

Briefing for House of Lords short debate on combatting neglected tropical diseases

March 2017

The British Society for Immunology is the largest immunology society in Europe. Our mission is to promote excellence in immunological research, scholarship and clinical practice in order to improve human and animal health. We represent the interests of more than 3000 immunologists working in academia, clinical medicine, and industry. We have strong international links and collaborate with our European, American and Asian partner societies in order to achieve our aims.

Key points

- Neglected tropical diseases (NTDs) affect close to one in six of the global population, and therefore represent a global public health crisis.
- Immunology plays a key role in the research of new drugs, vaccines and diagnostics for NTDs. However, since the London Declaration was signed, research progress has been slow.
- For example, there are currently no licensed vaccines for NTDs in the London Declaration.
- Better collaboration between academia, industry, and clinicians is needed to develop new treatments and administer them promptly in endemic areas. We believe the model of the UK Vaccines Network could also be applied to NTD research.
- The UK is well placed to lead the global fight against NTDs through its international reputation for immunological excellence. However, future challenges, such as our exit from the EU, do exist.

Introduction

Neglected tropical diseases (NTDs) are a diverse group of infectious diseases that disproportionately affect the world's poorest citizens. Almost every person living in conditions of extreme poverty is infected by at least one NTD,ⁱ which equates to around one in six of the global population.ⁱⁱ Following publication of the World Health Organization's 2020 Roadmap on NTDs,ⁱⁱⁱ a London Declaration was signed by a number of partners including pharmaceutical companies, the Department

for International Development, and NGOs, committing to contribute towards the goal of "*control or elimination [of] at least 10 of these devastating [neglected tropical] diseases by the end of the decade*".^{iv} The key aims of the declaration were:

- **Eradication** of Guinea worm disease (Dracunculiasis)
- **Elimination** by 2020 of lymphatic filariasis, leprosy, sleeping sickness (human African trypanosomiasis) and trachoma
- **Control** by 2020 of schistosomiasis, soil-transmitted helminthiasis, Chagas disease, visceral leishmaniasis and river blindness (onchocerciasis).

Tools to defeat Neglected Tropical Diseases

There are three key clinical tools available to address NTDs in addition to public health and education measures: drugs, vaccines, and diagnostics. Immunological research is fundamental to the development of each of these interventions and all three must be utilised in complementary fashion in order to achieve the London Declaration aims.

Vaccines

Vaccines are a preventative measure where the long term aim is the generation of "herd immunity", whereby community vaccine rates are high enough to prevent disease transmission in a population. Immunological study is crucial to vaccine design as scientists need to understand how the immune system reacts to a pathogen in order to design a vaccine to protect against it.

Drugs

Drugs are key to control diseases in endemic regions, as they can be given to large numbers of people to immediately treat the condition. As the immune system is integral to our defence against infectious disease, the study of immunology is invaluable for NTD novel drug discovery.

Diagnostics

Diagnostics are tests that are suitable for use in the clinic, which can quickly and accurately detect the presence of a disease, check the severity of the condition, and/or

Briefing for House of Lords short debate on combatting neglected tropical diseases

March 2017

confirm disease resolution in a patient post-treatment. In order to produce diagnostic tests, biomarkers for the specific disease need to be identified. Biomarkers are chemicals or proteins the body makes in response to an infection that can be used to diagnose the disease. Immunology plays a key role in discovering biomarkers, as many of these are produced by components of the immune system in reaction to the specific infection. Many diagnostic tests also rely on immunological understanding for their function. For example, a drop of blood can be tested for the presence of antibodies to a pathogen, in a similar way to how a pregnancy test works. These point of care tests are known as enzyme-linked immunosorbent assays (ELISAs).

Progress to date

At the time of the London Declaration, research on drugs, vaccines, and diagnostics for NTDs were chronically underfunded, and in many disease cases, were non-existent. Some progress has been made but specific goals for certain conditions have not been met.^v

Whilst drug treatment programmes may reasonably seek to eliminate some NTDs, such as lymphatic filariasis, river blindness and trachoma, this outcome is unlikely for other NTDs such as schistosomiasis and soil-transmitted helminthiasis.^{vi} This is due to high reinfection rates for these diseases, variable efficacy of drug treatments, and the risk of drug resistance emerging.^{vii} Vaccines for these conditions will be essential to prevent re-infection following mass treatment programmes, but **there are currently no licensed vaccines for any NTDs in the London Declaration.**^{viii} Candidate vaccines for schistosomiasis, soil-transmitted helminthiasis,^v leishmaniasis, and Chagas disease,ⁱ are currently in preclinical or phase I development.

The lack of reliable, cheap, diagnostic tools is also a major barrier to fulfilling the London Declaration targets. Progress has been made in diagnostics for some conditions such as sleeping sickness and schistosomiasis, but these have not been adequately implemented in endemic countries and in some cases their reliability has been found to be variable.^{ix}

Action required to meet the London Declaration aims

Vaccines

Going forward, immunology has a significant role to play in tackling NTDs, specifically in the areas of vaccines and diagnostics development. As previously discussed, certain NTDs will not be eliminated without vaccination programmes. There are also issues with regional conflict disrupting mass treatment programmes, therefore vaccination is a critical long-term approach to eliminate NTDs.ⁱ In recent years a new approach to vaccine design has arisen, with considerable advantages over traditional techniques: immunomics. Immunomics involves the screening of the immune component of human and pathogenic genomes to look for vaccine target candidates. This computerised approach is an improvement on traditional vaccine development as screening design is done virtually, saving both time and money. Funding should be channelled into these more efficient approaches to vaccine design. However, this technique has limited applications to complex parasites whose antigenic activity is poorly understood. Therefore, research into fundamental immunology is also required to increase our understanding of these complex parasitic organisms.

