Mathematics and Smallpox

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I am going to talk on mathematics and smallpox, but perhaps it is better to think of this is a meditation on the following passage from Voltaire: 'The Continentals consider the English to be fools and madmen: fools because they give smallpox to their children to prevent them having smallpox; and madmen because they wantonly infect those children with a certain and unpleasant disease to prevent an uncertain evil.'

Smallpox is a dreaded and dreadful disease. There are two forms of it and the serious form kills between 10% and 30% of those who catch it. It scars and sometimes blinds the survivors, and it was one of the great scourges of the 17th Century world.

In the 17th Century, people knew various things about smallpox: they knew that it was spread by close contact, and they knew that survivors were immune. Daniel Defoe, in his telling of the Fire of London, speaks of the survivors as 'Having survived smallpox, they now knew that nothing worse could happen.'

A more ready reference is, for those who have read Dickens or the interpretation on the television, in Bleak House when Dickens refrains from saying what the disease is that the street urchin, Joe, catches and which Esther catches from nursing him, but since she wakes up blind, and afterwards is scarred it must have been smallpox.

In Turkey at the time, there was a practice of inoculation. This consisted of the insertion of a small amount of matter from the pustule of a smallpox sufferer under the skin - that is, you deliberately gave a child the disease of smallpox. This was genuine smallpox, but for some reason not understood then, and to some degree still not understood now, much less often fatal. So the child, if it survived, had had smallpox and was immune for life.

Lady Montagu, whom I think of as a kind of 17th Century Germaine Greer, was the wife of the Ambassador in Turkey. She wrote a book explaining how the Turks were much more civilised than the English, and she also had her own children inoculated with smallpox, and tried to popularise it among her friends. Indeed, it did become fashionable, but it could not be denied that the inoculation itself could kill. You got smallpox and although it was milder smallpox, but sometimes it killed. This is a problem to which we will return, but since it is true smallpox, those inoculated got the disease perhaps mildly, but anybody who nursed them and who was not immune from smallpox would get the full-blown smallpox.

This practice of inoculation was then passed to England and, being English, it was bitterly opposed by the French doctors. But the question is: how can one decide whether the French doctors were right or the English doctors?

If you go through medical practice at that time, for serious diseases, such as TB, perhaps one in a thousand cases would better by itself, but with the best medical advice, one in a hundred would recover, so you were really saving ten times as many people. But there were a lot of competing medical procedures and some people were in favour of some and against others. There was not a consensus and with science as it was in the day, there was not the opportunity to find out which was actually the better. So how do you decide?

Well, there were three completely new sets of ideas that came about at that time. The first is the sudden birth of the Theory of Probability in the 1650s. People, particularly mathematicians, are very surprised that there was very little notion of probability before 1650. Of course there was betting and gambling, but they were more of the kind, 'My horse is better than your horse - 50 guineas if my horse beats your horse.' In the gambling games, it must be said, the odds were very favourable to the banker. So, all we have is the written evidence, and in something like this, the written evidence may not be sufficient. But from the written evidence, the first man to know how to bet correctly on the fall of dice was Gerolamo Cardano. Galileo was also able to do that, but neither of them published on it.

Eventually Pascal became interested in these questions, and wrote to Fermat about them, and the two together, in a very brief spurt of activity, discovered the notion of probability and expectation, and essentially discovered all of A-Level Probability and most of first year university Probability courses. But Fermat was not really interested in probability. What he wanted was to persuade Pascal to take up number theory. Pascal did not really want to be involved in it, because he was interested in mathematics against his will, since he felt that he should be giving himself to God. So, with occasional relapses, Pascal stopped doing mathematics.

The young Huygens, rightly called the Dutch Newton, was in Paris at the time. He heard that these things had been done, but had no details, so he reconstructed the Theory of Probability, wrote to Pascal and Fermat, and they said, yes, you have got it. He then published the first book on probability, which was well read throughout Europe, so probability was beginning.

The second new innovation that came about at this time, which is very suitable to talk about in Gresham College, was a growing belief in the utility of collecting facts, particularly numerical facts. This was a part of the Elizabethan Renaissance, a belief that man could conquer nature by learning facts and numbers.

