FT Health

Combating Neglected Diseases

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War waged on scourge of the lesser known

Killer infections are missing link in efforts to ease poverty in the developing world, says *Andrew Ward*

Emergency: a paramedic checks victims of a dengue fever epidemic that has recently hit Pakistan's Swat valley Aamir Qureshi/AFP

It is one of Africa's most feared diseases with symptoms including fever, swelling of internal organs and skin lesions. If left untreated it usually results in death.

This gruesome killer is not Ebola but a parasitic disease called visceral leishmaniasis which is spread by the bite of infected sandflies. It has killed hundreds in South Sudan over recent years and there are fears the outbreak could worsen amid renewed civil war.

Similar grim stories exist across the developing world. Only rarely does one of them break into the global consciousness as Ebola has this year. While nobody questions the horror of the epidemic sweeping west Africa, the death toll – 3,500 and rising – is dwarfed by the number struck down each year by a range of less notorious infections.

Dengue fever kills an estimated 22,000 people a year, mostly children, in more than 100 endemic countries. The mosquito-born virus is among the most deadly of 17 conditions identified by the World Health Organisation as neglected tropical diseases (NTDs). Together, they pose a public health burden comparable with better-known scourges such as HIV/Aids, malaria and tuberculosis. Yet their disparate nature and the fact they generally pose little threat outside tropical regions means they have struggled to attract international attention.

Ebola is not officially recognised as an NTD because the explosive nature of its sporadic outbreaks is different from the slow-burning but more enduring threat posed by diseases such as dengue and leishmaniasis. But Kamran Rafiq of the London-based International Society for Neglected Tropical Diseases says the crisis in west Africa has highlighted the vulnerability of the world's poorest societies to the worms, parasites, bacteria and viruses that bedevil the tropics.

He says: "All the things we're seeing with Ebola – lack of drugs, lack of vaccines, lack of diagnostics, lack of basic healthcare and sanitation – are the same issues that surround many NTDs."

As Tim Evans, director of health, nutrition and population at the World Bank says: "[They] are major constraints on the development of children and their opportunities for education, as well as the ability for adults to engage in productive work."

Yet, there are some cautious grounds for optimism. After the creation of the Global Fund to Fight Aids, Tuberculosis and Malaria in 2002, there was a growing recognition among international donors and policy makers that NTDs were the missing link in efforts to improve health and ease poverty in the developing world.

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Inside

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When you're healthy and strong, you can grow up to do anything.

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Epidemic Ignoring a sickness that has been confined to poor countries has rebounded on the rich world, writes *Clive Cookson*

Ebola thrives in absence of weapons to contain it

At the beginning of 2014, Ebola was very much a neglected disease, feared for its high mortality rate but not generally regarded as a grave threat to public health outside central Africa where sporadic outbreaks have been recorded for almost 40 years.

Low-key research into Ebola drugs and vaccines had been under way for a decade or more, funded mainly by the US government's biodefence programme and motivated in large part by fear that terrorists might conceivably turn the virus into a deadly weapon.

Nine months later, Ebola is the most discussed virus on the planet, as an exponentially expanding epidemic rampages through west Africa. The official toll is approaching 7,500 cases and 3,500 deaths, mainly in Guinea, Liberia and Sierra Leone. Unofficial estimates are two or three times higher than that. Terrifying projections by experts at the US Centers for Disease Control suggest that the worst extreme could produce 1.4m cases by January.

Threatened by a potential catastrophe with implications for global security, as well as human suffering on an enormous scale, western governments have belatedly pledged substantial financial, medical and operational assistance to help the World Health Organisation, affected governments and charities such as Médecins Sans Frontières fight the disease.

In the short to medium term, the war against the epidemic will be won or lost through intensive infection control methods. Hospitals or clinics need to be staffed by health workers equipped to

> 'It is a huge challenge to carry out clinical trials under such difficult conditions'

practise barrier nursing, sometimes referred to as bedside isolation, so that patients can be well tended – proper hydration for example helps survival – without the risk of passing the virus on to anyone else. When someone dies, traditional death rites and funeral practises must be adapted to avoid physical contact with the deceased.

Drugs and vaccines should be potent weapons against Ebola in the long run, but none is yet ready for large-scale deployment in the field. Laboratories around the world have a pipeline of some 15 medicines for people already infected and a dozen vaccines to prevent infection – most tested on animals but not people – which are urgently being evaluated for safety and efficacy.

