significant progress is being made in MERS-CoV R&D due to effective stakeholder collaboration[13]. This R&D roadmap should be emulated in other diseases prioritised by the WHO.

Whilst prioritising diseases for research is certainly a positive step towards developing therapeutics, the essential role the pharmaceutical industry plays in developing drugs and vaccines cannot be underestimated. To ensure the development of EID vaccines in the absence of an ongoing epidemic, significant financial incentives must be put in place to encourage vaccine developers to create products that may never be used. The Coalition for Epidemic Preparedness (CEPI) aims to invest in EID vaccine R&D and take promising candidates from pre-clinical development to proof-of-concept trials by filling in the funding gaps that would normal prevent so, thus correcting market failure in EID vaccine development[14]. With a large initial investment from its founders, almost half of the $1 billion required for the first 5 years of operating, CEPI seems financially capable of achieving its preliminary goal of developing 2 promising vaccine candidates against each of MERS-CoV, Nipah and Lassa viruses[15].

A Tale of Two Outbreaks: The Importance of Early Intervention

CEPI is not the first organisation aimed at co-ordinating a global effort to ensure adequate vaccine supply for future epidemics. Established in 1997, the International Co-ordinating Group (ICG) on vaccine provision continues today to monitor and stockpile vaccines against meningitis, yellow fever and cholera for deployment to an outbreak 10 days after a nation's request[16].

In 2014, South Sudan descended into civil war, displacing 20% of its population[17]. Assessment of the sanitation, rate of watery diarrhoea and nutritional status of inhabitants of the temporary camps prompted the Ministry of Health to request and receive just under 250,000 oral cholera vaccines (OCV). When cholera struck South Sudan in April 2014, the OCV program was successful in containing the outbreak to only a few regions that did not receive vaccination. Vaccinated camps only had sporadic cases suggesting that little, if any, transmission was occurring. 6,269 suspected cases were reported throughout the country during the epidemic[17].

The 2017 Yemen cholera outbreak, also due to civil war, has surpassed 1 million suspected cases, contrasting the success of the ICG's distribution of OCVs in South Sudan 3 years prior[18, 19]. Such a horrendous milestone shows that even with an adequate supply of efficacious vaccine the logistics required to plan and execute a vaccination program in a conflict zone can be too great in the narrow timeframe of an ongoing epidemic.

South Sudan's ICG request for 250,000 OCVs came months prior to the epidemic whereas Yemen's request for 1 million OCVs, which was later denied, was 3 months after the index case[17, 20]. The difference in the size and duration of these two epidemics illustrates the importance of early interventions, however, the speed at which epidemics arise and escalate pose a challenge for vaccine logistics. South Sudan received the OCVs 4 weeks after request submission, thus unless significant logistical advances occur, early planning and accurate forecasting is required for effective epidemic preparedness.

Forecasting and effective disease surveillance by Africa Centre for Disease Control (Africa CDC) could alleviate the logistical challenge of future epidemics. The Africa CDC, set up in 2017, co-ordinates with regional collaborating centres in Egypt, Nigeria, Gabon, Zambia and Kenya[21]. As each centre has their own lab with advanced diagnostic capabilities for emerging diseases the CDC will be able to rapidly identify known and unknown pathogens. A regional, dedicated workforce trained in disease surveillance and public health policy should result in earlier implementation of public health interventions, such as ICG requests, quarantine and treatment centres, that could contain an outbreak like cholera in its early stage.

Conclusion

The vast sums of resources invested into organisations involved in disease surveillance, epidemic preparedness and EID vaccine development only support the notion that the next epidemic is an inevitability. Vaccine design, development and delivery has improved significantly since the cowpox-lesion-inoculation days of Edward Jenner. Yet 2017's, cholera epidemic in Yemen illustrates that humans and epidemics have changed little since The Plague of Athens in 430BC. War, poor sanitation and overcrowding played a significant role in triggering both these and many other epidemics[18, 22]. Humankinds' long history with epidemics points towards a similarly long future with them unless these problems are tackled globally.

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