



The Neglected Tropical Diseases (NTDs)

Tremendous progress has been made since 2009

Annual Mass Drug Administration with safe and effective drugs, together with better water and sanitation, are the answers to many NTDs.

Report for the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases

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Chairman's Foreword & Introduction

to the 2011 APPMG Report



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The All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases

Our group continues to work with anyone and everyone who is committed to tackling NTDs. This work is not at the expense of what we do on malaria. As Stephen O'Brien MP (past Chairman of the group and now Under Secretary of State for International Development) recognised when he argued for their inclusion, it is complementary to it. Just as deaths from malaria can be reduced almost to zero within a decade, so can the ravages of NTDs.

I am pleased to present our second report on Neglected Tropical Diseases.

The Neglected Tropical Diseases (NTDs) Tremendous progress has been made since 2009

During the last two years our meetings have continued to be attended by biomedical scientists with a wide range of interests. Speakers have included researchers from pharmaceutical firms and international organisations specialising in NTDs as well as parasitologists interested in many tropical health problems.

The NTD community itself is broad. There are organisations which advocate increased funding to control the seven NTDs which lend themselves to control (or even elimination) using annual treatment of populations rather than reaching out to infected individuals. Then there are others who work on the diseases which suffer from even greater neglect and advocate greater recognition of the problems caused by these diseases which are largely unknown to the general public.

Since 2008 two bilateral agencies – the UK's Department for International Development (DfID) and the United States Government – have increased funding for the control of NTDs. This is in considerable part due to the advocacy of a group of international scientists who have developed strategies for their control. I mention in particular David Molyneux from the CNTD Liverpool, Lorenzo Savioli from the World Health Organisation, Alan Fenwick from Imperial College London and Peter Hotez from Sabin Institute. However, as you read this report, you will realise that, despite the considerable progress, there remains a huge amount to be done.

NTDs all have very complicated life cycles which, at first sight, makes one wonder how they can survive. But they do survive and infect billions of people, with terrible consequences for millions.

Throughout the developing world, we see children who are malnourished and stunted, not because of famine but because the food they are eating is being stolen by worms in their stomachs. We see people going blind because small worms destroy their retina, or infections cause eyelashes to scratch their cornea. We see gross deformity of the limbs because millions of people are afflicted by worms blocking their lymph drainage mechanism. Again there are people with urinary tract and intestinal damage, anaemia and bladder cancer; all caused by parasitic infections. And all these conditions could be prevented for a cost of less than 50 pence per person per year.

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Several APPMG meetings during 2010 and 2011 have been dedicated to NTDs. We have had vivid descriptions of the suffering caused and analyses of the burden of disease from these NTDs.

It is hard to believe – though true – that these infections of which few of us have heard of or even noticed have as great a disease burden globally as malaria and TB. They affect people differently, Malaria and TB kill; NTDs cause immense suffering and disability over many years. Our meetings have included presentations for the first time on some NTDs – including syphilis and sleeping sickness – as well as updates on the better known diseases. All the speakers remained true to two themes – that these diseases affect the poorest of the poor who cannot afford treatment and in most cases we have the tools to treat and protect people.

We have heard again how the pharmaceutical industry has increased its contributions to help NGO's and individual countries' Ministries of Health and Education to deliver tens of millions of drugs annually using the strategy of "Mass Drug Administration". Donated drugs have been used to treat leprosy, lymphatic filariasis, onchocerciasis, trachoma, and, since last year worms and schistosomiasis

But despite the fact that programmes have great benefits relative to their cost, they do not receive the attention and funds they need. NTD's need only £1 billion over seven years (£145 million per year). That is a fraction of the amount donated to malaria, HIV Aids and TB. Tackling NTDs is integral

to achieving many of the Millennium Development Goals (MDGs). So - at a time when attention is focused on the MDGs - it makes sense to put the money in. At £0.50 per person per year, many of the interventions which are possible are excellent value for money.

The Officers and Members of the All Party Group are grateful to all those who have contributed to its work and this report. They are particularly thankful to Professor Alan Fenwick of the Schistosomiasis Control Initiative (SCI, Imperial College) for his expertise and hard work in putting this report together and to Professor David Molyneux (Centre for NTDs, Liverpool School Tropical Medicine LSTM) who has had considerable input to the Report.

I am also personally grateful to Susan Dykes our Administrator for her tireless work and total commitment to the cause; also to Owen Meredith and Amy Gower for their assistance in arranging meetings and events.

I commend this report and its recommendations to you. It is amazing how much can be achieved for so many with relatively small sums.

Jeremy Lefroy MP

Chairman of the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases



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1. The Neglected Tropical Diseases

Box One briefly describes the status and strategy for the updated Neglected Tropical Diseases which are given prominence on the World Health Organization (WHO) website. This list has changed over recent years as the WHO has expanded its Department for the Control of Neglected Tropical Diseases to include control measures against additional diseases. In October 2010, WHO produced its **first ever report on neglected tropical diseases, entitled:**

“Working to overcome the global impact of neglected tropical diseases”

which is available online at http://www.who.int/neglected_diseases/2010report/en/index.html

Box One – the NTDs

NTD	Status	Control Strategy
Diseases controllable by Mass Drug Administration (“MDA”)		
Lymphatic filariasis (elephantiasis)	120 million people infected globally. A serious economic problem in Africa and the Indian sub-continent, but significant progress is being made towards elimination	Elimination by a minimum of five annual rounds of MDA with albendazole + ivermectin (in Africa where onchocerciasis is prevalent) or albendazole + DEC (elsewhere)
Onchocerciasis (River blindness)	An estimated at-risk population of 120 million people in Africa; 70 million currently have access to treatment. Elimination in some foci seems possible. Elimination is being approached in South America	Control of symptoms by annual treatment with ivermectin – 19 countries being treated managed by the African Programme for Onchocerciasis Control (APOC). Progress towards elimination in S. America and some foci in Africa
Schistosomiasis (Bilharzia)	200 million infected – over 85% of infected people live in Africa. Irrigation projects and dams exacerbate the problem – treatment coverage needs to be expanded	Control of symptoms Treatment with praziquantel protects children from future consequences. Improved socio-economic status, water supplies and sanitation are necessary for elimination
Soil transmitted helminths (STH)	Over 1 billion of the poorest children and adults infected globally – currently treatment is approaching 50% coverage	Control of symptoms. Annual treatment of pre-school and school aged children with albendazole or mebendazole
Trachoma (preventable blindness)	80 million infected, 8 million visually impaired. Already eliminated from Morocco; in other areas treatment is expanding satisfactorily	3 – 5 year programmes towards elimination. Annual treatment with azithromycin, as part of a “SAFE” strategy (Surgery, Antibiotics, Face washing and Environmental improvement)
One disease is close to eradication		
Guinea worm	Under 2,000 cases were reported in 2010. Less than 400 cases have been reported during the first quarter of 2011 – Sudan, Mali, Ethiopia and Chad are the only countries with continuing transmission	Provision of filtered water Individual case finding and case containment; clean water provision and filtration; vector control (using abate). Regular surveillance of endemic villages.
Diseases requiring individual treatment		
Buruli Ulcer	Endemic in 30 countries in the Americas, Africa and SE Asia	Case control Early diagnosis, treatment with antibiotics or surgery
Chagas disease	Limited distribution in South America – a disease due to poor housing because the parasite is transmitted by bed bugs. There is fear of immigration imports in to Europe.	Vector control of the bed bugs which carry the disease.
Dengue	250 million at risk and 50 million cases per year in over 100 countries. This infection is on the increase. Can be fatal if not managed in individuals.	Effective clinical management is important. Fluids and possibly transfusions - control of mosquito vectors.
Human African Trypanosomiasis (Sleeping sickness)	Distribution in Africa dictated by Tsetse fly ecology. Better diagnosis and treatment still required. Fatal if untreated	Case finding and treatment; vector control where appropriate. New drug development is ongoing.

1. The Neglected Tropical Diseases

Leishmaniasis (Cutaneous) (CL)	1.5 million new cases for CL are considered to occur annually, with an estimated 12 million people presently infected worldwide. 90% of cutaneous leishmaniasis cases occur in Afghanistan, Brazil, Iran, Peru, Saudi Arabia and Syria.	Early diagnosis and prompt treatment; control of sand fly populations through residual insecticide spraying of houses and through the use of insecticide-impregnated bed nets.
Leishmaniasis (Visceral)	500,000 cases per year. 90% of all visceral leishmaniasis cases occur in Bangladesh, Brazil, India, Nepal and Sudan; fatal if untreated.	Case finding and treatment with meglumine antimoniate (<i>Glucantime</i>) or sodium stibogluconate (<i>Pentostam</i>).
Leprosy	Close to elimination – in the last 2 years 5 more countries reached WHO target prevalence of less than 1 in 10,000 leaving just one endemic country – Brazil	Case finding followed by multi drug therapy (donated by Novartis)
Podoconiosis	Similar swellings of legs to LF caused by mineral irritant material associated with volcanic soils	Wearing shoes to protect feet
Yaws	A skin disease that affects people living in hilly, remote and inaccessible areas. No other host. About 5000 new cases annually in South-East Asia, and sporadic outbreaks in Africa.	Treatment is with a single injection of long-acting Benzathine Penicillin.
Zoonotic diseases		Case control and control in animal reservoir
Echinococcus	A life-cycle that normally stays in dogs and sheep but which can infect humans. Unknown numbers with cysts in liver	Tape worm control in dogs and careful surgery plus albendazole to remove unbroken cysts
Taeniosis/ Neuro-Cysticercosis	Caused by intermediate stages of tapeworm infecting man instead of a pig. Up to 20% infection found focally in rural Africa and South America	Tape worm control, improved sanitation, improved food hygiene and meat inspection
Snakebite	A major problem with an estimated annual mortality of 200,000	Anti snake bite venom made available where required
		Case control and control in animal reservoir/animal product
Brucellosis	Caused by drinking infected milk causing over 500,000 cases per year leading to fevers and serious consequences if untreated	Pasteurisation of milk; treatment of cases with antibiotics
Rabies	Animal reservoir – human infected from bite usually from an infected dog - Invariably fatal if untreated. Globally an estimated 55,000 deaths per year are reported, mainly in children in Africa	Dog vaccination and population control and prompt treatment of dog bites including post exposure prophylaxis

Progress since 2009

European Foundation Initiative for Neglected Tropical Diseases (EFINTD) Five European Foundations (Volkswagen, Nuffield, Merieux, Gulbenkian and Cariplo) have pooled resources to establish a post-doctoral research programme on NTDs for African scientists. A highly competitive programme for Fellowships has been established and to-date 20 Fellows have been appointed from over 200 initial applicants over two rounds. Fellows are based in their host institutions in Africa and

selected European mentors act as advisors and provide laboratory and technical support. Fellows hold their own budgets, devise the projects and are given administrative support. Fellows are brought together every year to interact, network and report results. A third round of proposals is currently being assessed with the expectation that a new group of African NTD Fellows will be appointed in 2012. Professor David Molyneux acts as an advisor to the Nuffield Foundation the UK Foundation which supports the initiative.

