The Neglected Tropical Diseases:
A challenge we could rise to – will we?

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

Using presentations made to the APPMG 2008/9

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Vice-Chairmen: Dr Evan Harris MP, Lord Rea, David Drew MP
Treasurer: Ashok Kumar MP  Secretary: Eleanor Laing MP
Coordinator: Susan Dykes
Website: www.appmg-malaria.org.uk
I am pleased to introduce and endorse the latest in our series of authoritative and influential reports: the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases (APPMG)’s Fifth Report entitled: The Neglected Tropical Diseases: A challenge we could rise to – will we? For the first time since the APPMG was established, we focus our report outside the Malaria field.

During the last two years our meetings have been attended by more and more biomedical scientists, particularly parasitologists, interested in the wider tropical health spectrum beyond Malaria. In particular presentations by Sir Roy Anderson, Professor David Molyneux, Dr Lorenzo Savai and Professor Alan Fenwick convinced us to turn our attention to these Neglected Tropical Diseases (NTDs), in addition to all our continuing work on Malaria. The case for more investment in the control of the NTDs has been promoted by a group of international scientists who have each worked on individual diseases for many years, developing and validating tools for their control. Armed with proven strategies they have now combined their efforts to advocate for both the case for control and funding for other NTDs.

The APPMG meetings during 2008 and 2009 have been dedicated to the NTDs. In particular, they have described the complex life cycles of the parasites which infect humans and sometimes their animals. They have stressed how these diseases affect the poorest of the poor who cannot afford treatment, and they have described how the pharmaceutical industry have come to the aid of these vulnerable populations by providing drugs free of charge. There is still a funding gap and money is needed for new drug development for some diseases. For other diseases funds are required for advocacy, for training, for drug distribution from the ports to the points of delivery, for health education, for delivery through schools, health centres or community selected drug distributors, and finally for monitoring and evaluation. However, the funding gap for all these activities is relatively smaller than the amounts required for HIV/AIDS, TB and Malaria. Despite that smaller demand, filling that gap is still proving to be problematic despite calls from the Commission for Africa, the G8, the UN Secretary General and the WHO Secretary General and contributions from USAID and DFID. The massive numbers of people infected with NTDs live mainly in sub Saharan Africa, although there are still infected populations in Asia, the Pacific, Central and South America. Because NTDs are not necessarily perceived as being responsible for the major burdens of disease as they are not serious causes of death, they are nonetheless an integral cause of poverty and suffering.

The APPMG meetings during 2008 and 2009 have on several occasions been dedicated to NTDs. Speakers have professionally presented the evidence describing the suffering caused, and quantifying the burden of disease, which remarkably has been shown to be as high as Malaria and TB in terms of “Disability Life Years” lost. They have described the complex life cycles of the parasites which infect humans and sometimes their animals. They have stressed how these diseases affect the poorest of the poor who cannot afford treatment, and they have described how the pharmaceutical industry have come to the aid of these vulnerable populations by providing drugs free of charge. There is still a funding gap and money is needed for new drug development for some diseases. For other diseases funds are required for advocacy, for training, for drug distribution from the ports to the points of delivery, for health education, for delivery through schools, health centres or community selected drug distributors, and finally for monitoring and evaluation. However, the funding gap for all these activities is relatively smaller than the amounts required for HIV/AIDS, TB and Malaria. Despite that smaller demand, filling that gap is still proving to be problematic despite calls from the Commission for Africa, the G8, the UN Secretary General and the WHO Secretary General and contributions from USAID and DFID. The massive numbers of people infected with NTDs live mainly in sub Saharan Africa, although there are still infected populations in Asia, the Pacific, Central and South America. Because NTDs are not necessarily perceived as being responsible for the major burdens of disease as they are not serious causes of death, they are nonetheless an integral cause of poverty preventing progress on the Millennium Development Goals. To achieve the MDGs, NTDs will need to be controlled, and that control to be sustainable. If this can be achieved, a heavy burden on vulnerable economies will be removed.
Chairman’s Foreword

The APPMG has played a major role in raising the awareness of NTDs. It has been heartening to see the group expand not only in its remit, but also in addressing a wider number of attendees as well as the variety of speakers and subjects. So the Group is now called the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases (retaining its abbreviation – APPMG). It remains a lively forum where, at least monthly, new ideas, technologies, methods and field work can be explained and debated from across the spectrum of all those involved in the battle against Malaria and the NTDs.

The UK Government and the Opposition Parties are now all equally committed to Malaria control and DFID has become one of the leading government departments in helping to bring tools to communities who need them. We still maintain that we must control Malaria in the highest transmission areas of sub-Saharan Africa and eliminate the disease country by country, as we all work together to ‘shrink the map’ of Malaria. It is vital that this political will is maintained to sustain the long term commitment required. However while this is being done our presenters have also shown that with a smaller and cost effective intervention of just 50 pence or less per person per year, many less lethal tropical diseases could be eliminated or reduced in prevalence and intensity of infection. We must not forget them because their control would alleviate the suffering on many millions, improve their quality of life, and to school-aged children give them a healthier start to life. Additionally, NTD infections may make children more susceptible to Malaria and HIV, and less likely to respond positively to vaccinations against a range of diseases.