One of the earliest collections of statistics are the London tables of mortality, and what was instigated was that each parish in London had someone who would collect, each week, the figures for the number of deaths and what people had died of. So, for example, the records would report that six people died of the fits, twelve of the Spanish pox, and so on. These were combined and printed. Nobody is quite clear why these tables of mortality existed. It is a plausible suggestion that it has to do with the Plague, but whether it was to enable anybody rich enough to leave town if there were signs that the Plague was increasing, or whether it was intended to reassure people that there was not a great deal of Plague about so they stayed in London, is not clear. I think, indeed, the purpose of the tables is lost, but it is very difficult to stop collecting data once you start it, particularly for governments. These tables turned out to be very useful, and they were first exploited by Graunt in 1662. In 'Observations made upon the Bills of Mortality,' for example, he attempted to compute the population of London from them, which was not easy, but he still tried.

Other people collected data. For instance, a man called Jurin specifically looked at figures for smallpox, and assuming that everybody would contract smallpox, suggested that the death rate is about one in 14, which is not implausible. It is clear, I think, that the death rate from smallpox did vary, so you got different proportions with different epidemics, but Jurin's figure is a reasonable amount.

The third new idea that is of importance to us which came about at this time was the annuity. Of course, like many innovations, it has classical roots, but it really was something new. When the Europeans were just hitting each other over the heads with iron bars, making war was very easy. The King called his knights together and said, 'You owe me loyalty - each you produce the number of followers required, and we will go and wage war.' But war then became more difficult and more professional: the way to win it was actually to use paid troops. In order to pay your troops, you need money. In order to get money, you either tax your population, which it does not like, or you borrow. It is true that, if you borrow, eventually you have to pay back, but it puts it into the future, and besides, if you win, your enemy can pay. So various schemes of borrowing are introduced, and one of them is the annuity, which is a very simple device: I give you a certain amount of money, and in return, you pay me so much each year until my death.

But why do I call this a great instrument of civilisation? Suppose that you have made your pile, so you have made the money and you now want to enjoy it. You can live off the interest but if you do that, when you die, there will be this great lump of money which you have not used. Alternatively, you can say, well, I will spend £100 a year. That is also fine, provided you do not outlive your fortune. Right? If you spend £100 a year, and you start off with £1,000, after ten years, or perhaps a little longer, with interest, you will have nothing. But an annuity removes this risk, so it is a very valuable innovation. However, an annuity is something like a bet - it is like horse racing - and that is where probability comes in. The man who provides the annuity is placing a bet that you will not live very long, so how long you are expected to live is expressed in the amount of time purchase. So if somebody had a month's purchase, that meant his life was not at all safe! Initially, annuities were just sold as is, a certain percentage in return, but the trouble was that you got lots of twenty-year-olds buying your annuities and very few eighty-year-olds. Therefore, clearly, you need to actually adjust for the fact that younger people live longer, and will therefore you have to pay more for their annuities.

In modern times, it has been said that everybody wants to retire at fifty and live till they are 100. It is just not possible. So you have got to price correctly, and to price correctly, you need to know how long you can expect somebody to live - what the probability is that they will die at the end of each year - which is precisely what this modern theory of probability will give you. That is, if you have the data, and what you need for that are life tables, which say, if you start with 1000 babies, how many will live to the age of one, live to the age of two, etc. and then you can work out, if you start with 1000 at the age of five, how many will live to six, and so on.

Now, Halley, known for his Comet and for the invention of a certain sort of diving bell, but known particularly because he is the man who got Newton to publish the Principia, he received a letter from a priest in Breslau, saying ,'We have very good records of births and deaths kept in our church registers - would you like them?' Halley said yes, and from those, he worked out the required thing - if you start off with 1000 children, how many will be alive at the end of the first year, and second year, and third year, and so on.