2. The burden of disease controversy

The first comprehensive study on Global Burden of Disease and Risk Factors was commissioned by the World Bank in 1992, and updated periodically, with the most recent update (using 2004 data) published in 2008. The Gates Foundation is now funding a review of the whole process comparing alternative methodological approaches, with the results due to be published in 2011.

Disability Adjusted Life Years (DALYs) are an attempt to quantify the overall burden of each disease via early death and the years lived with a disability. For each disease, the number of life years lost (LYL) are estimated, and the disease-specific disability weighting is allocated a value from 0 (no impact of infection) to 1 (death). The years lost to disability (YLD) are calculated as the years lived with the disability multiplied by the disability weighting. The total DALY estimate is then calculated as:

$$DALY = LYL + YLD$$

Unfortunately the DALY disease disability weightings, which subsequently form the basis for research and control funding allocations, are considered by some to be controversial and are not always seen to be a true reflection of a disease's impact. As an example, the weightings allocated to the NTDs are widely believed to be underestimates. In fact the impact of disfigurement, blindness and the social stigma of NTD-related disabilities need only be observed to convince people of the importance and impact of these diseases; unfortunately these are not considered in the DALY calculations. It is extraordinary that their importance for public health has not already attracted more effort to bring about a reduction in morbidity. Seven of the NTDs listed in Table 1 infect many millions of the poorest of the poor – “the bottom billion” (Hotez et al, 2009) - and many of those infected suffer the indignity of co-infections – “poly parasitism” (Hotez et al, 2009). The attribution of mortality and morbidity of several NTDs is included in other categories. For example, NTDs which cause cancers (schistosomiasis, worms of liver), neurological conditions (epilepsy, cysticercosis) or psychiatric illness are attributed not to the underlying cause of an NTD but to the sequelae caused by the infection. This failure to recognise the impact of NTDs reduces the reported burden of disease attributed to them.

Since the first report on the disability weights allocated to the NTDs, several peer-reviewed publications have subsequently attempted to make the case for a significant increase in these figures (for a comprehensive overview, see King et al, 2005). Indeed since 2006 the investigators working on many of these NTDs have come together thanks to the WHO. By combining their global burden figures, the result is that the overall burden of disease due to NTDs has been re-estimated at 56.6 million DALYs annually. This figure bears comparison to that for malaria (46.5 million DALYs annually) and TB (34.7 million DALYs annually) (Hotez et al, 2007).

King et al (2005) have made the case strongly and convincingly for an upward recalculation of the disability weighting allocated to schistosomiasis. The subtle morbidity caused by early and low intensity long term infections has previously been ignored but is thought to be significant. Equally, several more serious conditions (bladder fibrosis, liver fibrosis, portal hypertension) and the deaths which occur many years after infection (for example, due to bladder cancer; haematemesis) are often not recognised as being due to a childhood infection with schistosomiasis.

Impact of NTD on the attainment of MDGs

The G8 and G20 are committed to reaching the Millennium Development Goals (MDGs) by 2015. But how can this be achieved when so many people suffer parasitic infestation? How can poverty be reduced (MDG 1) when a billion people are caught in the cycle of poverty and disease, exacerbated by the high prevalence of NTDs? NTDs promote poverty, poverty promotes the NTDs.

How can universal primary education be achieved (MDG 2) when millions of children are undernourished and stunted? Children are hungry, anaemic, and have their cognitive ability impaired because they are infected with one or more intestinal worms which cause these conditions by consuming the food that the children eat and/or consuming blood from the child. These worms leave children too weak to go to school or unable to concentrate if they are there.

2. The burden of disease controversy

How can child mortality be reduced (MDG4) and maternal health be improved (MDG5) when one of the major causes of poor birth outcomes and a contributor to maternal mortality is anaemia caused by the parasitic infections carried by millions of women of child bearing age in rural developing countries (Abu-Saad and Fraser, 2010)? Studies have shown that pregnant women have a 40% increase in infant survival at 6 months when treated for hookworm infection in the second and third trimester of pregnancy (Christian et al., 2006). For sub-Saharan Africa which has a total target population of about 500 million, an estimated £1 billion over the next 7 years is estimated to be sufficient to be able to redefine these diseases as no longer posing a serious public health problem. (Fenwick et al, 2005; Fenwick, 2006a) Studies of the Global LF programme have shown that the cost saving to date of the Programme from 2000-2008 is of the order of US \$ 24 Billion (£16 billion)

Control progress since 2009

More and more governments in Africa are embarking on integrated control programmes targeting NTDs. This has been made possible by substantial allocations of funding by the governments of the UK and USA. The UK has committed £50 million to NTD control over 5 years while in 2010 USAID published a call for \$450 million for global control of NTDs again over 5 years. The Bill and Melinda Gates Foundation have allocated more funding for research into NTDs and a new fund has been launched (the END Fund) to raise private money for implementation of control in Africa.

3. Group One

Group One: Those susceptible to annual MDA (Fenwick, Molyneux et al. 2005)



Figure 1: Children with heavy soil transmitted helminth infections

(a) The Soil transmitted helminthiasis (Hotez et al., 2009)

There are three species of worms which together constitute the soil transmitted helminths (STH); so called because they do not use an intermediate host. They are hookworm (*Necator and Ancylostoma spp*) whipworm (*Trichuris species*) and the round worm (*Ascaris lumbricoides*). These worms inhabit the human gut, and their eggs are passed out in the faeces.

Hookworm infection is acquired when the free living larvae of hookworm which have hatched from the eggs, attach themselves to the feet and ankles of passers-by. They then penetrate the skin, migrate around the body, and end up in the gut where they attach and gorge on blood. When individuals have massive infections, anaemia is often the result, which has a major effect on young children but also on women of child bearing age because anaemia is the major cause of poor birth outcomes, infant and maternal mortality.

Whipworm and round worms are infections which are associated with poor hygiene. Good sanitation would remove faeces taking away the eggs, and regular hand washing when preparing or eating food would prevent the eggs or larvae being ingested. Heavy infections which occur in poor areas lead to malnutrition and stunting in children.

Elimination goes with socio-economic development - these three worms used to be common in Europe and USA, but with widespread water and sanitation, they have been eliminated from developed countries. Over a billion people do not have these facilities and are infected with one or more worms in developing countries.

Treatment. STH worms can be expelled by a single 400mg tablet of albendazole. An annual dose of deworming tablets throughout a child's life will have an amazingly positive effect on their growth and nutritional status, their school attendance and cognitive ability.

Progress since 2009

Two pharmaceutical companies have pledged drug donations to reduce the prevalence of these worms. Johnson and Johnson have increased their donation of mebendazole to 200 million tablets a year and these will be directed at Asia and the Americas. Feed the Children International also donate mebendazole through Deworm the World, which directs the drug to where it is needed. For Africa GSK announced in October 2010 that from 2012 they will donate 400 million tablets a year to target school-aged children in Africa. Over the next 5 years this will make a huge difference to the health and quality of life of African children. **DFID support this donation by providing essential logistical support for the distribution of the tablets currently in 8 African countries (Cote D'Ivoire, Liberia, Malawi, Mozambique, Niger, Tanzania (including Zanzibar), Uganda and Zambia)**



Figure 2: Successful early deworming of children stimulates growth

3. Group One

ESTIMATED NUMBER OF PRESCHOOL-AGED CHILDREN TREATED FOR STH DURING 2009 BY WHO REGION (WHO – WWW.WHO.INT)

WHO REGION	Pre-school-aged children	Number treated	%
African	93,834,170	42,711,551	45.52%
Americas	14,048,625	3,303,419	23.51%
South-East Asia	106,792,931	41,009,540	38.40%
European	1,223,098	30,547	2.5%
Eastern Mediterranean	24,461,154	877,363	3.59%
Western Pacific	32,973,548	4,141,501	12.56%
Total	273,333,527	92,073,921	33.69%

ESTIMATED NUMBER OF SCHOOL-AGED CHILDREN (AGED 5–14 YEARS) TREATED FOR SOIL-TRANSMITTED HELMINTHIASES, BY WHO REGION, 2009

WHO REGION	Pre-school-aged children	Number treated	%
African	189,950,147	48,314,312	25.44%
Americas	31,405,298	17,783,774	56.63%
South-East Asia	265,160,240	103,820,516	39.15%
European	3,054,623	339,289	11.11%
Eastern Mediterranean	53,491,766	1,609,882	3.01%
Western Pacific	66,148,854	9,986,576	15.1%
Total	609,210,927	181,854,349	29.85%

(b) Schistosomiasis (bilharzia)

Three major species of schistosome worms infect humans.