Stephen O’Brien MP
Chairman of the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases

Acknowledgements

The APPMG would like to express its deep gratitude to Professor Alan Fenwick, Director of the Schistosomiasis Control Initiative (SCI) Imperial College London, who has prepared the Report for the Group. Our grateful thanks go to all those who made presentations to the Group since the last report.

The Group would also like to express its grateful thanks to GlaxoSmithKline which has kindly sponsored the printing of this Report.

Presentations on Neglected Tropical Diseases during 2008-09

• Professor Sir Roy Anderson, Rector Imperial College, London
• Professor Alan Fenwick, Director SCI Imperial College, London
• Professor David Molyneux, Liverpool School of Tropical Medicine
• Professor Peter Piot, Director, Institute for Global Health at Imperial College London
• Professor Chris Whitty, Director of Research, DRD
• Chris Gilbert, Crown Agents
• John ‘Luc’ Lucas and Adam Ryan, Sumitomo Global Vector Control
• Dr Jan Kulaczkowski, NTD and Malaria Specialist, the Malaria Consortium
• Dr John P Rumausu, MPH, MB BS, Director General, Preventative Medicine, Ministry of Health, Government of Southern Sudan
• Dr Lorenzo Savoli, Director NTDs WHO, Geneva, Switzerland
• Dr Egger/Weinmiiller, Head of Corporate Affairs, BASF
• Andy Wright, Director of the Lymphatic Filariasis Programme, GSK plc
• Ivan Lewis MP (previously) Parliamentary Under-Secretary at the Department of International Development
• Prof. Michel Kazatchkine, Executive Director, the Global Fund

Many other organisations gave presentations during this period. They will all be acknowledged in the next Group’s Report on Malaria Control.

In addition, the Group would like to express its gratitude for the financial support it receives from The Malaria Consortium and Medicines for Malaria Venture.

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1. Introduction

The Neglected Tropical Diseases

The various speakers described some of the major NTDs which are listed below and a small description of each of these diseases is offered – along with some graphic photographs of serious cases taken from their presentations.

<table>
<thead>
<tr>
<th>NTD</th>
<th>Status</th>
<th>Control Strategy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Soil transmitted helminths (STH)</td>
<td>Over 1 billion infected globally</td>
<td>Annual treatment with albendazole or mebendazole</td>
</tr>
<tr>
<td>Schistosomiasis (Bilharzia)</td>
<td>200 million infected – mostly in Africa</td>
<td>Treatment with praziquantel, prontosil sulfat, or pirimetamidazol</td>
</tr>
<tr>
<td>Lymphatic filariasis (elephantiasis)</td>
<td>120 million infected in Africa and the Indian subcontinent, but elimination is possible</td>
<td>Elimination strategy by annual Mass Drug Administration with albendazole + Mebendazol (in Africa) or albendazole + DEC (in elsewhere)</td>
</tr>
<tr>
<td>Trachoma (preventable blindness)</td>
<td>80 million infected, 8 million visually impaired – eliminated from Morocco</td>
<td>Annual treatment with Zithromax, as part of a “SAFE” strategy</td>
</tr>
<tr>
<td>Onchocerciasis (River blindness)</td>
<td>50 million infections in Africa</td>
<td>Control of symptoms by annual treatment and Mass Drug MDA</td>
</tr>
</tbody>
</table>

Provision of filtered water

Guinea worm: Close to eradication

Individual case finding and case containment, clean water provision and filtration, vector control (planes). Regular surveillance of endemic villages

Diseases requiring individual treatment

Case control

Leishmaniasis

Infective in 30 countries in the Americas, Africa and SE Asia

Chagas disease

Lymphatic distribution in South America – a disease of poor housing

Hansen’s disease

Tropical distribution in Africa caused by Tsetse fly distribution

Cysticercus Leishmaniasis

15 million new cases for CL are estimated to occur annually, with an estimated 12 million people presently infected worldwide. 70% of cutaneous leishmaniasis cases occur in Afghanistan, Brazil, Iran, Peru, South Arabia and Syria.