Once Halley had done this, Daniel Bernoulli came along and carried the work further. What he did was to use this data, plus certain assumptions, to work out what the effects of smallpox are. To do this, he had to use modern probability theory, Halley's tables, and certain assumptions, to try to work out whether there is any advantage to smallpox inoculation. Now, because he still has not got all the data that he needs, he has to make certain assumptions. Firstly, he assumes, P, that the probability of contracting smallpox during a year, if you are not immune, is the same at every age, and the same is true of the probability, Q, of dying from smallpox once contracted. Of course, these are assumptions, and if you look at them finely enough, they are probably false, but they are pretty good to be going on with, and we might as well see what will happen if we make those assumptions. Having done this, Bernoulli has to find what those probabilities P and Q are.

So, what is the probability of dying if you get smallpox? Well, nobody knows exactly, but Q equals 1/8 is a very reasonable estimate given what people say about it. What about the probability, P, of catching smallpox? That, actually, is more difficult to estimate, but he knows that there are very few smallpox cases amongst those who are older than 23, which means, if you assume that almost everybody gets it, that they will have got it by the age of 23, and you have got to choose your P correspondingly. He also has another piece of knowledge, which is about one in 13 dies of smallpox. It is not the same as the probability of dying of smallpox if you have it, but the probability of dying of smallpox, because, if a child catches measles or mumps or something else and dies of that, they cannot then die of smallpox. So he has these figures, and what in effect he does is he draws up a spreadsheet.

You might be interested to know that the first column in the spreadsheet gave the number of survivors according to Halley. So, of 1,300 babies, only 1,000 will survive to the end of their first year, 855 will survive to the end of second year, and so on, down to the age of 24, when 572 of the original 1,300 are still alive. For comparison, take a group of 100,000 newborns in the UK, we get about 1,345 deaths before the end of the first year - about one in 100 - and thereafter, really very small numbers of deaths.

Now, because Bernoulli knows the probability of catching smallpox, he can estimate the number who have not had smallpox. He has each year, he knows how many, so he can work out how many ought to have had smallpox. He assumes that deaths from other diseases remains constant, and he can work out how many will have died of smallpox and how many of other diseases.

So, having done that, he can say: what would happen if there were no smallpox? Well, presumably, the proportion of people dying each year from other diseases would remain unchanged, and so we can work out this artificial life table, which shows how many people would be alive without smallpox. So he could create the life table without smallpox, and in it you can see, right at the end, that the figure starts to diminish, which is exactly as it should be, because now people are dying who would have died earlier from the smallpox, so there are more people around, so you are actually getting a diminution in the game.

So, that is not the end of matters, because there is a risk - what Bernoulli has done is said, if there is no smallpox, this is what would happen, but of course, he says, what are we doing to eliminate smallpox - we are inoculating at birth, so there is a risk that we will kill the child if we inoculate at birth, and he suggests that the risk is one in 200. That was, I think, optimistic for when he was writing, but probably true at the end of the century, because practices had improved and so on, so if you inoculated your child, you only had one chance in 200 of killing them.

He could then work out the expected length of life of a child at present is 26 years and seven months, and the average length of life if there was no smallpox would be 29 years and nine months. If we inoculate each child in birth, then we kill some, so it will reduce the expected length of life by one month and 20 days, but there is still a gain of about three years on the average in the natural state.

However, there are problems, as Bernoulli points out. He said a great deal of trouble has been taken to evaluate the gain which could be hoped from inoculation if it were generally introduced, and the advantage to each individual who was inoculated. It is, in general, clear that this profit and this advantage could not fail to be considerable and infinitely precious, but what sort of units could we use to measure it? By the average life which could be expected after inoculation? Are all the years of life equally valuable? Are three years when you are young the same value as three years when you are old? When you are young, you have no doubt about the answer; as you get older, your views tend to modify! He says, what about the advantage to the Prince, which we would now call the advantage to the economy, and he says that, even if inoculation killed as many children as were killed by smallpox before, there would be a net gain, because it would increase the wealth of the state since it would reduce the cost of supporting non-productive children who would not reach productive adulthood. That is the economic argument. It is unacceptable to most people, I would think. Most people are repelled by such calculations. It is said that if you use the standard programme to calculate where you should put zebra crossings, and you calculate the economic costs, then the programme will never put a zebra crossing outside an old person's home.