An international partnership, including the Wellcome Trust, University of Oxford, Médecins Sans Frontières, WHO, Institut Pasteur, Fondation Mérieux and the Global Health Network, has been set up to fast-track the most promising treatments into clinical trials in west Africa.

Details of the trial procedures and the pharmaceuticals to be tested are being finalised. Resources and local infrastructure will not permit all the candidates to be assessed. Factors in the selection include how quickly their production can be scaled up as well as their likelihood of success based on pre-clinical data. Companies collaborating with the initiative include Mapp Biopharmaceutical, Sarepta and Tekmira.

Mapp's ZMapp, a cocktail of three antibodies against Ebola virus, has had the most publicity of any candidate drug. The few available doses were given in August to seven patients, including four western health workers who were infected in west Africa. Monkey studies have given encouraging results. But the problem with ZMapp is that it will be slow to build up supplies because the drug is produced in genetically engineered tobacco plants grown in a research-scale facility in Kentucky.

Peter Horby of Oxford university, the consortium leader, says: "We urgently need to know whether any of these investigational treatments can save lives. In essence, we need straightforward clinical trials, as for any drug for any disease. However, new ways of working will be needed to provide rapid and reliable answers in perhaps the most challenging outbreak we have ever encountered."

Jeremy Farrar, director of the Wellcome Trust, adds: "It is a huge challenge to carry out clinical trials under such difficult conditions but ultimately this is the only way we will ever find out whether any new Ebola treatments actually work. Rapid trials, followed by large-scale manufacturing and distribution of any effective treatments, might produce medicines that could be used in this epidemic."

Two candidate vaccines are being fast-tracked through development. Initial safety trials of the first vaccine, co-developed by GlaxoSmithKline and the US National Institutes of Health, started last month in the US and UK. It uses an Ebola viral protein to generate an immune response but contains no infectious material, so there is no risk of accidentally transmitting the disease.

GSK will produce 10,000 doses, so that, if the initial trials go well, the vaccine can be introduced quickly to immunise health workers in the front line of the fight against Ebola.

As Margaret Chan, WHO director-general, points out, clinicians lack medicines because Ebola has been confined to poor African countries. The pharmaceutical industry has had no financial incentive to fund research and development.

The emergency has prompted a response, but the wider issue of how to pull in R&D investment for neglected tropical diseases remains unresolved.

Desperate times: a health official examines children infected with the virus in a Sierra Leone clinic — Tanya Bindra/AP

Outbreak points to need for behavioural change

The response

Given a lack of leadership from the top, the Ebola crisis highlights how much more action is required at local level, reports *Andrew Jack*

Mohamed Lamin Turay has seen the dangers of Ebola close up in Sierra Leone and it has only strengthened his resolve to help tackle the world's worst known outbreak.

One of his friends became ill after his father came home from a traditional burial where he had helped wash the body. "They thought he had a cold," he recalls. His friend and several other members of the family died.

He began work this month as one of 200 community volunteers recruited in Sierra Leone to a programme run by the charity Restless Development. It aims to change attitudes towards the disease, providing training, support and security to a network of "mass mobilisers" travelling to remote areas to share information on prevention.

He and colleagues are spreading messages including the importance of cleanliness, avoiding touching anyone suspected of infection including during funeral rites, remaining at home if at risk, and avoiding eating bushmeat.

"Ebola is really affecting us," he says. "It's an extraordinary challenge but it can be prevented."

Many local people are without access to healthcare workers and suspicious of government. Their traditions put them at high risk.

Jamie Bedson, Restless Development's Sierra Leone country director, says: "There's a strong belief in witchcraft that Ebola is contracted through a curse or in some cases that it is a white man's fabrication."

"There is a mistrust of foreigners, and in one place everyone threw away soap given out by the government because they thought it was poisoned."

Much attention has been paid to the short-term need for medical support and the long-term potential for innovative treatments and vaccines in tackling Ebola in west Africa, which has claimed more than 3,500 lives in the past 10 months. Far less effort has been on low-tech "behaviour change" that will prove essential to slowing the infection and limiting future outbreaks.

"What's missing is risk communication," says Nigel Lightfoot, head of Connecting Organisations for Regional Disease Surveillance (Cords), a Lyon-based group coordinating surveillance networks around the world. "It's not just about diagnosis and treatment but about getting people into local communities, to reach religious and community leaders and traditional healers."

