FLU AND POLITICS

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The author was born in Liverpool, the son of a minister. He was educated at Porthmadog County School, Friars School, Bangor, and Liverpool University. He graduated in 1938 and was awarded his MD in 1951. He was a lieutenant colonel in the RAMC in Europe and Burma during World War Two. Following thirteen years as county medical officer for Anglesey, he accepted an invitation to join the World Health Organisation to undertake research in South America. He returned to London, to the Ministry of Health and Social Security where he was responsible for international health and research and development. On retirement, he returned to Anglesey. His specialist field is epidemiology and medical statistics. He is an Honorary Fellow of the Royal College of Physicians and an honorary member of the Gorsedd y Beirdd1. He has published widely on epidemiology and public health.

Abstract

Following an outline history of flu, there will be a brief description of the virus in light of current knowledge. It will be noted that specific characteristics relating to flu correspond to the epidemiology of the infection. In light of the imminent threat of a pandemic similar to Spanish flu 1918-19 in the United States in 1976, the Administration’s response was a campaign to immunise the entire population. This attempt failed and the story is an example of the unfortunate way in which science and politics can react against each other.

1 Gorsedd of Bards – Gwilym was a member of the highest order under the name Gwilym Ddwylan, acknowledging his allegiance to both sides of the Menai.
‘What if...’ is a harmless way of passing the time. It is a simple game. Choose a person or a historic event and ask the questions ‘What if such and such’ and let your imagination flow. Blaise Pascal started the game when he asked ‘What if Cleopatra’s nose had been an inch shorter?’ and suggested that the history of the world would have been different. It is natural for a doctor to consider the consequences, sometimes far-reaching, that disease and illness has had. What if Lloyd George had been fully fit in August 1931 rather than being laid up following removal of his prostate? The epidemiologist is interested in the way infectious diseases influence the course of history; and there is an abundance of material to fire the imagination. The classic example is the Plague2 (or clwyf y marchogion3 – literally, the disease of horsemen according to Glyn Penrhyn Jones who associates the infection with that referred to as striking the Ashdodian armies) – the great epidemic that swept through all of Europe in the middle of the 14th century, resulting in revolutionary social change. A consequence of this enormous decrease in population was the collapse of the feudal system. In his recent publication Medieval Anglesey, Dr Anthony Carr provides a detailed assessment of the effects of the Plague on Ynys Môn.

There is a wealth of other examples of the critical impact of epidemics on the nations of the world. One remembers the fate of Senacharib’s army in the siege of Jerusalem. In the Second Book of Kings it is the ‘angel of the Lord’ who is credited with saving the city but it is more likely that the Assyrian armies were unexpectedly afflicted by some lethal disease. And, in truth, wherever armies were amassed, infections followed. Over the centuries, up to the Second World War, more died in the camps than on the battlefield.

When trying to equate past infections with diseases we are familiar with, we must remember that views about the nature of disease have changed greatly. As a result, the written evidence is often in terms which we find difficult to grasp. Sometimes, however, the description that comes down over the years is unequivocal. When the poet Ieuan Gethin over 600 years ago refers to ‘y swllt mewn cyswllt cesail’ (the shilling in the armpit), there is no doubt that he is referring to the Black Death.

**Flu in history**

We may wonder what suddenly infected Harry Tudor’s soldiers after the victory at Bosworth. The name given was the English sweating sickness but there is some doubt as to its nature. Over 60 years there were five epidemics of this disease and one of these spread through Europe as far as Vienna. Perhaps it was the flu.

In 1562, however, we have the first definitive description of the flu in Scotland, in the court of Mary Queen of Scots. There are, from then on, accounts of sporadic epidemics of the disease. Some can be traced in London weekly death statistics – the Bills of Mortality. The graph (Fig. 1) for 1679, for example, is very similar to the shape of an epidemic graph today. There will be no detailed discussion of the flu here (see Creighton for further information),

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2 in Welsh: *haint y nodau*, literally, the disease of the marks
3 Also, commonly used in Welsh for piles/haemorrhoids
suffice to note that even though there is some doubt about certain contemporary reports, when we are directly faced with a great epidemic, doubts disappear and it is only the flu that explain it. The biggest epidemic of all was the Spanish flu (1918-1919) as it was called which was the cause of between fifteen and twenty-five million deaths across the world. This is the greatest single epidemic in human history. We saw two big epidemics comparatively recently, Asian flu in 1957 and Hong Kong flu in 1968. These three epidemics were pandemics, that is, they weren’t restricted to one country or even one continent – they were world-wide diseases. In each of these pandemics, a high percentage of the population were stricken. It is estimated, for example, that 26% of the population of the United States came down with the disease between 1918 and 1919.