On the other hand, having held up our hands in horror at the use of economics to calculate the value of a life and said that every life is infinitely precious and that there is no amount of money that can compensate for even an hour's loss of life of any person, then, if we actually look at how we behave, it is clear that we do not behave in this manner. We do not behave as though lives were infinitely precious. We do not behave as though lives should be saved at any cost. We clearly operate on some sort of hidden mixture of the economic and non-economic, possibly an inconsistent one. After all, we are human beings.

D'Alembert, who I think was rather jealous of Bernoulli, wrote strongly against him and asked, as we have done, what the expected gain is? Here is a kind of strengthened argument which is worth looking at. Suppose that some benevolent and truth-telling being offers you a potion which will kill you instantly and painlessly, with probability P, but will obviously otherwise guarantee N further years of happy life. What will we choose if P is a half and N is a thousand? In this instance you are being offered a thousand years of happy life, but with probability a half. What will you choose if P is 1/1,000,000, so there is a tiny chance that it will go wrong, but N is a hundred? If P was 9/10, is there any N which would cause you to choose the potion? If N is a hundred, what is the largest value of P for which you will choose to drink? Now, I do not claim to answer those questions for myself, let alone for you, but this shows that there are difficulties with any calculation of this sort, and we just have to live with it. D'Alembert suggested that instead of using the expected gain you should use the mode, which means that anybody should be happy if he outlives half of his contemporaries, but that is simply D'Alembert's view of the matter. And in any case, mathematics is much easier to use making decisions for oneself than making decisions for others. It is very difficult to capture the dilemma of a mother balancing an increased danger of present evil against some distant danger.

So all the controversy went on, but it is rare that the arguments of mathematicians or philosophers have any instant effect. What happened was that Louis XV died from smallpox, the Royal Family immediately got itself inoculated, and the thing became fashionable in France. So inoculation was established in Europe.

Having put before you all the philosophical details, I nonetheless feel that Bernoulli shows that inoculation is worthwhile. So let us agree that it is, but there are problems.

It is restricted to the rich. There is an anecdote that Catherine of Russia, being a progressive monarch, decided to be inoculated, but Russia being what it certainly was, and perhaps still is, for the Scotsman who was to inoculate her, she provided a set of fast horses to enable him to escape to the Polish border if things went wrong!

So, can it be extended to the poor? Well, if you go to Coram's Foundling Hospital, which is quite close, you will actually see the instruments of inoculation. Every orphan who went into Coram's hospital was inoculated.

Washington, troubled by smallpox amongst his troops withdrew them to a quiet spot and inoculated the lot of them. Had the British Army known, they could have attacked then. But two weeks passed, and he then had an army which was free of smallpox.

So you could inoculate the poor, but the problem, as we have said, is that inoculation causes mild smallpox, and anybody who catches the disease got the ordinary form from them. If you are an aristocrat or a wealthy merchant, you could certainly find an isolated room and you could have your child nursed for three weeks by somebody who had already had smallpox. But the poor do not have isolated bedrooms, the poor mix with each other, so unless you inoculate everybody, what you are doing is actually spreading smallpox. You can inoculate an entire village at one time, and that was done, but you just cannot inoculate all of London, and if you do not inoculate all of London, inoculating half of London will be worse off than if you did nothing at all.

That led to lengthy controversy: had smallpox actually got worse since the introduction of inoculation? I think the answer is that it was not clear then, and there is no way of discovering now. It may be that the obvious answer, which is that smallpox inoculations must have been a good thing, is wrong; it may be that it is right. We just cannot tell now what the effect on public health was.

Then the whole matter was resolved by a country doctor named Edward Jenner, who observed that smallpox inoculation is not successful on some members of the farming community, and all those on whom it is not successful remember having cow pox. So he said perhaps having cow pox, which is a very mild disease, prevents one having smallpox. He took a young lad and inoculated him with cow pox, and then inoculated him with smallpox, and the smallpox did not take. Nowadays, this would all be considered deeply unethical, but certainly it was not unethical by the standards of the 18th Century, and it worked, and so Jenner soon became very famous in his lifetime. Chains of vaccination were set up to carry the vaccine to South America and so on. So if you had 12 orphans on your boat crossing the Atlantic, you inoculated the first one with cow pox, then after a couple of days on the boat, you inoculated the second one with the puss from the first one, and so on, and the chain got across the Atlantic and you got it to South America, and all the children were then given splendid education and so on.

