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Review Article

Have outbreaks of the World Health Organisation's Disease X been identified?

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Abstract

The World Health Organisation (WHO) has recently highlighted the possibility of a curious Disease X with potential to cause an international public health emergency. This research update details the progress to-date at identifying potential outbreaks of Disease X. During these outbreaks' medical admissions and deaths, but not surgical, increase for an approximate 12-month duration, before reverting to the baseline level. These outbreaks appear to initiate most commonly in the interval from the end of winter to the end of spring. A range of medical admissions increase which seemingly have a common immune function linkage, possibly related to certain types of inflammatory response. Research on alternative immune steady states presents a possible basis for this on/off switching of population health. As the WHO have noted, urgent research is required to further document these alarming disease outbreaks, which have eluded traditional disease surveillance methodologies.

Keywords: Disease X; On/Off Switching; Immune Function; Deaths; Medical Admissions; Nearness to Death Effect

Introduction

On the 6-7th February 2018 the World Health Organisation (WHO) held its second review of the 'Blueprint List of Priority Diseases' (WHO 2018). WHO experts developed the priority list to identify those diseases with the potential to cause a public health emergency in the absence of efficacious drugs and/or vaccines, and where there is an urgent need for accelerated research and development. The list includes a curious 'Disease X'. In respect of Disease X, for the past ten years I have been researching international outbreaks of a new type or kind of disease in which both medical admissions and deaths suddenly increase to an alarming degree, stay high for one year, and then revert to the baseline level. Both stay at the baseline level until the next outbreak. This behaviour has been called this on/off switching Jones [1]. Medical rather than surgical admissions are primarily affected Jones [2]. This research update will explain how these outbreaks have eluded current disease surveillance methods, look at the emerging evidence, give a tentative explanation for the one-year approximate duration, and show how deaths and medical admissions are linked via the phenomenon called the 'nearness to death effect'.

The Nearness to Death Effect

It is a common misconception that hospital admissions rise markedly with age, however, this seeming truism is an artefact produced by the omission of the nearness to death effect on admission rates. The nearness to death effect simply observes that around half of a person's lifetime hospital admissions and bed occupancy is compressed into the last year of life, irrespective of the age at death. This fact has been well documented for over four decades and in multiple countries Henderson [3], Busse [4], Payne, et al. [5]. During the last year of life there is a rapid decline in cognitive ability, increased frailty, increased reliance on others for the activities of daily life and increased long-term care outside of the home Rabbitt et al. [6], Kalbarczyk-Steclik & Nicinska [7], Aaltonen et al. [8], [9]. Failure to account for the nearness to death effect creates the illusion that age is responsible for higher healthcare costs and frailty Busse et al. [4], Payne et al. [5], Rabbitt et al. [6], Moore, et al. [10].

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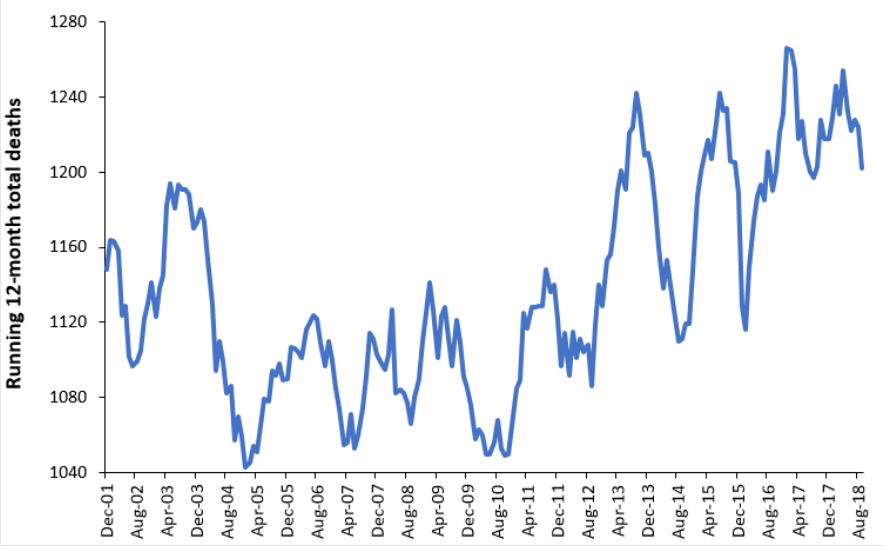
One-year Duration

Hence, any agent capable of tipping a significant proportion of the population into the rapid decline experienced during the last year of life will therefore simultaneously increase both hospital medical admissions and deaths (both in and out of hospital). Also, an outbreak of this agent would then last for approximately one year as the end-of-life cohort follow a trajectory to ultimate decease. Those already on this trajectory may have their decease hastened and symptom severity will be increased.

