THE FOUNDATION FOR SCIENCE AND TECHNOLOGY

DEBATE SUMMARY

What are the lessons learned from the response to the Ebola outbreak?

Held at The Royal Society on 25th March, 2015.

The Foundation is grateful to The Wellcome Trust for supporting this debate.

The hash tag for this debate is #fstebola .

Chair: **The Earl of Selborne GBE FRS**
Chairman, The Foundation for Science and Technology

Speakers: **Professor Chris Whitty CB FMedSci FRCP FFPH**
Chief Scientific Adviser, Department for International Development
Dr W Ripley Ballou
Vice President and Head, Clinical Research and Transitional Science
Vaccine Discovery and Development, GSK Vaccines
Dr Oliver Johnson
Programme Director, King's Sierra Leone Partnership

Panellist: **Dr Gina Radford FFPH FRCP**
Deputy Chief Medical Officer for England, Department of Health

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PROFESSOR CHRIS WHITTY said that Ebola was the most serious new threat in terms of infectious disease since HIV: a tragedy for the families directly affected. Health services in the countries affected had also broken down almost completely, creating an even bigger health impact. Above all Ebola was a disease of panic. As in the case of SARS, this was the reason for the disproportionate damage to the economies of Liberia, Sierra Leone and Guinea – which had been crippled.

Lessons had to be learned from the crucial delay in taking decisive action between April and August 2014 to counter the outbreak. During this period there was wide and increasing awareness of the emergence of the Ebola threat and a lot of debate and discussion; but nothing much happened. This was a serious failure of the international health system. The World Health Organisation (WHO) had taken this on board; but it was important that the right lessons were learned. There was a risk that conclusions would be drawn to support self-serving narratives. For example, the notion that more laboratory based surveillance should have been available was wrong. Existing surveillance systems had identified the problem. The evidence was there. The problem was the delay in responding.

The fact that potential Ebola vaccines were in the pipeline prior to the epidemic but had not progressed as far as a Phase I trial was another obvious learning point. So, too, was the fact that once the international response was in full swing, the UK had been too slow to mount research into simple clinical interventions. It was not the strategic priority in the first phase of the operation. There were also difficulties in working out the UK Government's responsibility for research in centres it funds, for example relating to ethics, the scope for local authorisation and the safety of NHS staff. But opportunities had been missed both to get early evaluation of different interventions being used and to do that research when the volume of patients in the centres remained high enough to support reliable and effective evaluation.

More generally, the international community needed to recognise that in some countries – the UK and Sierra Leone being honourable exceptions – hysteria about the epidemic was allowed to trump public health.

There were, however, a number of positive lessons to be learned from things that had gone well in handling the crisis from the perspective of the UK and Sierra Leone.

First, once mobilised from August 2014 onwards, the UK's response had been, in his view, remarkable. Multiple groups - from the UK Government Departments (with cross Departmental collaboration a notable feature in its own right), NGOs, Universities, the Wellcome Trust, the Medical Research Council, the NHS, the private sector - had acted, largely in concert, to provide a systematic response to this major global threat. This activity had been complemented and supplemented by courageous volunteers – clinicians and public servants – from the UK (and across the world) and of course by West African medical and nursing staff, who had borne the heaviest burden.

The decision of the UK to focus its strategy single mindedly on getting R_0[1] below 1 had also been vindicated. It had taken nerve to stick to the strategy as the total number of cases continued to rise; but because R_0 had started to come down it was possible to be confident – and crucially to be able to persuade decision makers – that the tide would turn. Indeed modelling of this kind was one of the successes of this period: for example in predicting the impact of delay in intervention by the week and in supporting what might have been as a counter-intuitive decision to locate a major treatment centre at Freetown on the basis of a prediction that it would become the centre of the epidemic in Sierra Leone – at a time when it was not.

The R_0 strategy had four goals: reducing transmission in hospital and other healthcare settings; reducing transmission around death and safe burial; reducing transmission in the community by shortening the time between first symptoms and isolation (much more difficult for this outbreak than in the past when Ebola had been largely confined to remote and rural areas); and increasing social distancing – primary prevention.

There were lessons to be learned in each of these areas and lessons still to be evaluated. For example, the heavy toll of the disease on health workers in the early stages meant that a balance had to be struck between the epidemiological pressure to intervene early and quickly and the need to put the right processes and infrastructure in place. The real time advice from anthropologists had been of great benefit in rising to the challenge of managing the vital period just before death and subsequent funeral rites (which in Sierra Leone involved washing and touching the body) in a socially acceptable way. Recognising the need to make rational, acceptable and achievable social interventions in primary prevention was also important: adjusting greetings to avoid handshaking worked; other measures (closing schools, roads, markets for example) had serious downsides and proper evaluation was required to see which actions had any real impact on Ebola.