This was a great advance, but, perhaps not unexpectedly, although many countries just said, 'This is marvellous - we will inoculate everybody,' once this was tried in England, it ran up against objections on the grounds of personal liberty - you cannot inoculate somebody without consent. This is one of the problems. People who are against something on grounds A then feel that their case will be stronger if it also has grounds B, so somebody who has an ethical belief that torture is wrong may then add 'and moreover, it never works,' but unfortunately, that weakens rather than strengthens the moral case, because sometimes such secondary arguments can come out false. So these people who objected on the grounds of personal liberty to vaccination then went on to say that really the decline in smallpox cases could be attributed to better sanitation, that there was a natural decline in the virulence of smallpox, that indeed smallpox had never been a very serious disease. If you want to read about these things, you only have to dig slightly on the internet to get people who are writing this even today.

Let me say that, in the 19th Century, none of these arguments was completely without foundation - sanitation has a lot to do with many things. It is certainly true that smallpox vaccination, although incredibly safe compared with inoculation, is not without its risks. So you could not say that nobody was killed by the cow pox, because people were. So you got this phenomenon of longstanding anti-vaccination societies and so on, with the result that the English became rather habituated to dealing with small outbreaks of smallpox because they had these non-inoculated groups. Indeed, there a serious one in Gloucester, where in 1895, which is terribly late, there were 434 deaths due to the virus. The local paper was strongly against vaccination, and amongst those who were unvaccinated, a death rate of 42%, which is really dreadful.

So, how did the English deal with it? They invented a procedure of ring vaccination. Of course, for 400 years had people quarantined anybody who had the disease. From this starting point of a quarantined group of sufferers, you vaccinated everybody who had come into contact with the person, and then everybody who had come into contact with anybody who had come into the contact with that, and so on. And that actually would limit the epidemic.

So, let us think more about the general spread of an infectious disease. We have somebody who arrives carrying a disease, in a town which does not have the disease, what will happen? Well, there is a certain probability that he will not actually pass it on to anybody. He may die. So it may just not be passed on. There is a certain probability that he will pass the disease on to, say, 1.1 or two people, but at the beginning, the whole thing is random - it can die out or not. So, with something which is not terribly infectious, it may just randomly die out. However, once enough people have caught the disease, the laws of large numbers step in, and the whole thing behaves as though everybody with the disease was giving the disease to a certain number of more people and so on, and you just get a steady rise in cases. So, the epidemic is not really probabilistic, and we can think about it quite simply.

So, clearly, the key is the number, alpha, that each case will infect. This number will tell us how infectious it is? If alpha is less than one, if everybody, on average, infects less than one person, the disease will die out. If alpha is greater than one, then the disease will go on growing. So, this number is very important.

But of course, if you have something like smallpox, or indeed any disease, where once you have had it once, you are not going to have it again, possibly because it has killed you, but in any case, you are not going to get it again, then, as the epidemic progresses, more and more people will have had the disease, so this alpha figure will be decreasing. If I am carrying influenza and none of you have had it, and I pass around shaking hands with you all, then, I will probably pass it on to a quarter of you or something like that. If most of you have had it, it is quite possible I shan't transmit it to anybody who has not already had the disease. So what will happen is, if alpha is greater than one, the thing will go on increasing, but it cannot increase forever, so it will have to start decreasing. If it drops below alpha, it will die out, so alpha will be one, or roughly one - it will be roughly stable.

It turns out that if alpha is one, then the disease will eventually die out. This is something that took mathematicians about forty years to work out. But, how long it takes to die out depends very strongly on how large a population you have. So if you have a large population and alpha equals one, it will take a very long time to die out - perhaps a time which is so long it is not really important. If you have a few, it will die out immediately. Indeed, very famously, Iceland had a population which was just too small to support measles. So, measles in Iceland would die out, and then some sailor with measles would come in, and they would have an epidemic, it would die out, and then it would be introduced from outside, and so on.

