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**Ebola: Emergence, Epidemic and the Global Response**

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*This lecture is dedicated to the men and women, local, UK and international, battling Ebola in Sierra Leone. Over 100 have so far lost their lives.*

At the time of delivering this lecture West Africa is in the grip of the largest Ebola epidemic by some distance that has ever occurred. An extremely dangerous disease, around 70% of those who catch Ebola currently die. It is a particular risk to health care workers and those who care for sick people and currently there is at this time no specific treatment or vaccine. This lecture will cover why Ebola has spread so widely in West Africa having not done so before, what we need to do now to control it, and prospects for future interventions such as vaccines.

The current outbreak began with a single child in Guinea in December 2013. How he got it we will never know for certain but the most likely cause is handling a dead bat or the guano of an infected bat. In the bat population Ebola is a relatively mild disease and African fruit bats, which are thought to be the main reservoir, are spread widely throughout Africa. Most of the outbreaks previously however had occurred in central Africa particularly DRC (formerly Zaire), Uganda and Sudan. Although there have been an outbreaks of Ebola, for example in Gabon, this outbreak is significantly further west and north from previous epidemics and possibly for this reason its importance was not fully appreciated when it first started. Within weeks all the child’s family were dead, a nurse who had cared for them was dead, and it had spread to several other villages. The early cases were in an area where three countries intersect; Guinea, Liberia and Sierra Leone. The virus spread through porous borders travelling from person to person and the epidemic gradually increased. Within three months a significant epidemic was occurring in all three countries increasing month on month.

To understand why Ebola from a very small number of cases initially managed to become such a large and still currently increasing epidemic, it is necessary to understand some basic epidemiology of infectious diseases. The central concept is the idea of R0 (or R). If on average one person gives an infection to one person to one further person a disease is stable in the population; it neither increases nor decreases. If R0 is 2 then one person gives it to 2 people who give it to 4 and so on. Where R0 is less than one the disease will die out in the population. Throughout the epidemic in the early phases the R0 of Ebola was somewhere between 1 and 2. It was not doubling every generation but it was increasing steadily with the doubling time in many areas of around a month. Because this compounds, it leads to the epidemic having exponential growth; doubling from 100 cases to 200 cases in a month which happened initially seems a relatively modest increase but as this compounds on it only takes a few months till the doubling is from hundreds to thousands. At the time of writing this at the moment Ebola is probably infecting roughly a 1000 new people a week. The majority of these will die.

What we need to do about Ebola is based on understanding how it is spread. All infections of humans have particular modes of transmission so for example influenza is airborne, HIV is almost exclusively sexual, salmonella is oral from contaminated foods. In the case of Ebola transmission is by direct contact with people who are sick, their bodily fluids (such as diarrhoea, vomit or blood) or contact with dead bodies. The last of these is extremely important because any funeral rites which lead to bodies being touched are dangerous to anybody who attends them.

The positive side of the fact that Ebola can only be caught by very close contact with people unless they are vomiting or bleeding is that in ordinary life it is actually very difficult to catch. If a member of this audience had early Ebola disease nobody who did not touch them in this auditorium would be expected to catch it. This is a very stark contrast to, for example, influenza. In the early period before Ebola-infected people exhibit symptoms they are virtually non infectious. It is likely they then become gradually more infectious all the way up to the period when they die (and beyond) or make a full recovery. This means that the group of people who are by far the most likely to catch Ebola are those who care for sick patients, whether they are relatives or medical staff, and those who handle their dead bodies. It does not look likely that Ebola survives for long in the environment outside humans particularly in tropical climates.

In previous epidemics two modes of transmission have tended to dominate. The first was transmission in hospitals and the first major outbreak that was fully investigated and led to the discovery of the Ebola virus by Peter Piot and other colleagues in what was then Zaire, was largely spread in hospitals, including by medical staff reusing needles to inject patients. The second major mode of transmission has always been funerals. In these previous epidemics therefore the key things have been to improve significantly the barrier nursing of patients with Ebola so as not to lead to transmission within hospital, and to make burials much safer. It has been possible to control epidemics by these two methods along with finding the relatives of people and other contacts with people who had Ebola in the community, isolating them at home for 21 days or until they have found to have symptoms, and then if they do get symptoms bring them to hospital for medical care.