Other lessons to be learned from what went well included: the positive role of the armed forces (both UK and Sierra Leonean) in hospital building, training, burials and command and control – and in managing a lot of the politics; the effective integration of different scientific disciplines – epidemiology, modelling, anthropology, water and sanitation, and clinical services and public health for the UK domestic response; and getting Ebola vaccines through Phase I trials very fast – to which UK organisations had made an important contribution

DR RIPLEY BALLOU said that the context for GSK's engagement had been its take-over of a Swiss biotech company which happened to be working on an Ebola vaccine. In the early stages of the Ebola outbreak GSK had put together a plan for development of the vaccine but struggled to get traction with WHO. When WHO finally declared Ebola a public health emergency in August 2014, GSK was in a position to accelerate development of the vaccine. FDA approval for their plan was gained in 48 hours; Phase I clinical trials began in September, with results through in November, confirming that GSK had a candidate vaccine; and Phase II trials were underway and licensing was in clear prospect by the first quarter of 2015. This was an unprecedented pace of development: doing in months what would normally take 5, 6 or more years.

The first lesson to be drawn from this was the power of partnership. As GSK had experienced with a number of its development programmes, strong partnerships make for good science, shared risks, and more efficient development of new medicines and vaccines. By tapping into an existing network of scientists, investigators, funders and advisors GSK was able to significantly accelerate the development programme of its candidate vaccine for Ebola; and with the help of WHO, it entered into constructive dialogue with regulators, government leaders and National Regulatory Authorities (including those in West Africa) to accelerate process development and manufacturing, to collect the clinical data needed to launch Phase III, and to begin to define regulatory pathways that could lead to the licensing of an Ebola vaccine in a timely manner.

While some of the apocalyptic predictions of the impact of Ebola – taken, for example, to imply the depopulation of West Africa by Easter 2015 – may have been effective in terms of grabbing attention and mobilising action, it was more questionable whether they were optimal for rational decision-making and planning. Indeed arguably they contributed to a sense of desperation, which blocked normal scientific debate, especially around study designs. For example they contributed to negative views on the ability to implement randomized controlled trials, despite local consensus on the ethical issues.

GSK also faced the challenge of a leak of its early, best estimate forecast of manufacturing capacity at that time, which now, in retrospect, was overly optimistic. And while high levels talks had been held with governments on the issue of loss mitigation – for resources diverted to fight Ebola and also for indemnification against claims that might be brought by trial participants, given the very early stage of the Ebola programme – and general commitments made, GSK continued to invest without a concrete mitigation plan and had been forced to acquire expensive supplementary trial insurance using its own resources.

Over the last decade the world had encountered a series of global health emergencies for which it was unprepared - H5N1, SARS, H1N1, MERS and Ebola. All these threats had a common theme – zoonotic diseases that jump from animal reservoirs to humans. Many more were known

[1] R_0 is the average number of persons infected by a single disease source

about and some were not. We were not prepared to respond to them. Ebola had created a major opportunity to bring about a substantial change; but it would take vision, political leadership, and a rethinking of how we address this class of infectious disease threats.

It was vital to seize this opportunity by creating: a global institution dedicated to surveillance and basic research on agreed prioritised emerging disease threats; dedicated R&D units embedded in an industrial setting to focus on developing drugs, vaccines and diagnostics for priority pathogens; mid-scale manufacturing capacity for lower volume stockpiles, a network of manufacturing capacity across the world for mass production and a payment system to ensure that supplies are available when and where they are needed; and a legal framework for indemnification, agreeing an acceptable clinical development approach that could work under outbreak conditions and new regulatory pathways for approval of the tools the world will need to respond adequately to future emerging diseases.

DR OLIVER JOHNSON emphasised that his perspective would be based on what it felt like to be on the ground in Sierra Leone -in the early days of the Ebola outbreak from March to July 2014, 'the gathering storm'; during the 'apocalypse' from August to November 2014; and through to 'the long last mile' since then. He echoed Professor Whitty's remarks about what had developed into an extraordinary response on the part of the UK Government; and he emphasised that any criticisms he had were of systems, not individuals – many of whom had performed heroically.

He and his small team in the King's Sierra Leone Partnership were embedded in the local health system and had worked closely with the Sierra Leone Government and Ministers prior to the outbreak. That was often helpful, indeed crucial, during the crisis. But the team was very small – originally three supplemented by two clinicians around the time of the outbreak. What had become apparent to him as the outbreak developed was the very limited depth of clinical resources available in Sierra Leone to deal with a crisis of this kind, not least among the international bodies, including the NGOs.