Schistosoma japonicum is found only in China and the Far East and infects humans and domestic animals.

Schistosoma mansoni (intestinal schistosomiasis) originated in from Africa, but spread to South America and the Caribbean; non-human primates sometimes also become infected (Standley et al, 2009).

Schistosoma haematobium (urogenital schistosomiasis) is found only in Africa and the Middle East and there is no animal reservoir.

The worms of each species live in the blood vessels of humans and the major symptoms are caused by the eggs laid by the female worm. The eggs escape through the urine or faeces and cause blood loss. Many eggs are trapped in tissue and the liver and cause serious liver and bladder problems in later life.



Figure 3: Bloody urine caused by *Schistosoma haematobium*



Figure 4: Advanced *Schistosoma mansoni* infection causes ascites

200 million people are infected globally with schistosomiasis with almost 90% of those infected found in Africa (Fenwick, 2006a; Stothard et al, 2009). Currently there seems to be little chance of elimination of schistosomiasis in rural Africa because of the poor water supply and sanitation in this continent. Only economic development will eventually rid the world of this disease. It has already happened in Japan and Puerto Rico (Fenwick, 2006b). However until that happens it is unacceptable that children in rural Africa are left with these infections because they cannot afford a treatment costing as little as 20 pence. An annual treatment reaching out to school aged children would have a massive effect on improving the quality of life of children, and protect them from the serious consequences of their infections in later life (Lammie et al, 2006).

Treatment

Schistosomiasis can be treated with a generic drug called praziquantel. One tablet currently costs about 8 cents (5 pence) which means about 20 pence for the tablets needed to treat an adult and kill the worms. Merck Serono have started a drug donation programme and pledged 200 million tablets over 10 years. Their 20 million tablets a year are used to treat 8 million children per year in high prevalence areas in Cameroon, Malawi, Mozambique, Nigeria and Senegal. It is hoped that Merck Serono may increase their donation; however the situation is complicated because the active ingredient for the tablets is in limited supply due to uncertainty in market demand. WHO is working with the drug companies to try and stabilise the market. Two papers estimate the needs for praziquantel in Africa (Fenwick et al, 2006; Hotez et al, 2010) (see www.schisto.org)

ESTIMATED NUMBER OF PEOPLE TREATED FOR SCHISTOSOMIASIS DURING 2009 BY WHO REGION

WHO REGION	Treated
African	14,498,101
Americas	30,418
South-East Asia	ND
European	ND
Eastern Mediterranean	2,550,763
Western Pacific	2,491,689
Total	19,570,971

Progress since 2009

Important research findings

- Schistosoma haematobium* which live in the blood vessels around the bladder have been shown not only to cause severe damage to the urinary tract and bladder cancer in later life, but also to cause lesions in their genital organs making them more susceptible to HIV infection. (Stoever et al, 2009; Kjetland et al, 2010)
- In Uganda it has been found that young children (aged 2-5) are infected which changes the perception that treating school aged children is enough. If children get infected earlier the damage could be severe before they get treated at school. High transmission areas we will need to consider treatment pre-school aged children (Stothard et al, in press)
- An initial survey to determine *Schistosoma haematobium* prevalence carried out in June 2011 in Cabo Delgado, Northern Mozambique, showed that in the 150 villages studied – 100% prevalence rates were recorded in many communities among children aged 9-12 years of age. As a result of these high infection numbers, SCl will contribute \$20,000 to help distribute the treatment to over 40,000 children and high-risk adults, such as fishermen, in this province in September 2011. DfID funding will reach Mozambique during 2011.

3. Group One



Figure 5: Treatment against schistosomiasis and other NTDs decreases prevalence

Improved funding

Thanks to DFID and USAID more resources have been made available through SCI Imperial College and RTI respectively to expand coverage of schistosomiasis treatments throughout Africa. By working together, several countries will receive the support they need to reach national coverage. Other countries will start implementation programmes in 2011 (Cote d'Ivoire, Liberia, Malawi, and Mozambique).

Although elimination is not generally a target in mainland Africa, Zanzibar is heading for elimination in 5 years thanks to a project supported by the Gates Foundation, DFID and WHO. Implementation will be by the Zanzibar government with assistance from the Ivo de Cameri Foundation on Pemba Island, The University of Athens Georgia, the London Natural History Museum, SCI Imperial College, and the Swiss Tropical Institute (Knopp et al, in press).

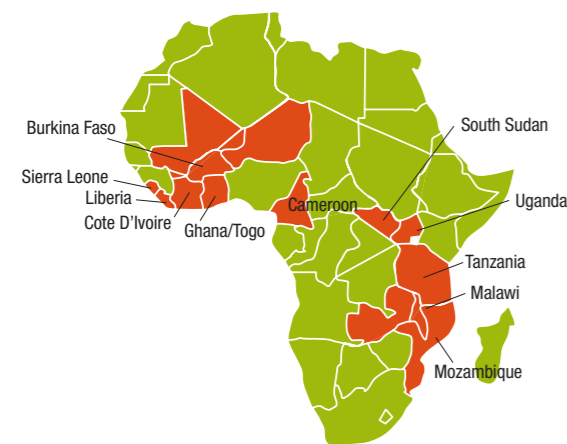


Figure 6: NTD control in sub-Saharan Africa: coverage leaves a lot to be achieved



Figure 7: Statue at the World Health Organization headquarters of sighted child guiding a blind adult

(c) Onchocerciasis (river blindness)

The onchocerciasis worm causes blindness because the larvae produced by the adult worms in the human body migrate across the eye. The parasite larvae also cause severe itching and skin irritation as they migrate. As recently as 1970, up to 50% of populations living on the banks of fast moving rivers suffered impaired vision thanks to the persistent biting of the vector of this worm which is the Black fly – a small biting fly that breeds in fast moving water.

Since 1986 the drug Mectizan which has a killing effect on the circulating larvae has been distributed widely and has saved millions of people from losing their sight. Merck & Co. Inc, recognising the fact that poor people in Africa would never be able to afford to buy even an annual dose of this drug, agreed to donate the drug to all who live in endemic areas "for as long as needed". Over 25 years later this donation continues, and in October 2010 their commitment was renewed. DFID has been supporting the river blindness programmes since their inception in 1974. Since that time there has been huge progress and in most of Africa people are no longer at risk of becoming blind from this scourge.

Complete coverage in Africa has not been achieved for reasons of access to areas where there has been civil unrest (DRC, Angola, South Sudan, Liberia) and to the problem of the risk of severe adverse events (SAEs) during MDA when those receiving the drug ivermectin are infected with another parasitic worm called *Loa Loa*, a worm causing a tropical eye infection. Patients with high parasite loads of *Loa* in the blood are at risk of encephalopathy resulting in the need for hospital treatment; if such treatment and care is not available

as it is often not in remote rural settings the patient may die. The Mectizan Donation Programme has developed guidelines for the treatment and care of such cases. Thus in parts of Central Africa where *Loa Loa* is endemic, both onchocerciasis and LF programmes have been impeded because of the risk of *Loa* induced complications. In addition because onchocerciasis programmes are dependent on support from NGOs there has been reluctance for them to be involved in high risk *Loa* areas. While this is a matter still to be resolved there are now available detailed maps of areas where the highest risk of side effects might be encountered. Alternative approaches may also be available (bed nets, use of albendazole alone at higher dosages; use of an antibiotic Doxycycline to kill adult worms which will not result in encephalopathies). Ongoing implementation research will continue to be needed but the situation has improved now other options are available.

Treatment

The African Programme for Onchocerciasis Control (APOC) oversees the distribution of Mectizan in 19 countries with the help of a number of NGOs (The Carter Center, Sightsavers, CBM Helen Keller International, World vision). During the current year some 70 million treatments with ivermectin have been given through APOC supported projects and through partnerships at country level and with NGOs who provide 25% of funding. Studies which were initiated within the APOC programme in a multi country study have also shown that community distributors can take on and indeed do take on additional health related activities (WHO; CDI study Group) such as bed net distribution, Vitamin A and albendazole distribution for LF. Recent studies in Senegal and Mali published in 2009 have shown that 15-17 years of treatment annually with ivermectin can reduce transmission by black flies to zero if regular high coverage is achieved. Similar results are being reported for parts of Nigeria, Cameroon and Chad giving hope that in some areas 10 years of high coverage will achieve local elimination.

In the Americas, The Onchocerciasis Elimination Program for the Americas (OEPA) is a regional initiative with the goal of eliminating morbidity and interrupting transmission of river blindness in six endemic countries in the Americas: Brazil, Colombia, Ecuador, Guatemala, Mexico and Venezuela. The OEPA strategy is to encourage the endemic countries to provide sustained ivermectin mass treatment every six months with the aim of reaching at least 85% of the 503,285 persons at risk of the disease. Results reported in the literature show that transmission has been eliminated in foci in Guatemala, Mexico and Colombia and interrupted in several others.

Progress since 2009

In Africa it has mostly been continuation with the successful programme, but for the first time WHO are considering with selected governments the concept of elimination to replace the annual MDA control strategy. It is thought that in many countries that have been offering annual Mectizan for many years that the worms are beginning to die out and so by increasing frequency of treatment for a short period elimination may be achievable. In the Americas, all six endemic countries have established effective national programmes and there are no new cases of blindness attributable to onchocerciasis in the American region.