There were, in all probability, other pandemics before our century. I suggested that the sweating disease was in fact influenza and there is very little doubt that there was a pandemic in 1889. What is common in all of these incidents is that significant pandemics occur from time to time and, in between these, there are more minor epidemics. When discussing the conduct of the virus and the human response to its emergence, this is the pattern that must be considered.

The altering virus

At the end of the 19th century, the belief was that the bacterium discovered by Feiffer, and which is named after him, was the cause of the flu. But by the 1920s it was evident that it was a virus and not bacterium that caused the flu. Shope’s 1931 discovery confirmed that it was a virus that was responsible for a disease similar to the flu in pigs. Two scientists in
London, Andrewes and Wilson Smith, were working on the challenge of isolating the virus in cases of the disease in humans. Their efforts were, however, unsuccessful until Wilson Smith happened to hear that a disease similar to flu had appeared in the Wellcome Institute laboratory. A group of scientists there were working on the canine disease distemper taking the ferret as a model. Flu was around at the time and a number of the Wellcome team were unwell with the illness. All accounts suggest that the ferrets also suffered from the same illness. As it happened, Andrewes himself was poorly with the flu and Smith took a sample from his colleague’s nostril and injected it to the nostril of a ferret. The poor creature went down with the flu. Sir Charles Stuart-Harris, one of the foremost authorities in the world on flu, was, at that time a young scientist working on the virus in Andrewes’ laboratory. One day, when he was handling a ferret, the creature sneezed into his face and within two days he became poorly with the flu. Therefore, it was not only possible to transmit the disease from human to animal but also from animal to human.

In 1935, Wilson Smith successfully grew the virus in chicken eggs and the following year it was possible to differentiate three strains of the virus: A, B, and C. We need not discuss strains B and C – it is influenza A alone that causes widespread epidemics and pandemics.

Under an electron microscope, the flu virus appears as a small ball about hundred nanometres in diameter. Within its shell are the proteins that differentiate the A, B, and C types. Hundreds of small bulges extend out of the shell, the majority are like small thumbs and the others are a mushroom shape. These are the two antigens, haemagglutinin (the thumbs) and neuraminidase (the mushroom) which stimulate the body to produce protective antibodies. The reaction which the haemagglutinin produces was discovered in 1941 but the neuraminidase reaction was not discovered until 1957. This then was the first time it was possible to classify the virus by type – A, B, or C – and by sub-strains – H or N. Furthermore, within the shell, there are 8 strands of RNA which makes the flu virus unique as each strand of RNA carries only one or two genes.

We now know the function of some of these RNA genes; gene number 4 regulates the production of haemagglutinin and gene number 6 is responsible for the neuraminidases. Genes 3 and 5 are thought to be linked to the severity of the virus.
From time to time, two types of antigenic mutations take place: one is called an antigenic drift and the other an antigenic sift. In the antigenic drift, the change in RNA is comparatively minor but that means that this year’s flu virus is not exactly the same as last year’s. Your bout of flu last year, therefore, will not result in full immunity from this year’s. Despite this, although the mutation in the RNA is comparatively small, it is likely that there is some cross protection from year to year. The drift phenomenon can be described in the familiar terms of evolution. But antigenic sift is an entirely different matter with major changes in the structure of the RNA which are evident in completely new types of haemagglutinin or neuraminidase, or both simultaneously. As the virus changes radically, the disease can spread both quickly and widely, though that does not necessarily happen.