In the current Ebola outbreak an additional method of transmission has however come to dominate particularly as hospitals are filled up and patients have delayed coming to medical care, and that is caring for sick patients in the community. This community transmission, which occurs between people first becoming symptomatic and first being isolated, is a very large part of the driver which led to the exponential growth of this 2014 Ebola epidemic.

In its simplest form the fact that these are the three methods of transmission means that these are the three areas where there need to be interventions to control Ebola. If we can reduce the R0 for transmission below 1 in each of these three components then the epidemic will begin to decrease and gradually die out.

The first aim therefore is to ensure that in formal medical care and also among more informal health care such as traditional healers, we minimise transmission from sick patients. The second is to ensure that burial rites do not lead to handling of the body. The third is to shorten the time between people first getting symptoms and being isolated. Each one of these has produced significant challenges in the current epidemic but if we can get all of them right the epidemic will be controlled.

It looks likely that from the time people first get symptoms they steadily get more infectious as they pass through their disease. By the time they are sick enough to be cared for in hospital they are very infectious, and may be vomiting, have diarrhoea, bleeding or other things which are likely to spread the disease. In the early stages of this epidemic a very large proportion of the medical staff who dealt with Ebola patients sadly caught the virus and most of them died. Even when people do have full protective kit for dealing with Ebola, unless routines are absolutely perfectly executed any small mistake in handling Ebola patients is potentially fatal. The fact that things can go wrong very easily has been demonstrated by outbreaks in health care staff in Spain, the USA and Nigeria.

The second major method of transmission, burials is also extremely difficult to address. The technical aspects of burying a body so that it minimises the risk of infection are well understood. The difficult thing is doing this in a way which is acceptable to families and communities. Every society has burial rites and in every society the burial of the dead is a very important rite of passage for loved ones and the wider community. Burial rites in this part of West Africa are, as elsewhere, highly complex and often involve touching and washing the bodies and other rituals which, if someone has Ebola, expose the mourners to the virus. In very prominent funerals of major figures multiple people may touch the body, either just before or after death, and this has led to super spreader events where just one dying or dead person can spread the virus to tens or even hundreds of individuals. The key thing here is to adapt rituals in a way that is acceptable to families and the community whilst also being safe. If people don’t do this the natural inclination of many grieving families will be to hide the body so that they can bury them in a dignified and culturally acceptable way and clearly this is very dangerous for all concerned.

The third issue of isolating people very early in their symptoms sounds easy but is very difficult. The problem is that the early stages of Ebola are extremely non-specific with fever, headache and feeling generally unwell. The great majority of people who have such symptoms will not have Ebola but will have things such as malaria or pneumonia or influenza. Sierra Leonean, Liberian and Guinean health services are extremely stretched with the ratio of doctors to patients of X to X in Sierra Leone. This compares to X to X in the UK. Isolating all these patients, even if people are prepared to be isolated, therefore presents a huge challenge and one of the major delays in keeping on top of this epidemic has been building up enough health capacity to be able to isolate them. Isolating them at home is extremely dangerous because whilst they start off relatively non-infectious as the disease progresses they steadily become more infectious; the longer the wait occurs, the more likely it is they will infect one or multiple other people. Building up enough bed capacity, and getting it near enough to the community where people do not have a huge delay between first getting symptoms and being able to get to isolation facilities, is therefore key to getting on top of this epidemic. Since it is essential to train people quite thoroughly before they handle Ebola patients, and understandably people are reluctant to volunteer for a nursing role which has a significant chance of killing them, scaling this up has proved difficult but at the time of writing has to a very large degree been achieved in much of Liberia, and is beginning to be in Sierra Leone. The epidemic in Guinea is currently a lot smaller.