Diagnostics

There are huge opportunities for progress in the development of rapid point of care diagnostics, which require little skill to operate. At present, seven of the ten NTDs in the London Declaration lack essential diagnostic tools.ⁱ Diagnostic tests that are available typically require a specialist and are not rapid point of care tests. For diseases that are being investigated for diagnostics, such as Chagas disease and soil-transmitted helminthiasis, research is still at the biomarker discovery stage.ⁱ For many conditions no diagnostic products are in the pipeline, and funding prospects are poor. Immunological study will play a critical role in identifying appropriate biomarkers for diagnostic tools, although more funding is desperately needed for these under-researched areas of NTD treatment. Government scientific agencies have already demonstrated that with the correct support they are able to quickly develop medical products for other diseases, such as the "rapid antigen diagnostic test" for

Briefing for House of Lords short debate on combatting neglected tropical diseases

March 2017

Ebola, pioneered by the Defence Science and Technology Laboratory (DSTL), and its industry partner BBI Detection.^x The Government should aim to replicate this success for the NTDs listed in the London Declaration, in collaboration with industry and clinicians.

How is the UK equipped to contribute?

Our reputation for immunological excellence

The UK ranks first in the G7 for the quality of its research in infection and immunity.^{xi} As a global leader in this area we are well placed to co-ordinate and lead the global fight against NTDs. The UK's scientific relationship with international partners faces uncertain times with Brexit, however our strength in immunological research is a platform from which we can develop an internationally leading role in the discovery and development of new vaccines and diagnostics that are so desperately needed.

The Government should capitalise on our immunological expertise by ensuring that research into NTDs is a discussion priority for international summits, and that the UK harnesses its clinical and research talent in order to engage productively with our global partners on these issues. For example, action against infectious diseases is currently a priority of Germany's G20 Presidency. This and other international fora are an excellent opportunity to discuss and develop coordinated global initiatives to support vital research efforts.

The UK Vaccine Network

One example where the Government has shown good leadership in the area of immunological research is the UK Vaccine Network (UKVN). This network brings together academic, industrial, and clinical scientists to mobilise research and manufacturing of vaccines against infectious diseases of pandemic potential. The UKVN has committed £120m between 2016 and 2021 to develop vaccines against such diseases, many of which are not financially attractive to the pharmaceutical industry. The network is organised through a series of working groups, working to target priority areas where investment would be most effective, and bringing a range of expertise together to build a full understanding of the pipeline of vaccine research, manufacture and deployment. While the UKVN's priority areas do not overlap with those in the London Declaration, the model could be replicated in order to advance clinical strategies to reduce the prevalence of NTDs.^{xii}

International funding instruments

Funding for the UKVN is one part of the Government's £1bn portfolio of projects supported by the Ross Fund. £200m has been set aside for NTDs to fund a variety of research areas, including work on new vaccines and drugs. Funding instruments such as the Ross Fund, which support UK research overseas, are a strong affirmation of our commitment to address the NTD challenge. Funding from European sources also helps UK-based researchers carry out important research on NTDs, including the development of new vaccines and diagnostics. Analysis of research funding under the previous EU science programme, Framework Programme 7, shows that between 2007 and 2013 more than €169m had been committed to NTD research activities^{xiii}. This makes the EU one of the top global funders of NTD research, alongside the Bill & Melinda Gates Foundation, the US National Institutes of Health, and the Wellcome Trust. NTDs remain a priority of the current funding framework, Horizon 2020, and although EU funding is competitive, the UK has an exceptionally strong track record of securing such investment and also in leading joint European research initiatives (for example, we currently take the lead in 34% of all EU funded health related projects). Therefore, as the UK leaves the European Union there is a danger we will lose access to this vital source of research income that supports work into NTDs.

ⁱ Hotez PJ *et al.* 2016 *PLoS Neglected Tropical Diseases* **10** e0003895

ⁱⁱ Terry FE *et al.* 2015 *Expert Review of Vaccines* **14** 21-35

ⁱⁱⁱ WHO 2012 *Accelerating work to overcome the global impact of neglected tropical diseases: a roadmap for implementation*

^{iv} WHO 2012 *London Declaration on Neglected Tropical Diseases*

^v Uniting to combat NTDs. 2016 *Fourth Annual Report 2016*

^{vi} Keenan JD *et al.* 2013 *PLoS Neglected Tropical Diseases* **7** e2562

^{vii} Global Network for NTDs 2017 *Vaccines are the future in the fight against NTDs*

^{viii} Walsh E 2016 *WIW 2016: Sabin Vaccine Institute vaccines for NTDs are a global health priority*

^{ix} Ochodo *et al.* 2015 *Cochrane Database of Systematic Reviews* **3** CD009579

^x House of Commons Science and Technology Committee 2016 *Science in emergencies: UK lessons from Ebola*

^{xi} APPG on Global Health 2015 *The UK's Contribution to Health Globally.*

^{xii} UK Vaccine Network 2017 *Competition brief: vaccines for global epidemics - clinical*

^{xiii} Olesen *et al.* 2017 *Comput Struct Biotechnol J* **15** 180-184