Very famously, as well, is the case of South America. How was America colonised? Well, so far as we know, there was a land bridge or short sea journey from Siberia to Alaska, and small groups of hunters would make the perilous journey, and then spread southwards, so America would be colonised by small groups of hunters. Now, if you have a small group, suppose you have smallpox. It may wipe out the entire tribe, or it may not, in which case, the smallpox has nowhere to go and it will die. So you have a number of small groups, some of them will die and some of them will not, but the smallpox virus will die. So smallpox is cleared by this method. South America is colonised, great empires grow up, but the Spaniards arrive from Europe, which is filthy, populous, and where none of these diseases had ever died out. So the Spaniards carry all these diseases, such as smallpox, and wherever the Spaniard sets his foot, the Native American dies, and a small group of men can conquer an entire empire.

But to return to the smallpox vaccine, anybody over the age of 50 will have a smallpox scar, because the rich nations kept smallpox at bay by vaccinating all their children. In the United States, you could not go to school unless you were vaccinated. With poor nations they cannot vaccinate everybody, because there isn't the manpower, there isn't the organisation, there are other priorities and so on, and so smallpox survives there. From time to time, because, although most diseases are diseases of the poor, the poor occasionally give them to the rich, and the rich countries would get an outbreak of smallpox. But even in the poor countries there was a fair amount of cover of smallpox vaccination, so this alpha is reduced. What was finally done was combining this with ring vaccination, so whenever a case appeared, you would immediately ring vaccinate and try to kill the disease in that ring. People are very prepared to be vaccinated if there is a case of smallpox, so it is relatively easy to vaccinate people when they know the virus is active in their area.

This is a great a great triumph. The only question is: why can't we do it with other diseases? Mathematics is very good about talking in general terms for extracting the general viewpoint about a multitude of things, but although there is a general viewpoint, sometimes the correct way of looking is to see them all as different. This is the case with diseases, where each disease is different. Well, actually, each human being is different, which makes everything much more difficult, but smallpox, it turns out, has certain peculiarities which made its eradication possible.

The first is the fact, if you vaccinate sufficiently quickly after somebody has been exposed to smallpox, you may actually be able to prevent smallpox developing. So, with smallpox, vaccination can be effective even after the disease is acquired.

The second peculiarity is that smallpox is not very infectious. That may sound extraordinary, because smallpox is a feared disease. You got it in the barracks, the barracks go done with it. One case in a prison, everybody from the judge downward got it. Smallpox was like wildfire. But, subject to lots of footnotes, you have to really come into contact with a smallpox case to catch the disease. It is not carried over long distances and so on. It actually finds it quite difficult to establish itself. So this alpha of which we were talking, the number of cases that you expect to infect, is actually quite small when compared with many other diseases.

The third peculiarity, which is very important, is that there is no non-human host, so if you can get it out of the human race you have got it all. That is very different, as we know, from flu, though it is terribly unfair to refer to the current outbreak of 'swine' flu because it was us who gave the pigs the flu in the first place! They are just the carriers of a remnant of the 1919 flu outbreak, so it is human flu that the pigs have got. But with the flu, there are pigs and ducks and fowl, so there are lots of hosts, so it is very difficult to eradicate through vaccination.

If I were asked for some conclusions at this stage, I do not think that I would try to say that history provides any solutions. I think everything is always so different from everything else that you cannot look back and say this was successful then and therefore it will be successful now, but I do think that history is the background against which we operate. If we have no feeling for what happens in the past, we will make more mistakes and worse mistakes than if we have some feeling. I do not say we will make few mistakes; I say we will make fewer mistakes than we would otherwise. But basically, I would like to leave you with this thought from Whitehead:

"I will not go so far as to say that to construct a history of thought without a profound study of the mathematical ideas of successive epochs is like omitting Hamlet from the play which is named after him. That would be claiming too much. But it certainly analogous to cutting out the part of Ophelia. The simile is singularly exact. For Ophelia is quite essential to the play, she is very charming... and a little mad."

Bibliography

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(Bernoulli's paper also appears in various other collections and on the web)