3. Group One

(d) Lymphatic filariasis (LF – elephantiasis)

The deformity and misery caused by this disease is horrific. The adult worms which are transmitted between humans by mosquitoes live in and block the lymph system preventing the drainage of lymph. This causes swelling of lower limbs,

secondary infections and in the case of men, the scrotum can become grotesquely swollen. Meanwhile the millions of larvae which the females produce circulate in the blood stream to be picked up by a mosquito for the transmission cycle to be completed.

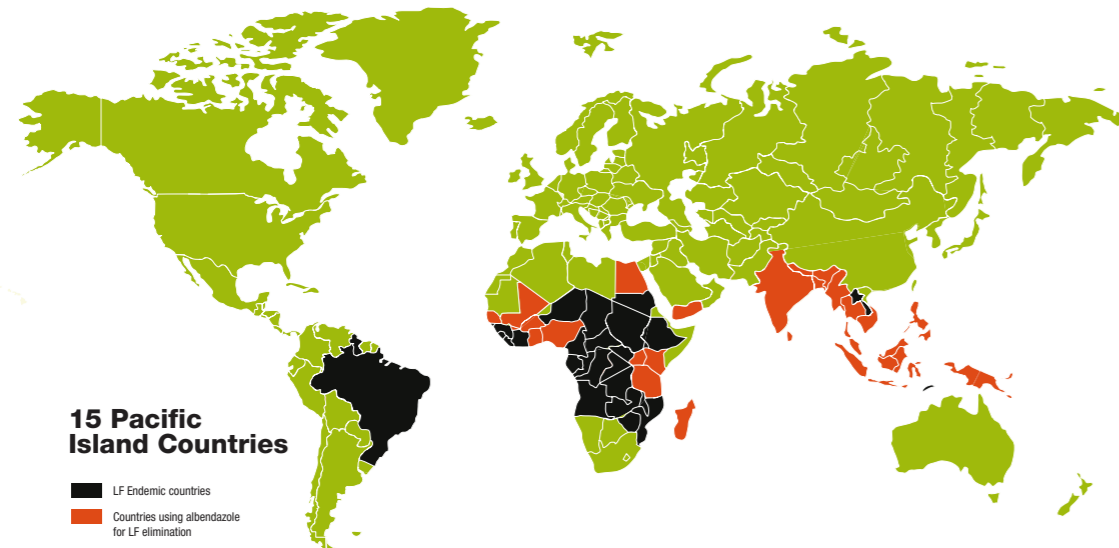


Figure 8: Many Central African countries still need LF elimination programmes

The Global Alliance to Eliminate Lymphatic Filariasis (GAELF) is supported by DFID and GSK and the Secretariat is based at CNTD, Liverpool School of Tropical Medicine. This alliance is probably the most effective alliance ever formed as evidenced by the expansion of treatment coverage against this terrible affliction; numbers of partners involved and the range of those partner interests; the commitment of pharma to long term donations (now three companies providing all the necessary drugs); as well as the total value of those donations of many millions

of dollars (see below). (see table and website www.filariasis.org) The GAELF 6 meeting was held in Seoul Korea, hosted by the Korean Centers for Disease Control in 2010 (See Addis 2010 for the full report); the meeting was used as a basis for reviewing the results after 10 years of the programme; assessing the challenges and providing WHO with a framework for its 2010-2020 Strategic Plan which was published later in 2010. The CNTD Liverpool was re-elected by GAELF to continue to act as the Secretariat of the Partnership.

TREATMENT OF LF DURING 2009 BY WHO REGION				
WHO REGION	Targeted Population	Countries MDA	Reached population	% age
(endemic countries)				
African (39)	79, 180, 429	17	51, 092, 260	64.53%
Americas (7)	3, 388, 920	4	2, 739, 610	80.84%
South-East Asia (9)	586, 676, 718	9	425, 628, 907	72.55%
Mekong plus (6)	25, 072, 271	5	15, 955, 918	63.64%
Eastern Mediterranean (3)	556, 499	2	509, 894	91.63%
Pacific (17)	346, 839	14	328, 333	94.66%
Total (81)	695, 221, 676	51	496, 254, 922	71.38%



Figure 9: Lymphatic filariasis causes swelling of limbs



Figure 10: Lymphatic filariasis causes swelling of the scrotum

The treatment regime for LF is a two drug combination – albendazole and Mectizan® (ivermectin) in Africa where onchocerciasis is prevalent. For the remaining endemic countries albendazole is given with the extremely cheap drug, DEC (1 US cent per treatment). A number of countries in Africa remain to launch an elimination programme and in parts of Africa civil unrest contributes to poor coverage in some areas.

Programme to Eliminate Lymphatic Filariasis (GPELF) represents an operational model of an effective public private partnership effective beyond the target disease but focussing on elimination of a global problem.

Albendazole is donated by GlaxoSmithKline (GSK) for as long as needed and Mectizan® is donated by Merck & Co. Inc. This partnership when it began was unique in demonstrating the capacity of two major pharma to work together to address a global health problem. The alliance between pharma, GAELF and the Global

Merck & Co. Inc. extended their donation of Mectizan® to include LF in Africa following the GSK commitment to donate albendazole. This emphasises the capacity of major pharma to work together on a major global health problem and the Global LF elimination programme (GAELF) is an alliance which represents an important operational model of an effective public private partnership effective beyond the target disease but focussing on elimination of a global problem.

Progress since 2009

A number of countries have stopped MDA because prevalence has reached below the level of 1% and have now entered into a surveillance phase. A new pledge was announced in October 2010 to donate diethylcarbamazine (DEC) by the Japanese pharmaceutical company, Eisai. DEC which is used with albendazole in those countries which do not receive Mectizan® will now be provided as a donation from Eisai – 2 billion tablets a year – enough to treat the sub-continent and raising hopes of reaching the goal of LF elimination by 2020.

evaluation; supporting capacity development and focussing on necessary operational research. CNTD support has resulted in the WHO announcing that several countries are free of LF reducing the number of endemic countries towards the target.

Meanwhile CNTD Liverpool, with DFID support is initiating LF programmes in DRC, Liberia, Malawi, Nepal, Mozambique, and Zambia whilst providing technical support to laboratories for monitoring and

Case management has improved. Leg washing has increased the care of elephantiasis patients and hydrocele surgery is growing as “surgery camps” are being established in different countries. In Niger SCI has supported over 600 surgeries in 2010. These have been extremely successful and hundreds of men have come forward requesting the 20-minute surgical intervention, performed under local anaesthetic. The cost of each intervention at one of SCI’s camps averages around \$200, which includes pre- and post-operative treatment as well as the surgery itself.

3. Group One

(e) Trachoma

Blindness due to Trachoma is the after effect of conjunctivitis caused by Chlamydia infections carried by flies. Trachoma is simply a disease of poor hygiene, plus dry and dusty conditions, and poverty. After severe infections around the eyes, eyelids become affected by scarring, and eyelashes are turned into the eye and destroy the cornea over time. For existing trichiasis cases simple surgery can correct the problem. Face washing and improved water and sanitation are essential components in a trachoma elimination strategy. The International Trachoma Initiative (ITI) promotes an integrated approach named the SAFE strategy – S for surgery, A for Antibiotics, F for face washing and E for environmental improvements to reduce the infestation of flies. The World Health Organisation promotes “GET 2020” and a number of NGOs are very active in promoting eye care and control of both onchocerciasis and trachoma. Excellent progress has been made in some countries, and ITI’s flagship programme has eliminated trachoma from Morocco.

Treatment

Early treatment is effective – ideally an antibiotic for active infection (Zithromax which is currently donated by Pfizer) should be taken annually. In 2011 it is estimated that approximately 70 million doses of Zithromax will be distributed.

Progress since 2009

ITI has expanded coverage with the donated drug Zithromax. A new website www.trachoma.org has been developed to provide information about trachoma and the treatments provided by ITI. This includes the target of elimination by 2020

- About 41 million people have active trachoma needing treatment
- 8.2 million are estimated to have an advanced stage and therefore are or are at risk of blindness
- 57 Countries are believed to be endemic with up to 1.2 billion living in at risk areas
- Since 1999 Pfizer has donated 225 million doses of Zithromax

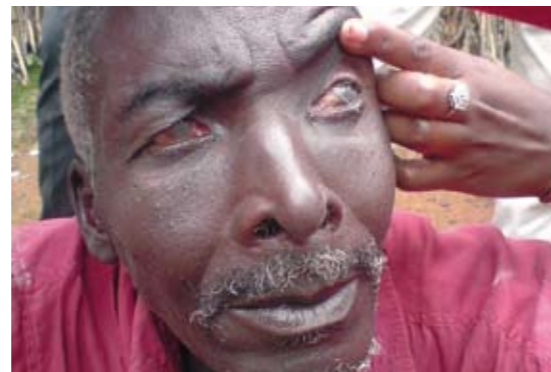


Figure 11: Trachoma causes eye damage

THE ESTIMATED TRACHOMA TREATMENTS BY COUNTRY FOR 2011:

COUNTRY	Population	2011 target
Guinea Bissau	1.7 million	599,644
Mauritania	3.1 million	7,669
Burkina Faso	14.8 million	5,071,302
Kenya	36.9 million	889,575
Tanzania	41 million	3,998,961
Uganda	28.5 million	8,280,081
Senegal	12.4 million	898,624
Zambia	13.5 million	783,542
Ethiopia	77 million	18,838,941
Ghana	24 million	eliminated
Mali	12 million	3,905,005
Sudan	31 million	450,964
Cameroon	18 million	974,718
Eritrea	4.2 million	713,990
Nigeria	144.4 million	3,174,250
Niger	14.3 million	7,954,651
Total		56,514,917

(f) Guinea Worm – a worm on its own

Guinea Worm has the distinction of being one of the longest human parasites, growing to 1 metre in length. The female worm which lives under the skin emerges after 12 months of incubation when she is ready to lay her eggs, forming a blister usually around the ankle. This creates an intense burning sensation hence the victim tends to seek the nearest source of water to cool the leg down – the worm then releases thousands of larvae into the water which are ingested by water fleas where they develop - and wait to infect humans who ingest the water fleas while drinking unfiltered water. This is guinea worm the fiery serpent of the Bible. Infection can only be acquired from swallowing infected water fleas and so case reporting and improved water supplies should lead to eradication. Guinea Worm is the only disease apart from polio which is targeted for eradication by a World Health Assembly Resolution – and massive progress is being made. The eradication strategy is based on simple measures of case containment, provision of clean water; filtration of potentially contaminated water; treatment of water with an “insecticide” to kill water fleas, surveillance and reporting and health education. The results speak for themselves as reported below.