First identified in Guinea last December, international and domestic recognition of the severity of the latest Ebola outbreak was slow. Neither African political leaders nor global bodies responded for months. Internationally, critics say the World Health Organisation lacked leadership on the issue. This

> 'These are countries with the worst health and development indicators that you can think of'

year, the UN agency downgraded its global alert and response team, dissipating expertise that it had built up in tackling Sars and pandemic influenza over the past decade.

Years of mismanagement and civil war have undermined the fragile health infrastructure in Sierra Leone and Liberia, which has also been hit badly by Ebola. "These are countries with the worst health and development indicators you can think of," says Peter Piot, head of the London School of Hygiene and Tropical Medicine, who first identified the disease in 1976 in what is now the Democratic Republic of Congo.

Healthcare workers are poorly paid and equipped and in extremely short supply. More than 100 local doctors and nurses have themselves died of Ebola. That illustrates the difficulties of diagnosing and isolating Ebola patients effectively and the practical problems of wearing stifling protective equipment – if available – in the local hot conditions.

Prof Piot stresses the significance of traditional practices – which include widespread touching and washing of corpses ahead of burial – and the need to build stronger relationships with local leaders including Sierra Leone's powerful secret societies. Instead, many cases have been driven underground. Some people avoid clinics for fear of infection.

Mass quarantine has not always helped, imposing formal travel bans that block access by specialists while doing little to prevent infected individuals from crossing borders. Dr Armand Sprecher, a Médecins Sans Frontières specialist who has seen many Ebola outbreaks, says his efforts to bring tents from Kenya into Liberia to construct a makeshift clinic were hit when the Kenyan authorities blocked flights. He worries how he would evacuate any expatriate medical staff for treatment if they were caught in a road accident.

Focus on Ebola has swamped medical facilities and downplayed the impact of other diseases that impose a far heavier toll in west Africa including HIV, TB and malaria. "Many more people will die because of Ebola than from it," cautions Jimmy Whitworth, head of population health at the Wellcome Trust.

For now, Mamusu Tarawalie, another Restless Development volunteer working in Sierra Leone, believes the burden of Ebola justifies her efforts. "There are lots of lives at stake," she says. "I am confident we can beat the disease."

War waged on scourge of the lesser known

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This led to the London Declaration in 2012, when organisations including the World Bank, the Bill & Melinda Gates Foundation and a dozen big drugmakers agreed to throw their weight behind a WHO target to control or eradicate 10 NTDs by 2020. Two years later, progress is well under way, with Guinea worm on the brink of becoming only the second human disease after smallpox to be eliminated and others such as trachoma and onchocerciasis in retreat.

At an NTD summit in Paris in April Bill Gates hailed the "phenomenal" effort to turn the tide but said there was still a long way to go. At that meeting, the Microsoft founder reinforced his status as the world's leading health philanthropist by pledging another $50m to the NTD programme, taking his foundation's commitment above $400m.

Meanwhile, drugmakers including GlaxoSmithKline, Sanofi and Johnson & Johnson, donated more than 1.3bn treatments to the effort in 2013, up 35 per cent since 2011. They are also training medics and helping improve health infrastructure and supply chain logistics to ensure medicines reach patients.

Mark Clark, analyst at Deutsche Bank, says: "We see the industry's efforts – especially in regard to strengthening local healthcare capacity – as a clear case of 'doing the right thing' while making a strategic long-term investment in the customers of tomorrow.

$500m	$130bn
Annual investment in tropical disease research and development	Pharmaceutical industry's total expenditure each year on research and development

Economic growth in the decades ahead will inevitably see many of these nations become increasingly important commercially to the pharma industry."

Annual investment in tropical disease research and development has risen to about $500m, according to Deutsche Bank, still just a fraction of the industry's total R&D expenditure of $130bn, but up significantly from a few years ago. GlaxoSmithKline and Sanofi are closing in on, respectively, the first vaccines for malaria and dengue.

Manica Balasegaram of health charity Médecins Sans Frontières says such breakthroughs remain rare. Ebola "is a case of chickens coming home to roost for an R&D system that is not aligned with global health needs. Society has to come up with a new way to incentivise R&D for neglected diseases".

Simon Brooker, professor of epidemiology at the London School of Hygiene & Tropical Medicine, says that drugs and vaccines are not always the answer.