Visceral Leishmaniasis

300,000 cases per year. 90% of all visceral leishmaniasis cases occur in Bangladesh, Kenya, India, Nepal and Sudan (if untreated) and in Ethiopia

Dengue

250 million: as risk and 50 million cases per year in over 100 countries

Effective clinical management; fluids and possibly transfusions; Vector control

Animal zoonosis

Haematozoonosis

Up to 20% infections in rural Africa and South America

Thick and acute pancytopenia

Thrombocytopenia

Unknown numbers with cysts in liver

Type a worms control in dogs and control surgery plus albendazole to remove unbroken cysts

Animal reservoir

Brucellosis

Pneumococcal of risk

Filariasis

Transmitted by dog listen Vaccination

The extent of the problem caused by Neglected Tropical Diseases

The NTDs have several things in common. They affect the poorest of the poor, but they rarely affect the well off, because usually poor hygiene is a high risk factor (Hotez, Ottesen et al. 2006). They are neglected in terms of the research and control funding allocated to them both by “developing world” governments and other donors. Less than 10% of research funds are received for NTDs compared with Malaria, HIV/AIDS and TB. Some of the NTDs (eg intestinal worms and schistosomiasis) infect many people but are chronic infections and so cause few deaths, while others (sleeping sickness and visceral leishmaniasis) infect relatively few people and are quickly fatal.

For illustrative purposes, the individual NTDs above have been divided into three groups:

1. those for which we have inexpensive, safe and effective drugs, which need to be administered just once a year (annual MDA) (Hotez, Raff et al. 2007); those for which improved drugs are needed, but for which there is no profitable market because those needing the drugs cannot pay; and

2. the “zoonotic” diseases, which are NTDs where human infections are derived from animals and predominantly infect those who work with livestock.

2. Group One

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

a. The Soil transmitted helminthiasis

(Hotez, Fenwick et al. 2009)

When individuals have massive infections, anaemia is the major result, and of course anaemia is the major cause of poor birth outcomes, infant and maternal mortality. Thus hookworms are particularly serious for pregnant women, while in children hookworm infections can cause stunting and retardation.

Whipworm and round worms are acquired when the eggs or larvae are ingested. Again heavy infections occur in poor areas and these can lead to malnutrition and stunting in children.

These three worms used to be common in Europe and USA, but with widespread hygienic conditions, they have been eliminated from developed countries, but over a billion people are infected with one or more worms in developing countries. Yet the worms can be expelled from the body with a single 500mg tablet of a drug called albendazole (an alternative drug is mebendazole), which can cost as little as one penny per tablet from a generic manufacturer. In practice an annual dose of deworming tablets throughout a child’s life will have an amazing positive effect on their growth and nutritional status.

Table 1: The NTDs

<table>
<thead>
<tr>
<th>NTD</th>
<th>Status</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Disease treatable by Mass Drug Administration (MDA)</td>
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Figure 1: Child with intestinal helminths

Three species of worms infect the “bottom billion” who are those people who live in poverty in the poorest areas of the poorest countries of the world. They are hookworm (Necator and Ankylostoma 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. They have no intermediate hosts but hookworm undergo a free living stage before reinducing a human host.

Hookworm infection is acquired when the larvae of hookworm which have hatched from the eggs and lie in wait in the grass, attach themselves to the feet and ankles of passers-by. They then penetrate the skin, migrate around the body, and end up finally in the gut where they attach and gorge on blood.

Figure 2: Successful early deworming of children stimulates growth
2. Group One

b. Schistosomiasis (bilharzia)

Three major species of schistosome worms infect man: one is found only in China and the Far East and is estimated that less than a million humans, but many domestic animals, carry that infection today. Another is found in Africa, South America and the Caribbean. The third species is found only in Africa and the Middle East. The worms of all species live in the blood vessels of the human host and the major symptoms are caused by the eggs laid by the female worm. The “African species” causes blood in the urine in children and severe damage to the urinary tract, as well as bladder cancer in later life (urinary schistosomiasis). Girls infected with these worms can develop lesions in their genital organs making them more susceptible to HIV infection (Stoeves, Molyneux et al. 2009).

The other forms of schistosomiasis (bilharzia) cause intestinal schistosomiasis because the adult worms live in blood vessels around the intestine and the eggs get trapped in the liver causing chronic liver damage and eventually liver fibrosis. Deaths in young African adults, from bleeding due to high blood pressure may well be due to liver damage caused by schistosomiasis during childhood. Infections are usually acquired when children swim, bathe or have contact with fresh water which harbours aquatic snails. These snails (intermediate hosts) become infected when human excreta (which is the route for the eggs to leave the body) is deposited in fresh water. The eggs hatch and larvae emerge and invade the snail, where they multiply before re-emerging to infect a human. The schistosomiasis larvae in water penetrate unbroken skin and migrate around the body until they reach the liver where they grow to over a centimetre in length before they pair up and start to lay eggs.