Treatment

There is no drug treatment for guinea worm; the only method to remove the worm is the slow extraction of the long creature from the skin by slowly winding the worm around a stick and pulling it out over several days.

Progress since 2009

Guinea Worm is moving towards eradication. The numbers of cases have been dramatically reduced from over 1 million in 1988 to 1797 in 2010; the disease remains endemic in just four countries- Chad, Ethiopia, Mali and Sudan. There are several countries which have not reported cases during the previous year (Burkina Faso, Cote d'Ivoire, Ghana, Kenya, Niger, Nigeria, and Togo) and are considered to be in precertification phase awaiting formal certification as being free of transmission. Post certification there is a continued need for surveillance until global certification is achieved. International Certification Teams have visited Burkina Faso and Togo to report on the status of the absence of transmission to the International Commission for the Certification of Eradication.



Figure 12: Emerging Guinea worm
(Photo Credit: The Carter Center/Louise Gubb, Ghana, 2007)

WHO REGION	Targeted Population	Countries MDA
Ethiopia	5	3
Ghana	83	0
Mali	7	0
Sudan	48	371
Chad	18	2
Togo	16	0
Nigeria	29	0
Niger	35	0
Total	243	376

4. Group Two

Group Two: Case finding and treatment – and the need for better medication

(a) Leprosy

There are now many fewer cases of leprosy than before, and the sight of people with gross disfigurement is now relatively rare compared to the last century, but cases do still occur and must be treated. This requires a multi drug therapy package which is donated through WHO by Novartis. The difficulty is the early diagnosis, and removing the stigma attached to leprosy. The number of countries where leprosy remains a significant problem had been reduced remarkably through multidrug therapy from over a hundred to six by 2009 – now there remains just one country.

Treatment

Multi Drug Therapy for multibacillary leprosy consists of rifampicin, dapsone, and clofazimine taken over 12 months

Progress since 2009

Of the six countries with prevalence above the 1 in 10,000 target towards elimination in 2009, five have reached their target – India, Madagascar, Mozambique, Nepal, and Tanzania.

The only country still to get down to below 1 in 10,000 is Brazil



Figure 13: Damage caused to the hands by leprosy infection (Photo Credit: The Leprosy Mission)

(b) Visceral Leishmaniasis

This is the serious consequence of Leishmania infection from a sand fly bite, and the resulting disease is called kala-azar or visceral leishmaniasis. The parasite invades internal organs, causing fever, anaemia, and an enlarged spleen. It is distributed in the tropical belt across the world and is caused by a single cell animal (protozoa) transmitted by sand flies. If this parasite invades the viscera and internal organs death is inevitable unless drug treatment is available. Sadly, these drugs are not readily available in rural areas, diagnosis is difficult and even if the drugs are available they have to be paid for. Since most infected people are unable to afford them, the death rate is high. New therapies to replace the more toxic compounds (based on antimony) are being developed.

Treatment

The current correct treatment with amphotericin B or meglumine antimoniate (Glucantime) or sodium stibogluconate (pentostam)

Progress since 2009

DNDi are working with One World Health on Paromomycin which it is hoped will become the needed new safe and effective drug to treat this disease. An effective drug, ambisome, exists but it is not donated hence the problems of affordability. Miltefosine is another drug which has become available and has the benefit of being taken orally. Combinations of these drugs are being tested to define the most effective treatments. WHO published an Expert Committee report on Leishmaniasis in 2010

(c) Cutaneous Leishmaniasis

The same organism as above if it remains in the skin at the site of the sand fly bite causes an unsightly and expanding ulcer which does not respond well to any known treatment. At least this form of the disease is not fatal! Fortunately the suppurating ulcer does not usually spread far from the site of the bite, and is self curing after about six months. Many animals act as reservoir hosts of cutaneous leishmania - often rodents in Asia, the Middle East and in the Americas. There have

been major epidemics of cutaneous leishmaniasis in Afghanistan associated with refugee camps and urban centres such as Kabul. Control of the sand fly is difficult and the costs of treatment as well as drug availability are often beyond the resources of the national authorities.



Figure 14: Impact of cutaneous leishmaniasis infection (Photo Credit: Stanford University)

(d) Chagas disease

Another protozoon – a trypanosome – causes Chagas disease in the Americas and Sleeping sickness in Africa. It is very similar to leishmaniasis when viewed under the microscope). It has been estimated that as many as 8 to 11 million people in Mexico, Central America, and South America have Chagas disease, but most of these do not know they are infected. Chagas disease in South America is a disease of poor quality housing because it is transmitted by Triatomine bugs (bed bugs). When a person is infected from a bed bug bite, the organism invades and damages the heart and other organs, although the pathology takes many years to develop. Economic development and improved housing and hygiene would eliminate this disease. Domestic transmission of the disease has been controlled in 5 countries (the southern Cone) by indoor house spraying with insecticide and other groups of countries in South America have similar control plans. However, the urgent need is for a new drug as the currently used drugs have many drawbacks. A complication is that Chagas Disease is also spread through blood transfusion and because of increased migration from endemic areas to USA and Europe (Spain and Portugal) and the donation of blood by migrants, the disease is being found in non South Americans through transfusion.

Treatment

A vaccine is currently being tested, and the antifungal agent amphotericin B has been proposed as a second-line treatment, but the high cost and relatively high toxicity of the drug have limited its use.

Progress since 2009

A backward step has been the apparent arrival of Chagas disease into Europe as migrants from Brazil and Spanish speaking countries in South America brought the infection into Portugal and Spain. Believed to have been transmitted through blood transfusions, steps are now taken to test blood for Chagas disease in Europe.

(e) Human African Trypanosomiasis (HAT)

HAT, also known as African sleeping sickness is transmitted by the tsetse fly that breeds in savannah and riverine woodland in a belt across Africa. The parasites first invade the blood and later invade the central nervous system with fatal consequences if untreated. Further research funding is needed to discover better drugs and treatment regimes. Early diagnosis is vital but methods need to be improved. Effective approaches to control have been based on mobile teams actively making microscopic diagnoses and giving early treatment to those found positive. However the reduced resources for the mobile team approach to control, and civil conflict in tsetse areas, led to a rise in sleeping sickness cases in the period of the 1980 and 1990's. Although according to WHO data, this has recently been arrested. The potential for epidemics remain and sleeping sickness is a disease which requires constant surveillance by national health authorities.



Figure 15: Effects of Sleeping Sickness

4. Group Two

Treatment

Treatment of HAT is less than satisfactory as we remain dependent on arsenical based drugs for Central Nervous system treatment which are themselves, dangerous and have a 5% mortality rate. However, a new combination therapy has been developed by DNDi which reduces the duration of treatment with the alternative drug eflornithine which requires two weeks infusion to one week by combining eflornithine with nifurtimox. These drugs have been approved by WHO for inclusion on the Essential Medicines list. All drugs for sleeping sickness are donated by the manufacturers (Sanofi-Aventis and Bayer) to WHO for distribution to endemic countries.

Progress since 2009

Recently developed innovative methods for the control of tsetse flies by insecticide treatment of the cattle reservoir as well as drug treatment of the cattle themselves have been developed by a UK based NGO (Stamp out Sleeping Sickness SOS) and the University of Edinburgh as well as private companies.

(f) Buruli ulcer

Buruli ulcer has been reported to WHO from 30 countries largely in Africa, but the geographical distribution of the disease is not fully known due to under-reporting and insufficient knowledge among both health workers and the public. It is caused by a Mycobacterium, *Mycobacterium ulcerans* similar to the organisms which cause TB. The costs of treatment if available are high as patients may require extensive surgery and such cases place a huge burden on the health facilities in hospitals. Buruli ulcer is a disease of people who live in remote, rural areas and having little contact with the health system. Infection with the bacterium often starts as a painless, mobile swelling in the skin but over time this leads to extensive destruction of skin and soft tissue with the formation of large ulcers usually on the legs or arms. Early stage diagnosis and treatment with antibiotics can prove successful, but if untreated the consequences can be irreversible deformity, extensive skin lesions and sometimes life-threatening secondary infections. The epidemiology of the disease and how people become infected remains to be clarified although there appears to be some association with water bodies.

(g) Dengue & dengue hemorrhagic fever (DHF)

Dengue fever and dengue hemorrhagic fever (DHF) are acute febrile diseases, found in the tropics, and caused by four closely related virus serotypes, transmitted by the Aedes mosquito which bites during the day.

The disease is now endemic in more than 100 countries in Africa, the Americas, the Eastern Mediterranean, South-east Asia and the Western Pacific. South-east Asia and the Western Pacific are the most seriously affected. Before 1970 only nine countries had experienced DHF epidemics, a number that had increased more than four-fold by 1995.

Not only are the number of cases increasing as the disease is spreading to new areas, but intense outbreaks are occurring. In 2007, Venezuela reported over 80 000 cases, including more than 6 000 cases of DHF.