During the early stages of the outbreak in West Africa, little was done by way of preparing Sierra Leone for a possible outbreak. Training for local health staff was extremely limited; stocks of relevant equipment were almost non-existent; no experts, including the representatives from WHO, were present at potentially vital training and planning meetings. At a point when Médecins Sans Frontières (MSF) were saying – correctly – that Ebola was out of control in the region, they were reprimanded by the Minister who pointed to WHO assurances that, on the contrary, things were under control. There was a clear disconnect between WHO in Geneva and WHO in West Africa – and the input of the latter could only have been hampered by the paucity of experts they had on the ground in West Africa.

During this period, the King's team had no budget, other than a donation from the Guy's and St Thomas' Charity; and they were unable to secure UK Government funding – in part because the ask was too small. Once the Department for International Development recognised the scale of the crisis, they were terrific. The Foreign and Commonwealth Office also gave the team invaluable practical and pastoral support. But in his view the later melt-down was avoidable had, at this earlier stage, quick, small scale investments been made to support infrastructure development in beds and other equipment (however rough and ready), working with the local authorities and not on a stand alone basis. His team achieved some successes in this direction; but it soon became swamped by the sheer volume of cases, the lack of beds, the lack of systems and the logistical nightmare of the distances between treatment centres. There was a high reliance on MSF as the only alternative means of support when capacity was needed; and they were stretched to the limit.

When the support began to become available from the UK Government it rapidly became clear that there was a market failure in terms of the willingness of the NGOs to create treatment centres, although one or two did step up to the plate. The solution was, therefore, to 'nationalise' the response by bringing in the Armed Forces. Notably by October even MSF were calling for the deployment of the military. This raised a key planning question for handling future crises of this kind: either military involvement should be assumed from the outset, or the 'market' had to be adjusted to support and incentivise NGO engagement. The key role played by the military (contrary to his, no doubt, false expectation that they would set about rapid construction of treatment centres) was in creating command and control systems, joining up processes and decision making on the ground. This was highly effective, although in terms of communications it did create a parallel system to the Sierra Leone Government teams like his.

The next phase saw the construction and eventual deployment of beds on a much bigger scale, to the point where the issue on the ground was about outbreak control, with the main emphasis on contract tracing and monitoring. There were, however, lessons to be learned from the experience of his team over these later phases of the management of the outbreak:

- Timelines remained too long. The construction of treatment centres could have been quicker, without prejudicing safety. The debate on the safest and most effective type of protective equipment was too prolonged and became confused. Issues such as this got bogged down by doing too much of the planning and decision-making in the UK. More scope should be given for decision making in the field, with closer engagement of local authorities and local people.

- The virtues of classic NHS operational management came into their own: supporting analysis of patient throughput, not just bed numbers, for example.

- Tricks were missed in terms of asking the right research questions – for example in relation to the merits of basic diagnostic and treatment measures - which could have had immediate impact, as well as lessons for the future.

- The current systems now being deployed on outbreak control were not as surgical as they should be. He would like to see Public Health England being deployed in supporting that function on the ground, not just in laboratories.

- There was an urgent need to strengthen health services, other than Ebola treatment, which had effectively broken down.

The speakers were joined on the panel for the subsequent debate before and after dinner by DR GINA RADFORD.

There was broad consensus that the UK had responded well – and in concert - to the crisis once the public health emergency had been called. There was no evidence that the humanitarian response had distracted from support to crises in other regions (such as Syria). On the other hand contributors agreed on the need to learn the lessons from the delayed international response to the outbreak. A number of contributors argued that WHO needed reform. Its resources were stretched. It did not have the right resources on the ground. Lines of accountability between the centre and the field were blurred. Politics sometimes got in the way of decisive action. The WHO had been successful at galvanizing support from member countries once the public health emergency had been declared. But the fault lines in the structure and resourcing of the WHO had long been apparent to member states. The problems with the organisation were political, not technical. It was for member states to take the lead on reform; and the UK Government accepted this. A new UN organisation was not the answer.

There were lessons for governments around the world in this; and there were lessons, too, for governments in the region. The heroes in West Africa were at the bottom or the middle of the social scale. There were some, at the top of these societies, who should be ashamed of their response. There was, inevitably, a risk that this would not be addressed honestly.

Other contributors confirmed that some NGOs had been slow to step up to the crisis on the ground in Sierra Leone. Their reluctance stemmed from lack of experience in such situations and associated risk aversion. The learning from this – and from the experience of those who had engaged – was being actively pursued.

The role of industry in providing capacity to develop new vaccines at speed and manufacture at scale was acknowledged. The unprecedented speed of the trials process and associated regulatory approach in this case must carry generalisable lessons for bringing other new medicines and technologies to market, even if moving at that pace would not be suitable in all cases. The response in West Africa to the vaccine, for example, in relation to trials and informed consent, was promising. The trials were on target. Decisions on the most effective deployment of the vaccine, taking account of possible side effects, were still to be determined.