200 million people are infected globally with schistosomiasis but almost 90% of those infected are found in Africa (Fenwick 2006). Can infected patients be treated? Yes - there is a generic drug called praziquantel which costs about 20 pence. As with intestinal worms, 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, Fenwick et al. 2006). Are there are other methods to rid the world of schistosomiasis? Yes - improved water supply, improved sanitation and snail control. Sadly, snail control has not proven to be effective, because chemicals which will kill snails are expensive, and environmentally unacceptable. However, economic development which will lead to improved water supplies and effective sanitation could eventually rid the world of this disease. It has already happened in Japan and Puerto Rico (Fenwick 2006).

c. Onchocerciasis (river blindness)

A scourge of Africa and totally neglected until the 1970s, this worm causes blindness because the larvae produced by the adult worms in the human body migrate across the eye. The most serious effect of the parasite larvae is irreversible blindness but infected individuals also suffer from severe itching and skin irritation. As recently as 1970, up to 50% of populations living on the banks of fast moving rivers suffered impaired vision. Why fast moving rivers? - because the vector of this worm is the Black Fly – a small biting fly that breeds in fast moving water. River blindness was the first disease to be tackled on a large scale in Africa in the last 4 decades. In 1974 the Onchocerciasis Control Programme (OCP) controlled river blindness by spraying insecticides using planes and helicopters into West Africa’s major rivers where the Black Flies breed. This approach controlled transmission over an area the size of western Europe and freed up previously uninhabitable land for development - some 25 million hectares in 10 countries significantly increasing food production. Subsequently, the ecological pollution caused by this chemical control became unacceptable. Fortunately, in 1986 the drug Mectizan was discovered, and its killing effect on the circulating larvae proved to be the salvation of sight. Merck and Co, recognizing the fact that poor people in Africa would never be able to afford to buy even an annual dose of this drug offered to donate the drug to all who live in endemic areas “for as long as needed”. Over 20 years later this donation continues. There is a bizarre complication to what seems to be a simple control programme using annual Mass Drug Administration (MDA), and that is a parasite called Loa Loa which is another worm with live larval circulating in the body. Mectizan also kills these larvae but sometimes with disastrous consequences [such as………]. Thus in parts of Central Africa where Loa Loa is endemic it is not safe to control onchocerciasis because of the possible dangerous complications. This is a matter still to be resolved.

d. Lymphatic filariasis (LF – elephantiasis)

Another family of worms cause LF, and the deformity and misery caused by this disease are horrific. The worms are transmitted to humans during a mosquito bite, and the larvae injected from the mosquito develop into adult worms which migrate and invade the lymph system which they can block, causing long term pathology. The lymph does not drain, which causes swelling of lower limbs, secondary infections and, in the case of some men, the scrotum becomes grotesquely swollen. Meanwhile, as the pathology is being caused by the adult worms, 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.
These infections could be eliminated cheaply and effectively because scientists have shown that an annual dose of albendazole plus either mebendazole (in Africa) or DEC (elsewhere) will prevent the worms producing larvae. Although the adult worms are not killed, no larvae can be picked up by mosquitoes and so transmission is stopped. An ambitious effort is being made to eliminate this disease: the theory is that since the worms live for an estimated 4-6 years, then six consecutive annual treatments given to everyone in an endemic area should lead to elimination because transmission will be stopped and eventually existing adult worms will die out. Of course to reach elimination it is vital that a high coverage with the annual drug regime is achieved; this is a challenge when only a small percentage of the population are infected. People are often reluctant to take drugs when they do not feel they need to. This leads to the need for effective advocacy. To aid that advocacy it is publicized that the LF drugs also bring additional benefits by killing intestinal worms and other parasites.

The elimination programme is being underpinned by the donation pledges of GSK (for albendazole) and Merck & Co. (Mectizan) as a result of which approximately 500 million people are currently being treated annually with free drugs or with the extremely cheap drug, DEC (1 US cent per treatment). Sadly many people in Africa who need the treatments are not yet receiving the drugs as some of the key endemic countries have yet to embrace the value that the LF programme brings. Civil unrest in many parts of Africa also contributes to the poor coverage in some areas.

Merck & Co. extended their donation of Mectizan to include LF in Africa following the GSK commitment to donate albendazole. This emphasises the capacity of global pharmaceutical interests to work together on a major global health problem: the Global LF elimination programme (GAEFL) is an alliance which represents an important operational model of an effective public private partnership beyond the target disease but focusing on elimination of a global problem.
3. Group Two

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

a. Leprosy

Everyone has heard of leprosy, and many probably think it is a cure or even extinct. Yet there are now many fewer cases of leprosy than before, and the site of disfigurement is now relatively rare compared to 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 beating the stigma attached to leprosy. The number of countries where leprosy remains a significant problem has been reduced remarkably through multidrug therapy from over a hundred to nine, and in these nine (Angola, Brazil, Central African Republic, Democratic Republic of Congo, India, Madagascar, Mozambique, Nepal, and the United Republic of Tanzania), the prevalence remains unacceptable and unnecessarily high.

b. Visceral Leishmaniasis

This is the serious consequence of leishmaniasis infection from a sandfly 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 sandflies. If this parasite invades the visceral and internal organs death is inevitable unless a correct treatment with amphotericin B or meglumine antimoniate (Glucantime) or sodium stibogluconate (Pentostam) can be administered quickly. 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. A new and effective drug is needed to treat this disease, and Drugs for Neglected Diseases Initiative are working with One World Health on Paramomycin. An effective drug, ambisome, exists but it is not donated hence the problems of affordability.