- During epidemics of dengue, infection rates among those who have not been previously exposed to the virus are often 40% to 50%, but can reach 80% to 90%.
- An estimated 500 000 people with DHF require hospitalization each year; a very large proportion of whom are children. About 2.5% of those affected die.
- Without proper treatment, DHF fatality rates can exceed 20%. Wider access to medical care from health providers with knowledge about DHF - physicians and nurses who recognize its symptoms and know how to treat its effects - can reduce death rates to less than 1%.

Treatment

Early treatment with therapy to tackle shock due to haemoconcentration and bleeding is important. Increased oral fluid intake is recommended to prevent dehydration. Internal gastrointestinal bleeding may occur requiring a transfusion.

Progress since 2009

Progress has been negative. Dengue fever is becoming more prevalent in some areas and is a cause for concern. The spread of dengue is attributed to expanding geographic distribution of the four dengue viruses and their mosquito vectors, the most important of which is the predominantly urban species *Aedes aegypti*. A rapid rise in urban mosquito populations is bringing ever greater numbers of people into contact with this vector, especially in areas that are favourable for mosquito breeding, e.g. where household water storage is common and where solid waste disposal services are inadequate.

5. Group Three

Group Three: Zoonoses – the even more neglected tropical diseases

By impacting on human health and also the health and productivity of livestock on which many families rely for a source of income, zoonotic disease impose a dual burden on affected societies.

(a) Neuro-Cysticercosis

Humans are accidental hosts to cysts which really belong in the pig, and epilepsy can be caused by the larval stage infection reaching the brain. The "normal cycle" is for the adult tapeworm to live in the human gut mostly in poor rural communities and the intermediate stage develops in pigs which become infected when they ingest human faeces containing tapeworm eggs. The larva develops in the pig forming cysts which if eaten as undercooked meat develop into the adult tapeworm in the human gastrointestinal tract. However humans can and do get infected accidentally by somehow swallowing the tapeworms eggs which were in their excreta. Humans can infect themselves under conditions of poor hygiene – not washing hands after going to the toilet for example. If this happens, cysts are formed in the muscle and brain tissue, causing a condition known as neurocysticercosis which may lead to epilepsy, epileptic seizures and severe neurological symptoms. Many of these cysts however remain in the brain and do not cause symptoms for many years. Pig keeping and pork consumption have increased significantly in eastern and southern Africa during the past decade.

The tapeworm that causes cysticercosis is endemic to many parts of the world including China, Southeast Asia, India, sub-Saharan Africa, and Latin America. The prevalence of cysticercosis in Mexico is reported to be 3 to 4 percent, and in Guatemala, Bolivia, and Peru rates as high as 20 percent in humans, and 37 percent in pigs have been reported. In Ethiopia, Kenya and the Democratic Republic of Congo around 10% of the population is estimated to be infected, in Madagascar and Tanzania 16%. The frequency has decreased in developed countries owing to stricter meat inspection, better hygiene and better sanitary facilities.

In Latin America, an estimated 75 million persons live in endemic areas and 400,000 people have symptomatic disease.

Treatment

People infected with the adult worm can be treated with niclosamide and praziquantel which will expel the worm. However praziquantel also may kill the cyst in the brain and we are unsure of the effect of death of a cyst.

Progress

Several studies, funded by a number of bilateral donors, are being conducted looking at the impact of different intervention techniques including both the veterinary and medical and food safety sectors.

A new project funded by the Gates Foundation in 2010-2013 aims to study neurocysticercosis in DRC, Malawi, Tanzania and Uganda over the next 3 years to determine the effect of praziquantel treatment delivered against schistosomiasis on epilepsy sufferers.

(b) Echinococcosis

Echinococcus is another tapeworm which normally lives in dogs with cysts in sheep. In this case the cysts can develop in man if the eggs in dog's faeces are swallowed. It seems unlikely to us but it does happen where young children live with their dogs in unhygienic conditions. With the adult tapeworm living in dogs, the eggs are normally transmitted from dogs to sheep that ingest the eggs from dogs' faeces while grazing. The cysts develop in the liver of sheep, and tapeworms get back to the dog when offal is eaten by or fed to dogs. If children have intimate contact with an infected dog and do not wash hands regularly, eggs can transfer into the child's mouth and then cysts will grow in their liver or other organs. These cysts can cause liver disease and can be mistaken for tumours.

5. Group Three

(c) Anthrax

This disease of cows which is a killer if man gets infected is spread by fungal spores and these spores can lie dormant for decades.

(d) Brucellosis

This disease is contracted from drinking unpasteurised milk and the consequences to women are serious because infection tends to cause abortion or other complications during birth.

(e) Rabies

Although UK is rabies-free, this disease which is mainly associated with dogs and foxes is prevalent elsewhere in the world wherever dogs exist. Over 90% of fatal cases occur in Africa and the majority in children. A bite from a rabid dog is fatal unless a vaccination is given almost immediately. Pre exposure vaccines for humans are expensive and not suitable for protection of endemic populations. Post exposure treatments can be given but are often not available in hospitals and clinics in areas where rabid dogs are most prevalent. Several studies looking at the most effective strategies for reducing the risk posed by dogs by vaccination and population control measures are being conducted.

6. Conclusions & Recommendations

Conclusions & Recommendations of the APPMG

The messages from the speakers which have been endorsed by those who have attended the APPMG are as follows:

Conclusions

- NTDs (Box 1) are a diverse group of infections which tend to affect the poorest of the poor.
- There are several countries in which a number of MDGs cannot be achieved without tackling NTDs
- For Group One NTDs, a cheap package of drugs with rapid impact can be delivered annually at a low cost. This could control or eliminate the suffering from these NTDs of up to a billion people. The estimated cost of controlling these infections is c £1.5 billion over a period of 7-10 years).
- Several pharmaceutical companies have been generous in donating their products which are unaffordable to those who need them in the poorest countries (see Box 2).
- Countries which are either still in conflict or have recently emerged from conflict have the greatest need for support.

Recommendations

- More donors need to be made aware of how much can be done for the health and life chances of a billion and more people through relatively small sums of money.
- New drugs are needed for some of the NTDs so there is a requirement for funding for research and development as well as for treatment
- **Zoonotic** diseases need greater attention.
- Countries in which **Buruli** ulcer is endemic – and their neighbours – need to introduce effective surveillance and reporting systems.
- Case finding and treatment should be encouraged; this will include leg washing and hydrocoele surgery for **LF** sufferers and surgery for **trachoma** sufferers.
- Every effort should be made to eradicate **guinea worm** from the few countries in which it is still endemic.

ANNEX I The UK Coalition against Neglected Tropical Diseases – due to be launched on September 13th 2011

The founder members of this coalition are:

- (1) Centre for Neglected Tropical Diseases (CNTD), Liverpool School of Tropical Medicine
- (2) Sightsavers, UK
- (3) Carter Center UK
- (4) Imperial College London, School of Public Health (Schistosomiasis Control Initiative and Partnership for Child Development)

- (1) Centre for Neglected Tropical Diseases (CNTD), Liverpool School of Tropical Medicine, Director: Professor Moses J. Bockarie

CNTD's mission is to support national NTD programmes, provide technical assistance to a global initiative, strengthen the evidence base to inform policy makers and identify and prioritise interventions that will eliminate filariasis and reduce the burden of other neglected tropical diseases.

The areas in which CNTD works

Mass Drug Administration: Support to 12 countries (Bangladesh, Burkina Faso, DRC, Ghana, Guinea, Ethiopia, Liberia, Malawi, Mozambique, Nepal, Tanzania and Zambia) to implement Mass Drug Administration for the control/elimination of multiple NTDs.

Capacity Building Laboratory support: In five countries (Kenya, Malawi, Ghana, Sierra Leone and Sri Lanka) CNTD has strengthened laboratory infrastructure and continues to provide ongoing support for staffing and consumables.

Post-graduate training for endemic country scientists: Six endemic country health professionals from Africa (Liberia, Malawi, Mali, Sierra Leone and Zambia) and 2 from the Asia-Pacific region (Bangladesh and Papua New Guinea) are registered for PhD studies with the University of Liverpool. Each study will contribute to national NTD programmes.

Operational Research: Nine research projects addressing identified critical unanswered questions are underway to support the evidence base for the elimination strategy and apply tools for assessing progress (Bangladesh, Ghana, Kenya, Philippines, Sierra Leone, Sri Lanka, Tanzania and Zanzibar).

Partnership Relations: CNTD has a role in ensuring successful global partnership in terms of advocacy, communication, resource mobilisation and co-ordination. CNTD is the elected Secretariat of the Global Alliance to Eliminate Lymphatic Filariasis (GAELF) a partnership of public and private sectors working towards LF elimination.

For the above activities CNTD is funded primarily from the Department for International Development with additional core support from GlaxoSmithKline

(2) Sightsavers

Sightsavers is an international development organisation which works with partners to eliminate avoidable blindness and promote equality of opportunity for disabled people in the developing world. Within neglected tropical disease control, Sightsavers holds programmes throughout Africa and Asia and is a leading partner in the control of two of the neglected tropical diseases - trachoma and onchocerciasis. Sightsavers works closely with governments, regional partnerships such as the African Programme for Onchocerciasis Control (APOC), non-governmental organisations, pharmaceutical companies and communities to deliver cost-effective and sustainable programmes in NTD control. In 2010, Sightsavers supported 23.1 million treatments for onchocerciasis, 1.8 million Zithromax treatments and over 15,000 trichiasis surgeries for trachoma. Sightsavers also delivers integrated disease control interventions, and in 2010 we supported 17.6 million treatments for lymphatic filariasis co-implemented with onchocerciasis.