By now, the sequence of the amino-acids in haemogluttinin molecules have to a large extent been analysed so that different types of the virus antigens can be compared. The results of these complex studies correspond closely with the epidemiological facts. It can be stated with confidence that recent pandemics, Asian flu in 1957 and Hong Kong flu in 1968 (Fig. 3) were the result of sifts. There is good reason to believe that a sift corresponding to swine flu was responsible for the great pandemic of 1918-19 and there is some evidence to suggest that the pandemic of 1889 followed a sift similar to that which was responsible for the Hong Kong flu of 1968. These similarities led to the notion that the flu virus seems to replicate itself every now and again but there is no real basis for this theory. Rather, by today, the belief is that the sift follows mixing genes from different sub-types of virus, a genetic form perhaps of sexual reproduction.

By the early 1960s, the understanding was that the flu virus was found not only in pigs but also in horses and birds – domestic birds such as ducks and turkeys and particularly sea birds. By cultivating human flu virus and bird flu virus in the same egg, it was found that it was possible to create a new sub-type. It is this genetic re-mix that is probably responsible for the sifts that precede pandemics. And if the conditions are favourable and the necessary characteristics present in the new virus, it will displace the sub-type that was previously common amongst humans. The new sub-type will continue for a period of time thus causing sporadic epidemics as a result of drifting until it too, in its turn, is superseded by a new sub-type. In nature, therefore, it is fate that decides when a new sub-type emerges and causes a pandemic and when the drift is sufficiently significant to cause an epidemic.

In addition to the three sifts this century, that is Spanish flu, Asian flu, and Hong Kong flu, Beveridge believes that we can be fairly certain about the seven other pandemics since the beginning of the 18th century. This suggests that a sift happens, on average every quarter of a century more or less but that the intervals between pandemics can range from ten years to almost half a century. There is, therefore, no predictability in the pattern and it would be a brave person indeed who is willing to predict when the next pandemic is due.

In January 1976, there was an outbreak of flu among the soldiers in Fort Dix camp, New Jersey. The cause was the sub-type A/Victoria which has struck the soldiers and it was fairly common throughout the world that year but five of the men had a different sub-type and one of them died. It was soon discovered that the unknown virus was closely related to the swine flu which was thought to be responsible for the massacre of 1918-19 and further
research found that blood samples from around 500 soldiers matched the new sub-type, suggesting that it was capable of spreading from person to person in the camp. The immediate question was whether the devastating Spanish flu was about to return. The Centre for Disease Control (CDC) in Atlanta, Georgia, sent out queries to establish whether or not similar cases had appeared in other parts of the country but only a handful of cases were found and those were in people with direct contact with pigs. Neither had the new virus spread within the state of New Jersey, beyond Fort Dix. By this time, the season when flu was widespread was coming to end. That could be the reason for the contained spread. Spanish flu had been comparatively harmless at its start in the spring of 1918 but it had become shockingly fierce by the following winter.

As it happened, one of the regular meetings of one of the advisory boards of the CDC, the Advisory Committee on Immunization Practices (ACIP) which is very influential in this field, was to be held on March 10 and naturally there was a discussion about this new flu and what should be done. Immediately after the meeting, Dr David Sencer, the head of the CDC, travelled to Washington to present the experts’ judgement to the government’s Secretary of the Department of Health Secretary, a position equivalent to the Minister of Health in Britain. The two met on Monday morning, March 15. In a memorandum presented to the Secretary by Sencer, the facts were presented: (a) that a new sub-type of the flu virus had emerged and that it was closely related to the sub-type considered to be responsible for the great pandemic of 1918-19 during which half a million people died in the United States; (b) that the majority of the population had no natural immunity against this new sub-type; (c) that the ACIP would formally and publicly recommend that the aim should be to immunise the whole population against the new flu; (d) that it was hoped that sufficient supply of vaccine could be produced in time, before the next flu season but the government would have to commit to the purchase of two hundred million doses immediately otherwise the commercial companies would not produce sufficient supply as it would, in their view, be a risky financial enterprise. He went on to outline the steps that could be taken: (i) that the health authorities in every state, county, and city should initiate plans immediately to ensure that they could start the vaccination plan without delay when supplies became available; (ii) that members of the public should be informed so that they were prepared to take advantage of the opportunity to be vaccinated; (iii) that Congress should be prepared to allocate the vital funding.