c. Cutaneous Leishmaniasis

The same organism as in (b) above if it remains in the skin at the site of the sandfly bite causes an ugly 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 leishmaniasis - often rodents in Asia, the Middle East and in the Americas.

d. Chagas disease

Another protozoa – 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 Triatomin 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. 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. Domestic transmission of the disease has been controlled in 5 countries (the southern cone in South America) by indoor house spraying with insecticide. The remaining 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 and the donation of blood by migrants, the disease is being found in non-South Americans through transfusion.

e. Human African Trypanosomiasis (HAT)

African Sleeping sickness is also caused by a trypanosome, but this one is transmitted by the tsetse fly that breeds in savanna and riverine woodland in a belt across Africa. When humans become infected from the bite of the fly, the parasites first invade the blood and later invade the central nervous system with fatal consequences if untreated. There is no satisfactory treatment for HAT as we remain dependent on arsencial based drugs which are themselves dangerous, although some recent progress on combination therapy has been reported. 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. Unfortunately the reduced resources for the “mobile team approach” to control, and civil conflict in tsette areas, led to a rise in Sleeping Sickness cases in the 1980s and 1990s. However, according to WHO data, this has recently been arrested. The potential for epidemics remain; Sleeping Sickness is a disease which requires constant surveillance by national health authorities. Recently developed innovative methods for the control of tsetse flies by insecticide based methods appear to work, and should be deployed to reduce transmission.

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 having little contact with any 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 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 distribution is from northern Australia and northern Argentina across the entirety of SE Asia, sub Saharan Africa, the Caribbean, and parts of South America. Dengue is transmitted to humans by the Aedes aegypti daytime feeding mosquitoes. 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.
4. Group Three

Group Three: animal zoonoses – the even more neglected tropical diseases

a. Neuro-Cysticercosis

Cysts in the human brain cause severe seizures, epilepsy and death. But what causes these cysts and what is inside them? In fact, humans are accidental hosts to these cysts which really belong in the pig. The pig is the normal intermediate host of a tapeworm which lives in the gut of man, and pigs become infected by eating the eggs which are passed out in human faeces. When ingested the eggs hatch and the larva of the tapeworm develop into a cyst full of fluid and new tapeworm heads, waiting for a human to eat the pig meat. So humans get infected accidentally by somehow swallowing the tapeworms eggs in their excreta. Under conditions of poor hygiene, man can infect himself – not washing hands after defecating, for example. If a person does ingest the eggs then they will develop into the cysts, but in humans they develop in the brain. Humans get infected with the adult worms by eating infected and poorly cooked pork, so meat inspection is important – but non-existent in rural village settings.

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 Brazil, Kenya and the Democratic Republic of Congo around 10% of the population is infected, in Madagascar 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.

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 who 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.

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 the UK is rabies-free, this disease which is primarily associated with dogs and foxes is prevalent elsewhere in the world wherever dogs exist, and the bite from a rabid dog is fatal unless a vaccination is given almost immediately. There is now a pre-exposure vaccine for humans which is expensive but a post-exposure vaccine should be available in hospitals and clinics in case of bites from suspect animals.

5. Lessons Learnt

Lessons learned from the speakers on the NTDs

Professor Sir Roy Anderson and Professor David Molyneux presented on one day as a double act and proposed a convincing argument for the APPMG to widen its remit from just malaria and embrace NTDs. Between them they described the life cycles of these NTDs and demonstrated graphically the horrific cost in terms of human suffering and economic losses. Professor Molyneux emphasised the advantage of controlling NTDs as a means of tackling poverty and addressing the MDGs. It was also emphasised that NTD control can be of great value in malaria control programmes and in reducing the spread of HIV. The importance of taking a holistic approach to the interventions available which are some of the cheapest and most effective available was emphasised. Some months later Professor Alan Fenwick and Dr Lorenzo Savioli each gave a different slant to the NTDs, again covering aspects of their life cycles (described above), their burden globally, numbers infected in different countries and regions, and describing attempts and progress towards elimination or control of these diseases. The efforts of a few dedicated individuals were first of all targeted against each of the individual diseases, but more recently the speakers explained how integration of NTD control had become the norm. WHO has established an NTD department, and countries were being encouraged to integrate their efforts to control NTDs.

The APPMG learned which drugs can be used to control the various diseases, and the costs of delivery have been calculated at approximately 50 pence per person treated per year.

Other presentations from Dr John Rumanu, Director Preventative Medicine, Ministry of Health, Government of Southern Sudan, and Dr Jan Kolażynski, NTDs and Malaria Specialist with the Malaria Consortium focused on the distribution and burden of NTDs in Southern Sudan and a plan was presented for their control after the recent ending of a very long civil war which had disrupted the health services in the region. These presentations emphasised the need for country commitment and NGO implementing partners.

The following table demonstrates the contribution that pharmaceutical companies are making towards NTD control.