Guinea worm is near eradication without the aid of either. "A vaccine can take 20 years to develop. In that time, I would hope we will have tackled most of these diseases through improved sanitation and hygiene."

Yet some countries are moving in the wrong direction.

Peter Jay Hotez, dean of the National School of Tropical Medicine at Baylor College of Medicine in Houston, says leishmaniasis and polio are on the rise in Syria and other war-torn areas of the Middle East are similarly vulnerable to NTDs.

"They are driven by social forces. The most important factors are poverty and conflict."

Sanofi squares circle of philanthropy and profit

Drug development

With dengue on course to be 'vaccine-preventable', the French company aims to cash in, writes *Andrew Ward*

For big pharma, tackling neglected tropical diseases is a largely philanthropic enterprise – something done to demonstrate commitment to global health while making the big bucks on treatments for rich westerners.

Just occasionally, however, a breakthrough comes along with the potential to address an unmet need in the developing world while also making lots of money.

Sanofi, France's biggest drug maker, has hit upon precisely such an opportunity through its work on the world's first vaccine for dengue fever – a debilitating virus that infects up to 100m people a year with half the world's population living in places where it is present.

Data last month from a big phase three trial – the final stage before seeking regulatory approval – showed that the vaccine reduced incidence of dengue by almost 61 per cent and hospitalisation by 80 per cent.

Olivier Charmeil, president of Sanofi's vaccines unit, says: "For the first time ever, after 20 years of research and industrial commitment, dengue is set to become a vaccine-preventable disease."

The dengue breakthrough represents a second significant public health success for big pharma this year after GlaxoSmithKline filed for European regulatory approval of the world's first malaria vaccine.

However, while GSK has said it is not looking to make big profits from its product, Sanofi is being more bullish.

The French company has invested €1.3bn in its dengue vaccine in anticipation of making a handsome return. Indeed, analysts at Deutsche Bank say it could become the world's best-selling vaccine with revenues of €1bn a year.

The contrast with GSK's vaccine reflects the greater concentration of malaria in poor regions. Dengue, by comparison, is also prevalent in middle-income countries from Brazil to

Long haul: 20 years of R&D have resulted in the new vaccine

Thailand. Dengue has been around for centuries but its spread was accelerated by soldiers in the Pacific theatre during the second world war. Incidence has increased 30-fold over the past 50 years.

Before 1970 only nine countries had experienced severe dengue outbreaks. Today it is endemic in more than 100 countries home to 2.5bn people across Africa, Asia and Latin America.

The mortality rate is relatively low at 1 per cent but the virus is a leading cause of death among children in affected areas. About 500,000 people a year have to go into hospital because of symptoms including high fever, severe headaches, muscle and joint pains.

There are signs of the disease spreading beyond its tropical strongholds. The US, China, France, Portugal and Croatia have had isolated outbreaks in recent years and scientists say climate change could make such cases more common. Japan has seen more than 60 infections in recent weeks, marking the virus's return to the country after a 70-year absence.

All this leads Christopher Pace, infectious disease analyst at GlobalData, a research company, to predict "rapid uptake" of dengue vaccines in Brazil, Mexico, India, Singapore and Thailand.

The failure of efforts to curtail the mosquitoes that carry the disease has left "a glaring void in the dengue prevention and control landscape," he says.

While Sanofi was on course to be first to market, it is likely to face competition from another promising dengue vaccine in late-stage development by Takeda of Japan, Mr Pace adds.

Rajeev Venkayya, head of vaccines at Takeda, says the company planned a tiered pricing structure that would provide affordable prices in poor countries while making a return on investment in more developed markets. Sanofi plans a similar approach.

Analysts at Deutsche Bank said the "huge demand" was such that "even with relatively low pricing, substantial sales are possible."

Sanofi aims to file for regulatory approval early in 2015 and launch by the end of the year.

Some scientists have expressed disappointment that the vaccine's success rate was not higher.

However, Christopher Viehbacher, Sanofi chief executive, insists a product capable of cutting the number of cases by more than half is a big step forward.

He says: "When I talk to health ministers they're pretty excited about this."

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Funds required in effort to find out what is wrong

Diagnostics

Cheap and simple tools of analysis that can be used in the field are as essential as drugs in the fight to control disease, says *Sarah Murray*

For those with sleeping sickness – a tropical disease transmitted by the bite of tsetse flies that is fatal if untreated – diagnosis has often meant undergoing a spinal puncture in a makeshift clinic under a tree. Although cheap and rapid testing is changing this, experts say diagnostics remains the poor relation in the fight against neglected diseases, .