Matthews and Ford

The Secretary was called Matthews and Sencer’s memorandum had put him in difficult position, particularly considering that the media could get hold of it. Matthews had been invited to Washington by President Ford, a few months previously, leaving his position as the President of the University of Alabama. Although his was a political appointment he had very little experience of national politics and as a layman, he had little ground to argue with
an experienced, single-minded, professional like Sencer. It is said that Sencer leaned heavily on the Secretary that morning to act decisively. Perhaps he did not need much persuading. Matthews was a comparatively young man, personable and laid-back with no evident political ambitions but who was also keen to use the authority of his new position for the good. The meeting with Sencer resulted in Matthews writing that same day to the Treasury chief, with a copy of the letter going to the White House, alerting them of the need for additional funding to meet the impending danger of a pandemic of the new flu.

One particular aspect of the letter, sent hurriedly, was that Matthews indicated the probability of the swine flu resulting in millions of deaths. I don’t know where that figure came from; it does not appear in Sencer’s memorandum but one wonders whether this was a figure noted when the two met. Did Matthews make a simple calculation: as the population had doubled since 1918 when there were a half a million deaths, a million deaths could be expected this time? It is a completely improbable figure as the percentage of deaths from the flu is now far lower than it was in 1918 due to the availability of drugs to treat complications such as broncho-pneumonia. Whoever was responsible, the figure stuck, and from then on that was everyone’s estimation, from the President down. Before the President could make a final decision, within two days arrangements were made to invite experts on health matters from across the country to an urgent meeting in the White House so that President Ford could hear the professional opinion for himself. Of those invited, the two most famous were Jonas Salk and Albert Sabin, two pioneers in polio immunisation and whose work had been so exceptionally successful at the end of the 1950s. Those in the know were aware that they had not been on the best of terms in the past and when it became evident that they were in total agreement in favour of the assertive programme of universal vaccination against the new flu, it was only natural to infer that this was the right path to follow.

Perhaps Ford had made his decision before he heard the expert views; certainly the White House staff were of the view that the President had already come to a decision. It was a large gathering and those present were unwilling to express, publicly, a view which was at odds with that of Salk and Sabin. Ford, to his credit and perhaps sensing that some in the room might have felt compelled to suppress their views, suspended the meeting and invited those who wished to speak to him in private into the Oval Office. No-one accepted the invitation. Ford prepared a statement for the press. Some time later, some of those who attended the meeting noted that they had misunderstood its purpose, having assumed it to be a meeting to alert them to what was being planned rather than a real opportunity to express an opinion. However, the White House staff had arranged for Ford to appear before the cameras immediately after the meeting with Salk and Sabin on either side of the President. The purpose was to launch a national campaign against the swine flu. Some of his advisers had suggested that perhaps it would be wiser for Matthews to make the announcement but Ford insisted that this was a matter of sufficient gravity for him to undertake the task himself. This meant, of course, that he would claim the credit for such a bold move, decisively meeting the challenge of this danger; not perhaps an insignificant consideration in his view. Who knows? No doubt he was conscious of the disadvantage to him were the media to discover this from an alternative source. Some leading media figures
were sceptical from the start, sensing that this was motivated by political considerations, particularly when some of them discovered that not all the experts, not even within the CDC, were of a unanimous view. Some thought that the best approach, in taking the threat seriously, would be to accumulate stocks of material, to be used if needed, rather than attempting to vaccinate everyone against an epidemic that might, perhaps, never come.

In order to fully understand the media cynicism, we need to recall the situation in which Ford found himself in March 1976. He was a comparatively obscure senator when he was chosen to run as Nixon’s vice president in the election of 1972 which the Nixon-Ford ticket, of course, won. But Nixon was forced to resign following the Watergate scandal and Ford became President. As President, he was, at least in name, the leader of his party, the Republicans, although he had inherited the post rather than winning it. He was, naturally keen to be elected in his own right next time. In March 1976, he had his eye on the first stage which was to be adopted as the party’s candidate in the general election to be held the following November. At the time, all indications suggested that Edward Kennedy would be the Democratic candidate (as it turned out, Carter was chosen) and Kennedy was chair of the important Senate committee on health. Ford could not afford to have Kennedy appear to ahead of him, particularly in matters of public health.