At a global level, Sightsavers works to influence multilateral institutions, international agencies and donors to invest and include eye health, disability and NTD control policies and programmes within wider health systems and development frameworks. Sightsavers works collaboratively with a number of international, regional and national networks and we are currently Vice-Chair of the Neglected Tropical Disease NGDO Network, which incorporates the LF NGDO Network, the International Coalition for Trachoma Control and the NGDO Coordination Group for Onchocerciasis Control. Our regional offices maintain several strategic regional relationships including with the West African Health Organisation (WAHO), APOC, and the New Partnership for Africa's Development (NEPAD) and the African Union (AU).

(3) The Carter Centre United Kingdom and Foundation,

A non-profit organization and charity, support the work of The Carter Center—based in Atlanta, Georgia, U.S.A.—founded more than two decades ago by former U.S. President and Nobel Peace Prize laureate Jimmy Carter and his wife, former First Lady Rosalynn Carter. The Carter Center advances global efforts to wage peace, fight disease, and build hope by engaging with those at the highest levels of government and civil society. Working in close partnership with The Carter Center, The Carter Centre United Kingdom supports the Center's work by raising funds and increasing awareness in the United Kingdom and Europe. The Center's programmes, implemented to date in more than 70 countries around the world, prevent and resolve conflicts, promote sustainable development and human rights, enhance freedom and democracy, and improve people's health and quality of life, including the near eradication of Guinea worm disease globally and the near elimination of river blindness in the Americas. Chaired by Dame Marjorie Scardino, the board of trustees decides and supports the mission of The Carter Centre U.K. and manages its assets.

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(4) Imperial College School of Public Health

4.1 The Schistosomiasis Control Initiative (SCI)

SCI was established in 2002 at Imperial College with funding from the Bill and Melinda Gates Foundation. The SCI originally targeted schistosomiasis in 6 African countries and assisted Ministries of Health and Education to deliver treatments with praziquantel against schistosomiasis in highly endemic areas, adding in albendazole treatments against concurrent soil transmitted helminth (STH) infections.

Since 2006, when additional funding sources were brought in and the WHO moved towards integration of NTD treatments, SCI amended its aims to "the control or elimination the seven most prevalent NTDs (soil-transmitted helminths (STH)-ascariasis, hookworm infection, trichuriasis), lymphatic filariasis (LF), onchocerciasis, schistosomiasis, and trachoma) from sub-Saharan Africa". This means that our ultimate target would be 500 million people, two-thirds of the total population of Africa, who have two or more NTDs and need regular treatment.

SCI has been funded by the Bill and Melinda Gates Foundation, the USAID NTD control program through RTI, Legatum through Geneva Global and the Global Network for NTD Control, SCORE (UGA) and private donations.

Currently SCI's main funding comes from DFID, UK and SCI together with partners CNTD Liverpool, is committed to delivering 75 million treatments against schistosomiasis and STH over the next 5 years. SCI works closely with WHO and with African governments to achieve the targets.

SCI is supporting schistosomiasis and NTD control programmes in Burundi, Cote D'Ivoire, Liberia, Malawi, Mozambique, Niger, Rwanda, Tanzania, Uganda, Yemen, Zambia, and Zanzibar.

Staff capabilities include programme management, biostatistics, health economics, and veterinary medicine.

Director, Professor Alan Fenwick OBE **Deputy Director,** Dr Wendy Harrison

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4.2 The Partnership for Child Development

The Partnership for Child Development (PCD), Imperial College London, works to improve the health and nutrition of school-aged children across the globe.

PCD's ongoing research and operational activities in the field of school health and nutrition provide an evidence-based platform that assists countries and international agencies turn such findings into national interventions. PCD is recognized internationally for its focus on quality science in development and this work has shown how simple health and nutrition interventions, implemented through schools can improve not only children's physical wellbeing, but also their education and life choices.

Deworming programmes can act as a springboard for more comprehensive school health and nutrition interventions. To this end PCD, in partnership with Innovations for Poverty Action, supports and co-ordinates the work of Deworm the World (DtW). This global initiative aims to improve the health and education of school-age children by working directly with Ministries of Education and Health to help launch, strengthen and sustain school-based deworming programmes.

To date, programmes supported by DtW have benefitted over 20 million children across 27 countries. Through school-based programmes these children will be dewormed repeatedly throughout their schooling. DtW achieve this impact by identifying what is needed to launch or sustain effective school-based deworming programmes and coordinating the assistance needed to regularly treat many millions of children each year. Find out more at www.dewormtheworld.org

PCD will continue to use deworming as the starting point for more comprehensive school health and nutrition programmes.

To read the latest school health and nutrition research findings, news and events visit www.schoolsandhealth.org

ANNEX 2 Summary of the six presentations on NTDs

- Syphilis – A silent Killer of Babies - David Mabey and Rosanna Peeling (LSHTM)
- Building capacity in post conflict countries to utilise the increasing support for control of NTDs: the case for Sierra Leone and Liberia – Moses Bockarie (CNTD Liverpool)
- The current status of funding and support for control of NTDs Professor Alan Fenwick (SCI Imperial College)
- The Global Burden of Leprosy: Priorities for Action Cairns Smith (University of Aberdeen) and Sian Arulanantham (The Leprosy Mission)
- Controlling Sleeping Sickness in Uganda through a DFID and private sector partnership Professor Sue Welburn (University of Edinburgh)
- Sightsavers and NTDs in Africa – Simon Bush and Sunday Isiyaku (Sightsavers)

During this year the presentations have widened in scope from covering the most common of the Neglected Tropical Diseases, to covering the “even more neglected” diseases of Syphilis, Leprosy, and Sleeping Sickness. Also covered were the financial commitments to NTDs, the important contribution of capacity building and then the diverse interventions supported by Sightsavers in Africa.

Some of the facts presented by the presenters were new even to the knowledgeable audiences that the APPMG attracts.

For example Professors Mabey and Peeling from the London School of Hygiene and Tropical Medicine showed that while the progress towards achieving the MDG 4 to reduce child mortality is on track for the older children, it has not improved as well for children in the first week of life. Thus in Africa, there are an estimated 1.2 million newborn deaths/year and 880,000 stillbirths/year. Thus the total number of “perinatal” deaths is over 2 million.

Of these

- malaria causes up to 200,000 perinatal deaths/year
- Syphilis causes almost 500,000 perinatal deaths/year

Most pregnant women with syphilis show no symptoms, but 25% of them deliver a dead baby, and 33% deliver a low birth weight baby. Yet a single dose of penicillin given before 28 weeks prevents these bad outcomes, - one of the most cost-effective health interventions, at \$10.5 per life year saved.

Pregnant women could and surely should be screened. There is now a simple rapid test that is easy to use, does not require equipment, and gives a result in 15 minutes. And yet in a survey of syphilis screening practice in Geita district in Tanzania, 60% had the capacity to screen, but only 14% were doing so. The reason for the low screening rates were lack of reagents, which need refrigeration, and a lack of electricity to use testing equipment or refrigerate reagents

Simply stated if 50 million women could be screened at \$2 per test, the cost would be \$100 million and the potential would be 500,000 babies lives saved.

Professor Cairns Smith and Dr. Sian Arulanantham reminded the group that despite the huge improvements due to better diagnosis and treatment, there are still an estimated 250,000 new cases of leprosy per year globally. However some 15 million have completed treatment, 3 million + with continuing disability, and the estimated burden is 194,000 disability adjusted life years. In fact all but one country (Brazil) has now reached the WHO target of less than one case per 10,000 population. India, Madagascar, Mozambique, Nepal, and Tanzania were the last five to reach this goal. They urged that the global strategy be continued to ensure that the 2015 target to reduce new cases with visible disability by 35% is achieved, and the tools to be used would be early case detection and treatment, household contact surveillance +/- chemoprophylaxis, prevention of disability and community based rehabilitation.

Professor Sue Welburn’s presentation to the APPMG on February 8th 2011 described the burden of sleeping sickness (the disease caused by the trypanosomes *T. rhodesiense* and *T. gambiense*), the current situation in Uganda with respect to the Tsetse flies, animal infections, human outbreaks, diagnostic advances and the aptly named campaign SOSS - Stamping Out Sleeping Sickness. In 1896 a devastating epidemic of Sleeping sickness affected Uganda killing an estimated 300,000 people. By 1908 300,000 were dead in Bugoba district, and in 1909 the Lake Victoria shoreline was evacuated. With such extreme fatality rates it seem amazing that sleeping sickness should be still a “neglected tropical disease” but as Professor Welburn explained, it suffered from the prioritization using DALYs because the evidence base is poor and so the burden of these diseases are difficult to define. Because of the high death rate, there is gross under-reporting. In Uganda today, the privatisation of veterinary services has meant that zoonotic disease control fell down the cracks between medical and veterinary services. It is estimated that today there are annually 300,000 cases and 50,000 deaths. Sleeping sickness is still difficult to diagnose, therefore underreported, and still no new drugs despite there being 200 disease foci. Having said that, from 1985 – 2005 an EU Programme for sleeping sickness control used active case detection and vector control. Now the SOSS aims to deliver Cost – effective intervention for Zoonotic sleeping sickness by

- (1) treating the 220,000 in cattle 5 high risk zone districts with trypanocide, led to a 75% reduction of all trypanosomes in cattle (human and cattle pathogens)
- (2) preventing reinfection by follow on application of ‘pour-on’ insecticides. Tsetse mostly feed on legs and belly of cattle and so insecticide (dip formula) applied to tsetse predilection sites where cattle act as live baits maintained prevalence <1% all trypanosomes. There was no re-infection with *T. brucei*. The treatment is affordable (10 cents), quick, effective and convenient – and has the added bonus that it kills ticks

- (3) stopping market introductions by reinforcement of Government policy for point of sale treatment – which still needs to be enforced.
- (4) using one health messaging

The project consists of many partners, namely Industri Kapital/ IKARE/ CEVA Sante Animale/ COCTU/ WHO/ Ministry of Health/ Ministry of Animal Industries and Fisheries/ University of Makerere/ University of Edinburgh DFID Research Into Use.