"It's considered an add-on to treatment and other programmatic needs rather than a priority," says Anurag Mairal, technology solutions leader at PATH, a Seattle-based global health organisation. "Vaccines and drugs typically take those priorities."

Now, non-profits are working with companies to launch new products. For example, a rapid test to screen for sleeping sickness (also known as human African trypanosomiasis, or HAT) was introduced in 2012 by the Foundation for Innovative New Diagnostics (FIND) and South Korea's Standard Diagnostics.

In 15 minutes, using fresh blood from a finger prick, the test (known as SD Bioline HAT) detects antibodies against the parasite responsible for more than 90 per cent of cases. Health workers with minimal training can perform the test.

While drugs and vaccines are fundamental to combating neglected diseases, cheap, easy-to-use diagnostic tools are critical. This is particularly true for tropical diseases, which are prevalent in some of the world's poorest communities and places where few people have access to sophisticated medical services.

Yet for many, fast and accurate diagnosis can mean the difference between recovery and death. "Diagnostics are the starting point for treating people," says Mark Kessel, chairman of FIND.

Such tools play a role in the entire treatment chain – from identifying an illness to discharging patients once cured. In many cases, verifying that someone is no longer infected can be hard. Nathalie Strub-Wourgaft, medical director at Drugs for Neglected Diseases Initiative (DNDi) cites visceral leishmaniasis, which is caused by a parasite that enters through the bite of a sandfly.

The symptoms – which include fever, weight loss and enlarged spleen – are hard to distinguish from those of other conditions. The only way to verify that patients are free from disease is to re-test them six to 12 months after treatment, which may mean they have to travel miles to a clinic, often on foot.

Dr Strub-Wourgaft believes that access to cheap and simple diagnostic tools is critical. "It's a package," she says. "You can have a very good treatment but if you can't diagnose the patient and administer it in a field-adapted way, you're not going to meet your objective."

Dr Mairal agrees: "There's an increasing recognition that without diagnostics, you're in the dark as to whether your programme is having an impact." Yet despite strong arguments for developing these tools, more investment is needed. "Diagnostics always gets the short end of the stick," says Mr Kessel.

Part of the difficulty in scaling up the use of diagnostics is technical: since they will be used in places with few medical resources, they need to be simple to use. Local conditions throw up hurdles, too. The extreme temperatures and humidity in the places where these diseases occur mean diagnostic tools must be very robust. For PATH, this means testing the tools in humidity- and temperature-controlled chambers.

> 'There is a recognition that without diagnostics you're in the dark as to whether you are having an impact'

In addition to technical hurdles, structural barriers prevent widespread investment in diagnostics. The return on investment is often poorly understood. Without diagnostics, health ministries may implement blanket treatment, paying for drugs for large numbers who are not in fact ill.