Furthermore, Ford had to keep an eye on another opponent. As you know, in the United States both parties choose their candidates in huge conventions held in the summer. But before that, a number of primary elections are held in a number of states when candidates compete for the state votes in the summer conventions. Ford was set on winning the Republican nomination in 1976. But competing against him was a man named Ronald Reagan – who almost defeated Ford in the first primary in New Hampshire. Ford did better in the following two or three primaries but he was shaken when Reagan won the North Carolina primary held the day before Ford held his meeting of experts in the White House and made his announcement to the media. It was clear then that he was under considerable pressure to take advantage of the opportunity to appear before the nation – a decisive and determined leader in a crisis that threatened the lives of millions of his fellow Americans. It should also be remembered that Ford was not held in particularly high regard as President. His detractors considered him incompetent and awkward. Lyndon Johnson said of him that he could not walk straight and chew gum at the same time.

Once the President had decided, things began to move. Congress passed the requisite order releasing $135 millions as requested. There were detailed consultations with the commercial companies that would be producing the vaccine products. Meetings with local authorities were held to ensure that their plans were in place. In short, people were doing what they could in their own areas to reach the goal of vaccinating the entire population of the United States before the winter.

The process of producing vaccines on a commercial scale is complex. To begin with, the virus must be grown in chickens’ eggs and if you want to vaccinate 200 million people, you need a lot of eggs. The Secretary of Agriculture did not anticipate any problems. ‘Mr President’ he said, ‘you can rely on the roosters of America to do their duty’.
It was essential to find a strain of the virus which would grow quickly and from an extracted line that would stimulate the production of antibodies. The hope was to overcome the two problems by cross-fertilising the strain of virus which grew quickly but which was ineffective with a strain which grew more slowly but that was effective as an antigen. Another difficulty, and one which relates to all types of vaccination, was the unpleasant reactions to the vaccine, for example painful arms, rise in temperature and so on. This was an important consideration in relation to a vaccination against the flu, in case the reaction was worse than the infection. By chemically splitting the virus it was possible to separate the haemaglutinin and neuraminides antigens from the unwanted proteins, resulting in a purer viral form. A number of other processes needed to be undertaken before the supply would be ready for bottling and distribution but they are not for discussion here. In addition to the production problems, field tests needed to be undertaken to ensure that the vaccine was effective in people of different ages. Three thousand volunteers offered themselves up for these tests.

'Murphy’s Law’

You will all be familiar with Murphy’s Law. This is the general principle that states that if anything can go wrong, in all probability, it will go wrong. And that was what happened with this story about the massive campaign against swine flu, as one thing after another went awry: the virus growth was slower than expected; one of the companies used the wrong sub-strain resulting in the loss of millions of portions. Then, the field tests indicated that the vaccine was not sufficiently effective with children and young people if only one vaccination were offered, as was the intention. Two injections would be needed for a vast number of the population which would require far more eggs than had been anticipated. A thorny legal problem emerged as the production companies were unable to get insurance against any possible harm caused by the vaccine. As the Government was unwilling to indemnify the companies, they were unwilling to release the material. (It is worth noting that they did not fear the cost of compensation in successful cases – they were confident that their material was safe – but rather the enormous costs they would face as a result of groundless actions that would never end up in court.) The Government could not shoulder this responsibility without Congress passing specific legislation and Congress was not particularly inclined to do anything of the sort. Some viewed the stance of the insurance companies as being unreasonable and others were concerned about setting a worrying precedent. By the end of July, therefore, the campaign seemed to be over before it had properly begun. The impasse with Congress was still not resolved when suddenly, at the beginning of August, a very serious disease emerged suddenly in Philadelphia. By now, we know to have been Legionnaires’ disease. In August 1976, this appeared to be an entirely new disease and its cause a mystery, striking like an epidemic with many sufferers dying of pneumonia. Was this the return of the 1918 flu? It only took CDC a few days to announce that whatever its cause, this new disease was not swine flu. Even so, the coincidence reminded everyone of what could happen (a million Americans dying?) and this spurred Congress to the legislation required for the campaign to start. October 1 was the agreed
start date, two months after the original date and with no hope of vaccinating everyone before winter. Some two weeks following the start of the programme, news came from Pittsburgh that three men in their seventies had died soon after being vaccinated. Immediately, the CDC looked for similar cases and found 33 deaths identified as being linked to similar cases since the start of October. In the United States at that time, the expectation was that 10 to 12 in every 100,000 people in their seventies would die every day, and considering the number vaccinated, 33 was close to the number of predicted deaths, vaccinated or not. Unfortunately no-one had anticipated that the coincidence was inevitable and so there had been no prior warning that this was certain to happen. It was, therefore, a natural reaction for many local authorities to abandoned the programme. Ford did his best to support the campaign. He appeared before the cameras to be vaccinated, both himself and his family. A case of swine flu surfaced in Wisconsin and received much press attention and that was a boost to the campaign. However, within the month, the first news emerged of complications which would prove a mortal blow to the campaign. A case of Guillain-Barré syndrome, a comparatively rare condition, appeared in mid November. The patient had been only recently vaccinated.