Sightsavers:

Dr Simon Bush, situated in Accra, informed the group that Sightsavers is an international organisation working with partners in developing countries to eliminate avoidable blindness and promote quality of opportunity for disabled people. Building on their experience in Nigeria Sightsavers is currently developing pilot programmes combining NTD work with malaria programmes. As for Trachoma, 40 million people estimated to be suffering from active trachoma but some 1.2 billion people live in endemic areas, and so are at risk. 48% of the global burden of active trachoma is concentrated in five countries: Ethiopia, India, Nigeria, Sudan and Guinea (Conakry), and not surprisingly Africa is the most affected continent: 27.8 million cases of active trachoma (65% of the total). Prevention is with Antibiotic Zithromax but for those with advanced trichiasis, surgery is needed and the estimated backlog of surgeries worldwide is 9 million people - 5 million of which are in Africa.

In total the International Trachoma Initiative which handles the drug donation for Pfizer has delivered some 220 million doses. Of these 991,000 Zithromax treatments were supported by Sightsavers in 2009 and blinding trachoma close to elimination in 2 Sightsavers-supported countries Ghana & the Gambia. In addition, over 13,000 Sightsavers-supported trichiasis surgeries performed in Africa in 2009.

In addition to Trachoma, Sightsavers also assists The African Programme for Onchocerciasis Control which is the most successful community health programme/public-private partnership in Africa delivering Mectizan against Onchocerciasis (River blindness).

Onchocerciasis is a parasitic worm disease spread by the bite of infected black flies that causes blindness and skin lesions. 84 million people are currently infected, 1.2 billion at risk. However as little as 50 years ago, up to 40% of villagers over the age of 40 would be blind near to the rivers in Africa but thanks to control programmes and particularly annual doses of Mectizan® through community directed treatment/intervention, blindness has been controlled. Sightsavers have contributed to this successful programme, delivering 22 million supported treatments in 14 African countries (out of 68 million treatments in Africa, Yemen and Americas) during 2009. The 150 millionth treatment supported by Sightsavers was delivered in 2010.

Sightsavers are part of a network that supports 1 million ‘community directed distributors’ in 146,000 communities (CDTI). After years of aiming purely for control, there is now evidence from Senegal, Mali, Guinea-Bissau and Nigeria that elimination of onchocerciasis transmission is possible in defined geographical areas in Africa: Our new aim is ‘the shrinking of the onchocerciasis map in Africa’.

What Simon Bush emphasized was that with only a minimal increase in implementation costs at health district and first line health facility, the CDTI process achieved higher coverage for all NTD interventions, while increasing the geographic and therapeutic coverage for the onchocerciasis control/elimination programmes.

He stated that if we are to eliminate trachoma and onchocerciasis this will only happen in the context of NTDs control, as they not attract enough attention on their own.

In Zamfara state in Nigeria, Sightsavers have an integrated programme, and during 2010, treatments were expected to be:

Schistosomiasis and STH	153,124
LF	636,147
Onchocerciasis	201,000
Trachoma	205,000
Total treatments	1,195,271

Over 1 million people were treated within 12 weeks with a total expenditure of **£90,853 (0.07p per person treated)** – and the extra expenditure for STH, schistosomiasis and LF was **£35,295.18**

In conclusion, Dr Bush stated that Trachoma needs to be a core part of NTD support – particularly on the integration of water and sanitation within elimination plans. However, continued financial support to NTD mass drug administration through increased donation programmes is essential – this has been the key to success to date of the NTD programmes.

Could we somehow recruit the G8 governments which have not contributed significant funds towards NTD control and elimination and to do so in line with 2009 G8 commitments. UK and USA have done so, but what of the others?

This recommendation leads into Professor Alan Fenwick (SCI Imperial College) who summarized the current state of support for NTD control. He reminded the group that 1 billion people live on less than £1 per day and in Africa over 500 million in rural areas are infected with at least one if not more of the Neglected Tropical Diseases. ...and that for less than 50 pence per child per year these infections could for the most part be eliminated. There are globally over 200 million cases of schistosomiasis, 807 million cases of Ascaris worms, 604 million cases of Trichuris worms and 576 million with hookworm which causes severe anaemia. The LF at risk ate about 1 billion with 120 million infected, and trachoma cases may number 80 million.

He praised the pharmaceutical industry for their often unrecognized donations towards the control of NTDs (see tables). In particular the donation over 25 years from Merck of Mectizan against river blindness and LF in Africa and GSK for albendazole – 1 billion tablets a year – against LF and intestinal worms in Africa. Then he mentioned Pfizer’s donation of Zithromax against trachoma (70 million annually by 2011). Two new donations were announced at the WHO meeting in October 2010 – GSK offering up to 400 million tablets a year for school based deworming in Africa and EISAI – a Japanese company who pledged 2 billion doses of DEC for LF control in the Far East and Indian subcontinent.

The German company Merck Serono has donated 60 million tablets of praziquantel over the last 3 years to encourage new countries in Africa to start schistosomiasis control programmes. Their current commitment is 200 million tablets over 10 years – enough to deliver about 8 million treatments a year. A good start but well short of the amount needed to treat 200 million people infected and many more at risk.

As for financial support Professor Fenwick noted that only two governments, USA and UK, support the implementation of NTD control programmes despite the fact that they represent the best buy in public health and are described by Margaret Chan as “low hanging fruit”. Where are the other G8 countries? Why are they missing this opportunity to help reach several of the MDGs including reducing poverty, increasing primary education and reducing maternal and child mortality? The USA support was originally \$100 million over 5 years. For the next 5 years (subject to Congress approval) up to \$450 million may be made available globally - \$250 million for Africa. The British government commitment from 2008 was £50 million split between schistosomiasis, LF, onchocerciasis and guinea worm. There are a few private initiatives trying to raise funding for implementation of control of NTDs. The Gates Foundation is supporting a fund raising campaign. SCI has its own fund raising campaign but the most investment and most successful is Sightsavers.

For the next 7 years to eliminate the seven “low hanging” NTDs from Africa we estimate that approximately £1 billion would do the job. Not that much compared to what is available for HIV and malaria – but we need a three-fold increase in currently available funding.

Professor Moses Bockarie from the CNTD Liverpool provided a specific case report on **Building capacity in post conflict countries to utilise the increasing support for control of NTDs: the case for Sierra Leone and Liberia**. He noted that the USAID model was significant in supporting the scaling up of mass drug administration (MDA) on the platform of integrated control of multiple diseases. However, capacity building was limited to the training of community drug distributors with no support offered for laboratory strengthening or operational research and for direct health systems strengthening through long-term training.

DFID support through CNTD has been substantive for scaling up mass drug administration (MDA) on the platform of integrated control of multiple diseases. The support has been innovative by including capacity building to enhance monitoring and evaluation of output focused projects; support for laboratory strengthening and operational research to improve existing tools and provide an evidence base for the current strategy and support for post-graduate training to ensure sustainability. With the £10 million awarded to CNTD for LF control, Liverpool is supporting Burkina Faso, DRC, Ethiopia, Ghana, Guinea, Liberia, Malawi, Mozambique, Tanzania and Zambia in Africa, plus Bangladesh and Nepal.

The progress against LF has been remarkable. 81 countries are noted by WHO to be endemic with 1.3 billion at risk; 52 countries are implementing annual MDA, 10 may not require MDA, as a consequence only 19 countries remain to launch an elimination programme. Currently circa 650 million receive annual treatment.

In Liberia, technical assistance for mapping of NTDs was provided by Dr Koroma from Sierra Leone, and CNTD has funded operational research on alternative intervention strategies in urban settings and Louise Kpoto from the Ministry of Health has been awarded a PhD fellowship to work on alternative treatment interventions. As Liberia has demonstrated preparedness for implementation and operational research it has been selected as a project country within a \$10m Bill and Melinda Gates Foundation project on alternative treatment strategies for filariasis and a CNTD funded laboratory in Ghana provides technical support and training for malaria vector control activities in Liberia. In addition a DFID grant to SCI, implemented by CNTD in Liberia will provide support for the control of schistosomiasis and soil transmitted helminths. Thanks to the support provided by CNTD and the in-country commitment, Liberia is rapidly becoming a flagship country in Africa to address NTDs.

In Sierra Leone NTD MDA is supported by USAID, APOC and NGDO partners. CNTD support focuses on operational research (alternative intervention strategies in Freetown and Monrovia), capacity building by providing PhD training to 2 nationals and laboratory strengthening and support.

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BOX 2 The pharmaceutical industry contribution to NTD control

	<p>Merck & Co Inc has reconfirmed their commitment to donate Mectizan for as long as needed for both onchocerciasis and filariasis in Africa</p>
	<p>GlaxoSmithKline has already donated almost 2 billion tablets of albendazole for lymphatic filariasis and will continue until elimination is achieved</p> <p>In October 2010 GSK committed an additional 400 million tablets a year for 5 years to deworm school aged children in Africa</p>
	<p>Johnson & Johnson has for several years donated up to 50 million tablets mebendazole per year for intestinal worms – next year this will be increased to 200 million tablets per year</p>
	<p>Pfizer committed to provide doses of azithromycin for trachoma. In 2009 alone they donated 50 million tablets – in 2011 that number will reach 70 million tablets</p>
	<p>Novartis is continuing its commitment to MDT for leprosy</p>
	<p>EISAI In October 2010, EISAI committed to provide 2 billion tablets of DEC for LF which is used with albendazole outside of Africa</p>
	<p>Medpharm (a generic manufacturer) has donated praziquantel through SCI</p>
	<p>E. Merck has committed to donate 200 million tablets of praziquantel through WHO over 10 years</p>