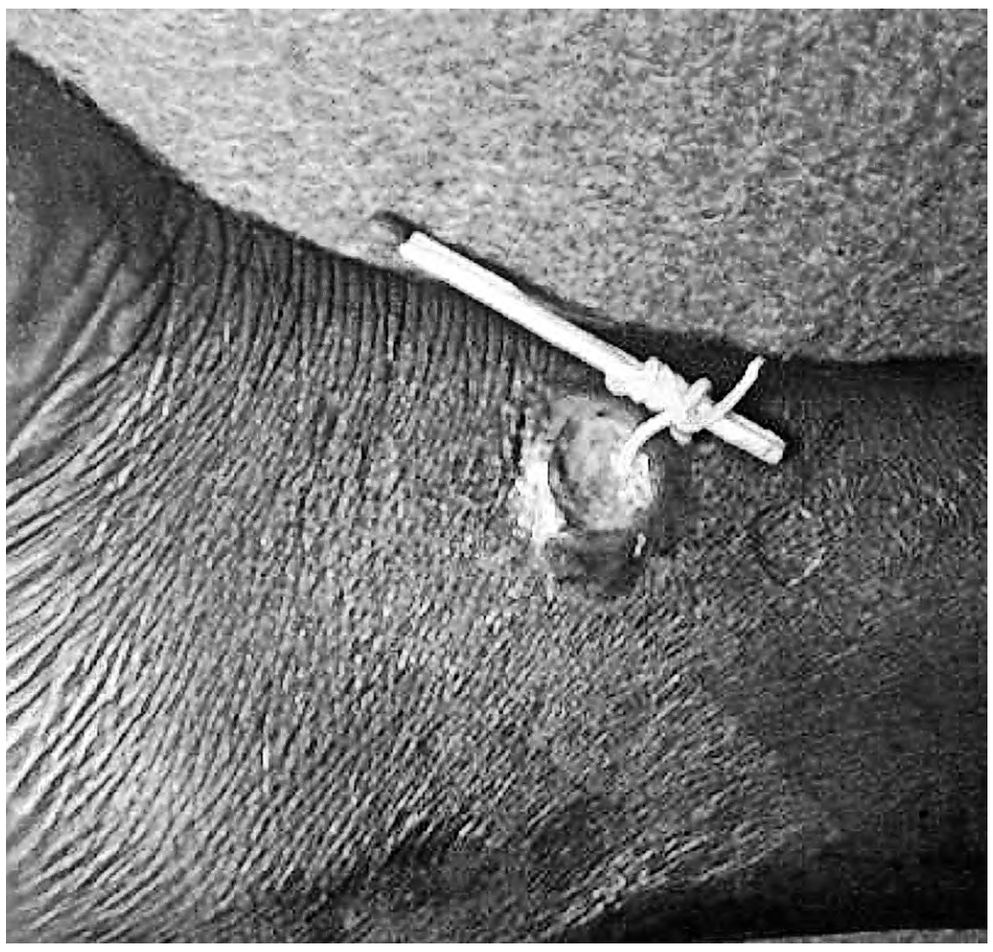
"It's a lot easier for politicians to understand what a vaccine is and the need for drugs," says Mr Kessel. "They don't appreciate the value of diagnostics to the health system – and the economic payback on a diagnostic is enormous."

Yet, given the need to produce tools that can be afforded by the poorest communities, it is tough to find a business model that can attract private sector investment. What also makes it hard for companies is that regulatory guidelines are often less clear than they are for a new drug. "In many places clear regulations don't exist, so it's not obvious to manufacturers how to get a diagnostic into the communities," says Dr Mairal.

For this reason, many argue that to increase availability of diagnostics for neglected diseases, greater collaboration between governments, non-profits and companies is needed.

From presidential office to parasitic disease control: the Carter Center

Guinea worm After three decades' work, a plague may be close to eradication, reports *Andrew Ward*



Excruciating: the only treatment for Guinea worm infestation is to wind the worms out of the body on a stick, which can take weeks

Becoming US president from a humble farming background in rural Georgia is hard to surpass. However, the biggest achievement of Jimmy Carter, who turned 90 this month, could yet be to come.

Since 1986 – five years after he left the White House – he has been pursuing a goal arguably more ambitious than anything he did in office: the eradication of Guinea worm disease.

Nearly three decades later, success is tantalisingly near. In 1986, the disease afflicted an estimated 3.5m people a year in 21 countries in Africa and Asia. So far this year, fewer than 100 cases have been reported in four countries.

"We are so close," Mr Carter said this year. "I look forward to personally announcing that we have stopped transmission of Guinea worm disease worldwide."

Should that happen – and Mr Carter believes it will "within the next year or two" – Guinea worm disease will become only the second human disease, after smallpox, to be wiped from the face of the earth.

This would further embellish the reputation of the peanut-farmer-turned-president from Plains, Georgia, as "the best ex-president in US history". By setting up the Carter Center in Atlanta to promote global peace and health, he established a model now common among former statesmen looking for a globe-trotting political afterlife.

But whereas other former politicians such as Bill Clinton and Tony Blair have been criticised for mixing philanthropic and commercial interests, Mr Carter has taken an unshowy approach to brokering peace talks and tackling obscure diseases.

"When organising the Carter Center, I have to admit my first projected goal was to bring peace to people," he says.

"But then we began to see that the main goal . . . would be to fill vacuums in the world; that is to do things that the UN or the US government or Harvard University were not doing."

Guinea worm disease was an ideal candidate. Some academics suggest that the Bible's mention of a "plague of fiery serpents" refers to this unpleasant parasite. The infection is contracted when people drink water from ponds infested with worm's larvae.

Once inside the host, the larvae mate and mature. The female worms – which can grow up to three feet long – emerge about a year later through painful sores in the skin. The best way to soothe the pain is by submerging the affected area in water. But this triggers the worm to release her eggs, and the cycle repeats.