There are some 4,000 cases of the syndrome annually in the United States and its cause is not known. It was not unusual to hear of one case following vaccination but the CDC began detailed questioning, through its surveillance procedures to ascertain whether there had been other cases. By mid December, 54 cases, in 10 states, of the syndrome had been identified with 30 of them following vaccination. It was no longer possible to ignore the possibility that this was nothing more than a coincidence. Having hurriedly consulted with a number of experts, Matthews decided, and Sencer agreed, to halt the vaccinations until a full investigation had taken place. An announcement was made on December 16, with Presidential approval, that the campaign was to be suspended. This time it was not Ford who appeared before the cameras and neither did Matthews do so. The grim task was given to two civil servants, Sencer being one of them.

The end of the story? The campaign was not revived but the pandemic of swine flu did not materialise in the United States, nor anywhere else through the world either. The detailed enquiry found that Guillain- Barré syndrome was not as serious as originally feared. Some 46 million people were vaccinated and there were 532 cases of the syndrome following vaccination or one case in every 86,000 vaccinations. The vast majority of these patients made a complete recovery but 32 died, on average one for every million and a half vaccinations. These figures are, of course, misleading because there would have been cases of Guillain-Barré if no-one had been vaccinated. There is no doubt, however, that the swine flu vaccination had, to some extent, increased the risk of contracting the disease.

By now, a new President had been elected and he had appointed his cabinet. Matthews returned to his university in Alabama and his successor decided that Sencer’s time was up. He had been the head of the CDC for ten years and the feeling was that a new person was needed. And, the errors made in the campaign against swine flu had undermined his authority in the Centre and his influence elsewhere. There were a number of enquiries into
the campaign’s failures. Congress undertook an official post-mortem and at least two books on the business were published.

Wisdom after the event is easy and there is no time here to summarise the censure of the critics. Go to the sources to learn the lessons from the story. What if the effort to vaccinate everyone had been a total success? What if Spanish flu had returned and swept across the world, sparing only the citizens of the United States? Would Ford have been elected President and would Reagan now be in the White House?

The ways of the political mind are not the same as those of the scientist. When I was younger and more naive than I am now, I remember being more than a tad shaken by an observation, made in private of course, by a member of the Cabinet. He acknowledged that he had been convinced by the scientific evidence that he needed to commit to a certain course of action. But, he would not act as ‘there is’, he said, ‘no political mileage in it’. I am not suggesting for one moment that such factors always prevail but it must, at times, be difficult for politicians to discount them, even if they are no more than unconscious considerations. In dealing with politicians, scientists have to constantly remind themselves that this affects them also. There are two critical questions which need to be pondered seriously: scientists need to consider the reliability of the bases of their assertions, and politicians need to consider honestly the validity of their recommendations. Blessed is he who can pray with the Psalmist: Examine me, O Lord, and prove me; Try my mind and my heart.

Bibliography