<table>
<thead>
<tr>
<th>Pharmaceutical Company</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>E. Merck</td>
<td>Has donated praziquantel and deworming drugs via Canadian donations</td>
</tr>
<tr>
<td>Novartis</td>
<td>Has a continuing commitment to Multi-Drug-Therapy for leprosy</td>
</tr>
<tr>
<td>Johnson &amp; Johnson</td>
<td>Has committed to donate up to 100 million praziquantel tablets over 10 years</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Has committed to donate up to 120 million doses of azithromycin for trachoma</td>
</tr>
<tr>
<td>GlaxoSmithKline</td>
<td>Has donated albendazole for lymphatic filariasis globally and up to 2020</td>
</tr>
<tr>
<td>Merck &amp; Co Inc</td>
<td>Donates praziquantel for schistosomiasis and lymphatic filariasis in Africa</td>
</tr>
<tr>
<td>Medpharm (generic manufacturer)</td>
<td>Has donated praziquantel and deworming drugs via Canadian donations</td>
</tr>
<tr>
<td>Pfizer</td>
<td>Has committed to donate up to 100 million doses of albendazole for onchocerciasis and lymphatic filariasis in Africa</td>
</tr>
</tbody>
</table>

The process of establishing a control programme and the possible strategies were also described by several speakers. In summary there are seven NTDs which are extremely prevalent globally, but which today are almost never found in the developed world. These seven (Group One above) are now known to be controllable at minimal cost using an annual dose of what has been termed a “rapid impact package” of four drugs.

However the process for control was shown to have been a complicated exercise in funding, advocacy and planning, with the first obstacle to be overcome being that most governments, even the Ministries of Health in endemic countries, do not encompass these diseases in their plans.

Table 2. The Pharmaceutical company donations
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:

- NTDs are a diverse group of infections which tend to affect the poorest of the poor.
- Without something being done for the NTDs, the MDGs will not be attainable.
- For the first group of NTDs a cheap rapid impact package of drugs can be delivered annually at minimal cost and could easily control or eliminate the suffering of up to a billion individuals (the estimated cost is about $200 million per annum for 5-7 years).
- A number of global pharmaceutical companies have been generous in donating their products which raise revenue in the west but are unaffordable to those who need them in the poorer countries.
- Post-conflict countries and countries still in conflict probably have the greatest need for support.
- For some diseases new drugs are needed so further R & D should be funded.
- Greater attention needs to be focussed on Zoonotic diseases.
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- NTDs are a diverse group of infections which tend to affect the poorest of the poor.
- Post-conflict countries and countries still in conflict probably have the greatest need for support.
- For some diseases new drugs are needed so further R & D should be funded.

Annex 1

List of Presentations made to the APPMG on Neglected Tropical Diseases in 2008-09

A Summary of presentations

Professor Sir Roy Anderson, Rector, Imperial College, Department of Infectious Disease Epidemiology Faculty of Medicine

Sir Roy presented a strong case for the control of Neglected Tropical Diseases (NTDs). He pointed out that at present control was disjointed there were many NGOs, and many diseases but there was little co-ordination between them. Disease control was separated as for malaria, HIV and TB in the Global Fund.

There was a need for co-ordinated logistics, delivery and management for all these diseases, including NTDs. The disease burden was high but much of this was preventable with simple low cost but effective interventions. Governments needed to focus on keeping their structures simple.

Amongst the UN Millennium Development Goals combating HIV/AIDS, TB, Malaria, and other diseases, NTDs were included in “other diseases”, he said.

An estimated 500 million people in Africa infected with one or more infections which constitute the Neglected Tropical Diseases (NTDs), the burden as measured by DALY’s was as great as malaria and TB. But unlike many diseases safe and effective drugs existed for at least seven of these diseases which should make morbidity unnecessary. Sadly those who needed them could not afford them.

The pharmaceutical industry had helped in this respect with drug donations from GSK (Albendazole), Merck (Medik, Pfizer (Zithromax)), Johnson and Johnson (Ivermectin) and smaller donations from MedPharm and Merial (Plasmepartal to SCI and WHO) respectively.

In conclusion, Professor Anderson said that advocacy, mapping, training and drug delivery were needed to complete the treatments. They were relatively inexpensive when conducted at scale. Treatment could do so much good at an extremely low cost.

Professor David Molyneux, Liverpool School of Tropical Medicine

NTDs: Malaria: Realities and Operational Opportunities

Professor Molyneux, who has had experience in both onchocerciasis and lymphatic filariasis, reminded the meeting that the Blair Commission for Africa Report recognized the gap in funding for NTDs with the statement

“Donors should ensure that there is adequate funding for the treatment and prevention of parasitic diseases and nutritional deficiencies.”

He said that the targets of the Millennium Development Goals also needed NTD control because this would have a significant effect on MDG 1 (Eliminate extreme poverty and hunger): MDG 2 (Reduce child mortality); MDG 3 (Reduce maternal mortality); MDG 4 (Combat HIV/AIDS, malaria and other diseases) and MDG 5 (Develop a global partnership for development).