Current Disease Surveillance is Inadequate

Many disease surveillance methodologies rely on the detection of levels of deaths which are above the upper confidence interval. These are typically conducted at national or regional level. This new type of disease outbreaks has the unique feature that deaths and admissions jump suddenly and then stay high for 12-months. The full effect can only be observed in a 12-month moving or running total, and the initial step-like increase is usually below the detection threshold of current surveillance methods Jones [11] which are basically fine-tuned to detect spike-like events such as an influenza epidemic. In addition, the outbreaks occur at neighbourhood level with variable synchrony between neighbourhoods Jones [12]. In one study in England outbreaks were observed in around 1% of neighbourhoods in any month of the year Jones [13]. The level of synchrony between the neighbourhood outbreaks then determines the shape of the 12-month total time trend at local authority, regional and national level. This is further complicated by the fact that males and females behave as separate compartments and can lag each other Jones [13] and that certain social groups are affected more than others Jones [14].

In a running 12-month total, seasonality is effectively removed, and initiation of the sudden 12-month increase in deaths occurs at the foot of each peak, while the full extent of the sudden increase is revealed at the peak some 12-months later. Switch-off then occurs. Up to the present such switch on/off was not thought possible, so no one thought to look. Figure 1 gives a typical example of a 12-month running total of deaths in an affluent local authority in the south of England. The large 2012 event seen in Figure 1 has been extensively investigated at small-area (neighbourhood) level across the six local authorities in Berkshire. The effect on medical admissions at the local hospital was also documented Jones [15], Jones and Beauchant [16]. As can be seen sudden and large increases in deaths commenced (foot of the valley) for the four most recent events in October 2010 (+9%), October 2012 (+14%), September 2014 (+11%) and March 2016 (+13%). All these increases exceed the 99.99% confidence interval. There is currently no official explanation for this concerning behaviour.



Footnote: Monthly data on deaths by usual area of residence is from the Office for National Statistics (2018) https://www.ons.gov.uk/peoplepopulationandcommunity/birthsdeathsandmarriages/deaths/datasets/monthlyfiguresondeathsregisteredbyareaofusualresidence

Figure 1: Running 12-month total of deaths in the West Berkshire local authority in the south of England.

Features of the New Disease Outbreak

The key features of each outbreak have been summarised in several reviews Jones [2,17,18] however, the salient points are:

i. Certain medical conditions are most affected Jones [17,19,20].

ii. The increase in admissions does not imply increased incidence but rather increased disease severity.

iii. Other conditions show an unexplained reduction Jones [21].

iv. Persons suffering from Alzheimer's and dementia experience the highest increase in deaths, followed by respiratory infections Jones and Goldeck [22].

v. Medical admissions rise first followed by in-hospital and out-of-hospital deaths around two months later, i.e. illness precedes eventual death Jones [23,24].

vi. Staff sickness absence in hospitals likewise increases before deaths, infection due to proximity Jones [25].

vii. A time cascade for certain illnesses appears to exist, i.e. certain illnesses take more time than others for the effect to reach the level required for an acute admission Jones [15].

viii. Single-year-of age specific patterns appear to be involved which suggests the possible involvement of the immune phenomena known as antigenic original sin (the Hoskins Effect) Jones [2].

ix. The rise in respiratory illness suggests that aerosol is one route for transmission Jones [18].

x. The effect on deaths has been characterized across Europe, USA, Australia and New Zealand Jones [26].

A Possible Candidate

Such widespread increase in deaths and medical admissions suggests a common pathogen whose acute effects have been previously discounted. Evidence suggests that the immune modifying virus Cytomegalovirus (CMV) may be involved via sub-clinical immune manipulation Jones [25,13], Rocha et al. [19]. This requires extensive clinical validation.

A Possible Mechanism

Research suggests that the immune system can exist in discrete steady states Craddock et al. [27]. A pathogen capable of modifying immune function therefore has the potential to shift the immune steady state of a susceptible proportion of the population. Further metabolomic and immune studies are required. The possibility exists that several inflammatory markers may rise during the events [28,29].

Conclusions

Recurring outbreaks of a powerful new type of kind of disease have been occurring for many years. This has evaded traditional disease surveillance which looks for spike events such as an influenza epidemic. The aetiology for this disease appears to be immune-based with secondary effects against disease severity and progression across a range of illnesses. Whether the outbreaks affect both incidence and disease severity need to be investigated. No official explanation has been offered for these recurring events.

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