The rapid development of vaccine research in this case had been facilitated by the fact that it started in non-endemic countries. That was in contrast to clinical research on diagnostics and treatment on the ground, where it was agreed that opportunities had been missed because of the focus on immediate operational priorities. This was a difficult balance to strike; but again, there was endorsement of the points made by the speakers about the need to build such processes into pre-planning for future outbreaks of this kind.

There was general acceptance of the need to make effective command and control process an early priority in creating the infrastructure needed to handle such an outbreak: treatment facilities, protective equipment and clinical processes and protocols. More use could be made of NHS clinicians, particularly if training programmes could be made more flexible. On the other hand there was considerable debate and discussion about the lessons learned in terms of effective community engagement: Was the use of anthropologists a legitimate substitute for direct engagement with local people? Were local communities effectively engaged in local prevention measures? Were international partners on transmit, rather than receive mode?

The difficulties were acknowledged. Elite capture was a problem. It was difficult to get past leaders who had the authority to take action, but who had their own reasons for avoiding responsibility. Secret societies held sway in religious and local communities. Families had protected incubators. Smuggling of infected people had occurred. The fact that the outbreak had occurred in populous regions with porous borders, had compounded the problem. For example, people could be summoned quickly and in numbers to burials through mobile technology. This confirmed the importance of recognising that the spread of Ebola was down to people not the virus itself. It would be vital to continue to work at the balance between anthropological support and genuine engagement with local communities on prevention and outbreak control. Building trust with local people was vital for international partners; and history cast its own shadow in this respect.

It was recognised that the UK domestic response to Ebola had been exemplary: from the public health and prevention perspective, to NHS front-line preparedness and the specialist treatment given to returning, infected health workers. Impressively, national communications had been based on public health science; and the Chief Medical Officer's early public warning that we should expect a handful of cases had been

powerful in setting the right tone and avoiding an over hysterical response. It was nevertheless important to review the measures taken, not least for proportionality. Was it right, for example, to halt direct flights from the affected areas? Might it not have been easier to screen visitors if they had continued?

The role of Public Health England in setting up laboratories abroad was acknowledged – and, specific tribute paid to their role in Sierra Leone. The organisation had recognised the scope for it to be involved on the ground with outbreak control in future outbreaks, if it could be resourced accordingly.

A number of contributors stressed that the outbreak was not over. Dealing with the tail of the disease to the point of eradication could still go wrong for social and political reasons; and the dilemma for focussing on that goal while rebuilding the damaged health services was real. More people were dying in Sierra Leone from other diseases and from poverty than they were from Ebola; but we had to get rid of Ebola.

Throughout the discussion tribute was paid to the heroism of West African and international workers who had led the response to the outbreak on the ground; and, summing up the discussion, the chairman acclaimed, on behalf of all the participants, DR Johnson and his team who embodied that commitment.

He thanked all the speakers for their contributions – and for the contributions of their organisations which had rightly been praised in the course of the debate. This had been a rich and open discussion. The global health system had been challenged by this outbreak, as had governments and individual organisations. There had also been genuine successes. It was evident that learning had been taken from the outbreak. There was still more to be done and more lessons to be learned.

Sir Hugh Taylor KCB

Open the summary with Adobe Reader outside the browser and click on the URL to go to the sites below.

ActionAid UK
www.actionaid.org.uk

British Red Cross
www.redcross.org.uk

Centres for Disease Control and Prevention
www.cdc.gov/vhf/ebola/outbreaks/2014-west-africa/

Ebola virus: UK Government response
www.gov.uk/government/topical-events/ebola-virus-government-response

Department of Health
www.gov.uk/government/organisations/department-of-health

Department for International Development
www.gov.uk/government/organisations/department-for-international-development

Disasters Emergency Committee
www.dec.org.uk

Economic and Social Research Council
www.esrc.ac.uk

Foreign and Commonwealth Office
www.gov.uk/government/organisations/foreign-commonwealth-office

GOAL
www.goalglobal.org

GlaxoSmithKline (GSK)
www.gsk.com

Government Office for Science
www.gov.uk/government/organisations/government-office-for-science

Jenner Institute, University of Oxford
www.jenner.ac.uk

King's Sierra Leone Partnership
www.kslp.org.uk

London School of Hygiene and Tropical Medicine
www.lshtm.ac.uk

Medical Research Council
www.mrc.ac.uk

Médecins Sans Frontières
www.msf.org

MRC National Institute for Medical Research
www.nimr.mrc.ac.uk

Oxfam
www.oxfam.org.uk

Public Health England
www.gov.uk/government/organisations/public-health-england

Research Councils UK
www.rcuk.ac.uk

Restless Development
www.restlessdevelopment.org

Royal Free Hospital
www.royalfree.nhs.uk

Save the Children
www.savethechildren.org.uk

The Academy of Medical Sciences
www.acmedsci.ac.uk

The Royal Society
www.royalsociety.org

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