Professor Molyneux stressed that NTDs affected the poorest people. “They live in areas where there are no roads, no doctors, and no drugs. Hunger and food security are the greatest threats incomes are very low and the communities are in greatest need.”

There have been successes: in China 350 million are now free of threat of lymphatic filariasis disease, because transmission has been arrested. In sub-Saharan Africa, in 10 countries, onchocerciasis (river blindness) was no longer a public health problem. In South America, domestic transmission of Chagas disease had been eliminated in 5 countries and transfusion transmission eliminated. In China and in Egypt, schistosomiasis had been controlled – though not yet eliminated.

In Morocco, active trachoma prevalence in under 15’s had been reduced by over 90%.

In Cambodia, soil transmitted helminths control had reached the World Health Assembly target of 75% children under regular treatment at an estimated cost of US$50.

In Peru, the elimination had been achieved as a public health problem through Multi Drug Therapy. Prevalence had been reduced by 90%.

The Guinea Worm Eradication Programme had reduced global infections from circa 900,000 in 1990 to 25,500 in 2006. It cost around $50 per person per year for treatment, often much less, he said.

Andy Wright, Director of the Lymphatic Filariasis Programme, GlaxoSmithKline

Mr Wright said that private sector companies had a role to play in malaria and NTD control. GSK cared for their staff in endemic countries, cared for communities in which the company operated (mining, oil companies) and GSK believed in local and international corporate responsibility.

GlaxoSmithKline in particular was one of the world’s largest pharmaceutical companies with 100,000 employees in over 100 countries. Their expertise was to develop medicines and vaccines for medical needs globally, as required.

GSK was heavily involved in the development of anti-malarial drugs, development of a malaria vaccine, and developing and using community partnership programmes.

The GSK CEO Andrew Witty, made commitments in a speech delivered at Harvard, where he stressed GSK’s flexible approach to Intellectual Property for Less Developed Countries (patent pool for medicines for NTDs). He committed GSK to reduce prices for patented medicines in the Less Developed Countries (LDCs), greater collaboration in R&D for developing world diseases, and a move to be a partner in delivering solutions (GSK would remit 20% back into the field).

GSK had a portfolio of anti-malarials (Halofantrine, Malarone, LapDap, CDA), and a drug discovery unit at Tres Cantos, Spain.

GSK continued to support research into Malaria, TB and other NTDs. There were 100 scientists, who were in partnership with the Gates PATH Malaria Vaccine Initiative.
Dr. John P. Rumunu (MPH, MB.BS), Director General, Preventive Medicine, MoH-GoSS, discussed the local challenges and strengthened health systems in the process. Schistosomiasis & soil-transmitted helminths (STH) and by strengthening community-based delivery. He said he would use the drug administration (MDA).

Presenting his overview of NTD control, Dr. Kolaczinski suggested that the integration of NTD control was intuitively appealing, because disease burden. He said that the death rate due to NTDs was relatively low, probably about 500,000 per year, much less than HIV, which was a simple question of getting drugs distributed to those who needed them. For Human African trypanosomiasis, Chagas disease, Buruli ulcer, Leishmaniasis, and, Dengue, case management in the field was essential. Meanwhile new drugs were required.

For NTD control the need was for simple and inexpensive diagnostic tool, oral inexpensive drugs that did not have side-effects and integration within existing health structures if possible. This would lead to sustainable control and eventual elimination. Dr. Kolaczinski stressed that mass drug administration was the way forward, not individual diagnosis, nor the use of delivery through the community. He showed that there was a template produced by WHO that would determine the best timetable for interventions according to the overlapping distribution of the NTDs. WHO’s recipe for success was a focus on populations to improve access to essential interventions. They would look to:

- Integrate ‘strategies’ to improve effectiveness
- Improve education, environment, and local empowerment as a core for success
- Expand the control programs
- Deliver preventive chemotherapy on large scale
- Reinforce Primary Health Care
- Deliver focused interventions and innovation
- Empower peripheral systems through training and equipment
- Advocate access to care and mainstream society for the neglected communities
- Measure diseases and development indicators

Professor Alan Fenwick, Director of the Schistosomiasis Control Initiative, Imperial College London. The Burden of the Diseases and their Impact. This presentation complemented Dr. Savioli’s. Professor Fenwick described in more detail some of the life cycles, the consequences of long term infections and attempted to describe the burden of the diseases. He also costed the control measures taking into consideration the value of the drug donations, and suggested that control of NTDs, at least the seven that could be controlled by mass drug administration, was the best buy for public health. He also pointed out that there were other NTDs for which we did not have adequate diagnostic techniques, nor safe and effective chemotherapy.