One of the major concerns that people have is the possibility of Ebola spreading substantially outside the three main affected countries. Individual cases are likely to spread outside the three countries unless they are completely shut off from the world, which would be a disaster for them and essentially impossible to achieve anyway. Where patients with Ebola present in countries with well established healthcare systems, the possibility of a few onward transmission cases, until Ebola is recognised as being present, is there and this has occurred already in Mali, Nigeria, the USA and Spain. In each of these countries by then finding the contacts of the affected people and isolating them early, it has been possible to get on top of the mini outbreak extremely quickly. This means that the first generation (the importing case) can spread Ebola to a number of people in the second generation before it is recognised, but the second generation is likely to spread it to a much smaller number in the third generation, generally there will be no onward transmission to a fourth generation of Ebola sufferers. The chance therefore of a significant propagated Ebola outbreak in a country with a highly developed health service such as the UK is therefore as close to zero as makes no difference, although a mini outbreak could in theory occur before the first patient was identified as having Ebola. The fact that Senegal, Mali and Nigeria have all managed to get on top of small outbreaks very rapidly demonstrates that even in countries with healthcare systems not as well resourced as the UK this is possible with well established public health methods.

Unfortunately despite this Ebola is much a disease of panic as it is very serious disease for those who catch it. The reaction of the outside world to Ebola in West Africa has been to reduce economic activity with affected countries (eg mining), whilst gatherings including markets and other events which keep very poor people alive by providing income have been significantly curtailed. The impact on the lives of very poor people, most of whom have absolutely no contact with Ebola, has been profound. The first has been that the health services have been overwhelmed and also dangerous to go to because they are the one area, other than funerals, where there is significant risk of catching Ebola. We do not yet know how many extra people have died from preventable diseases such as malaria or childbirth complications but it is likely that more people have died as a result of the collapse of health services caused by Ebola, than died of Ebola itself during this period in these countries. The second impact has been economic with major falls in the economies of three very poor, but until this epidemic, rapidly expanding economies. The remarkable ability of infectious diseases to have an economic impact way beyond their medical impact can be demonstrated in a different context with the SARS epidemic which killed less than 1000 people and is thought to have wiped around $40 billion off the global economy whilst flights were cancelled and economic activity was slowed down. Supporting the wider health services and the general economy during an epidemic such as this is therefore essential along with trying to make sure that people respond reasonably rationally to what is a significant but not uncontrollable threat.

If we do not manage to get on top of the current epidemic with conventional public health methods which have been adapted with local circumstances, largely consisting of safe burial, isolation and better in hospital barrier nursing, what are the prospects for a vaccine? Currently three vaccines are being trialled in humans which are capable of being scaled up commercially if they are successful, and a further variant has already been tried in humans. None of them have yet been used in an Ebola outbreak and we do not know their effectiveness in humans. So far data suggests that they are relatively safe but we do not know if they will be efficacious. However we are encouraged by the fact that all of these vaccines produce significant protection from Ebola for non human primates, which in the case of Ebola have a disease which is very similar to that seen in humans. There is therefore a fair chance that a safe and effective vaccine can be developed, although whether it will be done in time to have a big impact on this epidemic remains to be seen. International bodies including the UK Government are doing their best to push the development phases through as fast as possible, at a rate very much accelerated compared to normal development pathways.

It is also clear that best medical management at the moment can reduce mortality from Ebola. In the general population the Ebola epidemic mortality has been around 70%. Excellent nursing care, in particular managing fluids seems to reduce this but current data suggests not much below about 50% mortality. Even in high intensity western settings once people are very sick with Ebola they certainly have a significant chance of dying. There are now a range of possible experimental treatments including better fluids, antivirals, Z Mapp (antibodies to Ebola grown in tobacco plants which have been genetically modified) and immune plasma from patients who have had Ebola. Better diagnostics are also being developed. So far we do not which if any of these are going to have a significant impact on the disease but we hope that by the time another Ebola outbreak occurs there will both be a wider range of options and hopefully better knowledge about what are the effective interventions.

At the time of giving this lecture the epidemic in Liberia appears to be subsiding, although by no means gone. In Guinea it has always been a much less severe outbreak but is not yet obviously decreasing. In Sierra Leone, the country where the UK has taken the lead in supporting the Government of Sierra Leone, the epidemic is still increasing although we hope and expect it will peak in the next 2-3 months. By the time it is over this epidemic will have killed over 10,000, has already spread to seven countries, (excluding people who were imported with known Ebola and treated which includes the UK and Germany) and had a massive impact on the lives, health and economy of very vulnerable populations. Only because of the selfless actions of doctors, nurses and other healthcare workers, both local and from international voluntary and medical groups, has this epidemic any chance of being brought under control. It is to their dedication and courage that this lecture is respectfully dedicated.

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