Professor Fenwick described the financial resources needed to control the seven NTDs in Sub-Saharan Africa, approximately $1 billion over 5 years. He pointed out how little was spent on NTDs in contrast to the funds available for HIV control. He described how the American people through USAID and a private donor Legatum had increased the funding. The three major donors were the American people through USAID, the British people through DFID and a private donor Legatum, who had donated to SCD and the GNNTDC.

The coverage of each disease was shown on maps, and the various organisations involved, the WHO APOC for Onchocerciasis, GAELF for Lymphatic filariasis, ITI for trachoma and SCI for Schistosomiasis and intestinal helminths. They were credited for their efforts. The Global Network partners were now moving towards integration of NTD control, as were the gatekeepers supported by the Global Network, the contractor RVI. They were now expanding control in 10 countries with time, more to be added as funding was increased. The private donor Legatum supported the integrated control of NTDs in Rwanda and Burundi he said.

Despite all this progress, in 2008 the WHO believed that schistosomiasis and intestinal helminth treatment reached less than 10% of those who needed to be reached.

Professor Peter Piot, Director of the new Global Health Institute, Imperial College, London. Professor Piot presented a wide ranging overview of the concept of global health as perceived today. He dealt the progress that has been made in the separation of the concept with ARVs in Africa to several million at a cost reduced in 10 years from $1,000 per person down to less than $100 per person. He cited how quickly the WHO responded to the SARS threat and how a similar threat (swine flu) was being tackled in 2009. Professor Piot described the “unfinished business” in global health which is an ongoing scenario because of climate change. However there was a need to focus on seven major categories if the world was to become a better place for those in the bottom billion in terms of wealth.

The Ministry of Health (MoH) had prioritized the control or elimination of some diseases e.g. Onchocerciasis, Guinea worm and Trachoma, as well as through strengthening the health system at all levels. In particular there must be a commitment to increase and strengthen the coverage of the primary health care system and services, including the referral system. In order to achieve this, the Ministry of Health would need resources both in terms of man power, funding, partnerships with international agencies, NGOs and effective planning and training.

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- Infectious diseases (TB, Plasmodium and NTDs)
- Maternal mortality
- Child health
- Neglected tropical diseases
- Reproductive health
- Malnutrition
- Primary health care

The message from Professor Piot was that we needed to finalize the unfinished agenda tackle chronic diseases, mental health, urbanisation, climate change, water and population. This could only be done if we delivered new prevention & treatment technologies and ensured population had access to more effective health systems.
Since 1999, the funding available for the control of diseases of poverty (neglected diseases) has increased mainly due to leverage resulting from donations by the Bill and Melinda Gates Foundation and loans from the World Bank. Many countries have embarked on control programmes on a national scale due to drug donations by pharmaceutical companies through vertical programmes. The Schistosomiasis Control Initiative has expanded its operations to cover six countries in sub-Saharan Africa, but overlap of treatments between different vertical programmes is now a reality, and so care is needed to ensure that too many different drugs are not given together. Dialogue between programme managers has increased, and integration of some programmes may offer chances of synergy.

The development of water resources, particularly in Africa, has changed the face of the continent, opening up land for agriculture, providing electric power, encouraging settlements adjacent to water bodies, and bringing prosperity to poor people. Unfortunately, the created or altered water bodies provide ideal conditions for the transmission of waterborne diseases and a favourable habitat for intermediate hosts of tropical parasitic infections that cause disease and suffering. The recent progress in control of these waterborne and vector-borne diseases, such as guinea worm, schistosomiasis, lymphatic filariasis, and onchocerciasis, suggests that many of them could be controlled effectively by 2015, which is the target for reaching the Millennium Development Goals. Donations of safe and effective drugs by several pharmaceutical companies, funds for delivering these donated drugs from foundations and bilateral donors, and effective global health partnerships should make these diseases history.

Three years have passed since the publication of the first of a series of policy papers, which first highlighted the under-appreciated global burden of the neglected tropical diseases (NTDs) and then outlined a rationale for linking vertical control strategies for the seven most prevalent NTDs in a cost-effective pro-poor package of preventive chemotherapy. Since then, global advocacy for these conditions has increased and, with it, new funds for scale-up of integrated NTD control in sub-Saharan Africa. Recent speeches by the Director General of the World Health Organization at regional meetings have referred to NTDs as important global health priorities (www.who.int/dg/speeches/2007). Outlined here is a summary of the recent progress in global efforts to integrate NTD control, with an emphasis on the challenges that lie ahead.

The rapid expansion of chemotherapy-based control programmes for neglected tropical diseases has been catalysed by funding from the Bill and Melinda Gates Foundation, donations of several drugs from pharmaceutical manufacturers, and the reduced price of the drug praziquantel. Focussing on lymphatic filariasis, schistosomiasis and soil-transmitted helminthiasis, we review here the progress made to date with the implementation and integration of large-scale control programmes. Unresolved issues include a means for rapid identification of communities at highest risk of co-morbidity, cost-effective approaches for integrating the technical interventions into setting-specific packages, and determination of the most appropriate and sustainable delivery systems.