Although not usually fatal, the disease incapacitates people for extended periods, making them unable to care for themselves, work or attend school.

The only known treatment has been used for thousands of years: extraction of the worm by winding it around a small stick – a slow, painful process that can take weeks.

So how has this ancient scourge been brought to the brink of extinction without a medical breakthrough?

The answer could hold lessons for tackling other neglected tropical diseases. Rather than hunting for a medicine or vaccine, the Carter Center focused on community-based intervention to educate and change behaviour. This included teaching people to filter drinking water and keeping anyone with an emerging worm away from sources of drinking water.

Working with partners including the World Health Organisation and national health ministries, the Carter Center has trained thousands of local volunteers to provide grassroots support and surveillance.

Financial rewards are offered to anyone reporting a confirmed case – ensuring that most are caught quickly and prevented from spreading.

Efforts are now concentrated on the four remaining countries where the disease is present: Mali, Chad, South Sudan and Ethiopia. It would be the first parasitic disease to be eradicated, and the first disease of any kind to be eradicated without use of a vaccine or medicine.

However, nobody is taking success for granted, when just one case can lead to dozens more if the larvae are spread.

Few people understand what is at stake better than Abdullahi Rabiu, a Nigerian farmer who holds the dubious record for having the most Guinea worms emerge from his body at one time: 84. "I couldn't move because the worms were coming from so many different places," he recalls of the experience 15 years ago.

Mr Abdullahi, now 40, recovered and went on to marry and have 14 children. Others were not so lucky. "It was hard to believe that one day this disease would be gone from our communities for ever," he says. "But today, people in Nigeria are no longer crippled or disabled because of this disease. They are back to their normal business and are carrying on with their lives."

For that, Mr Abdullahi and millions of others across Africa have President Carter to thank.

GUEST COLUMN

Roy Anderson

US and Europe must lead way in tackling Ebola

Far from abating, the Ebola epidemic in west Africa goes from bad to worse, as the global response to it has been too little and too late. Exponential growth continues, each case generating on average two further cases in ever-expanding chains of transmission in Liberia, Sierra Leone and Guinea.

Case numbers are doubling every 15 to 20 days, with a fatality rate of about 70 per cent. Only a radical and immediate improvement in the key control measures – isolation of infected patients and quarantine of contacts – will halt the spread.

Substantial help is needed immediately from the US and Europe, in the form of field isolation and treatment hospitals, supported by trained military units working in collaboration with NGOs such as Médecins Sans Frontières.

Hopes of an immunotherapeutic treatment for the many patients in need and a vaccine in the near term are not realistic. Even if trials go well and approval for use is rapid, it could be a least a year before manufacturing facilities can meet demand. In the mean time, it seems likely that the virus will spread to other regions of Africa and perhaps beyond.

The epidemic emphasises a series of factors that have inhibited effective control of a wide variety of neglected tropical diseases (NTDs) in resource-poor countries, despite growing donations of money and drugs.

NTDs include dengue virus transmitted by mosquitoes (perhaps the world's fastest growing infection), bacterial infections that cause blindness (trachoma), and parasitic worms (either transmitted by contact with infective soil or water, or insect vectors). The global burden of people suffering worm infections is in the many millions and an estimated 100m cases of dengue arise each year.

For worms and bacteria, effective drugs are available, and much is known on how best to deliver community-wide treatment and control. In poor countries, especially sub-Saharan Africa and parts of southeast Asia, control is prevented by the absence of an effective healthcare system and infrastructure to ensure continued treatment.

In west Africa, the lack of proper health infrastructure lies behind Ebola's growth and greatly limits our impact on NTDs. Aid from western governments and numerous NGOs is often disease-specific, treatment-orientated and ill co-ordinated.

Local governments must insist on much closer co-ordination of the many health-orientated NGOs to integrate education, healthcare, and supply. It is not uncommon to find a number of NGOs administering drugs to treat soil transmitted infections in the same villages in sub-Saharan Africa, without knowledge of each other's activities. Western government agencies, such as Dfid and USAID, could do much more to help such co-ordination.

> A greatly enhanced international response is vital to bring Ebola under control

Aid agencies must focus much more on strengthening health systems and delivery platforms, such as schools, primary healthcare settings and hospitals. This facilitates early disease detection and a rapid, appropriate response in the case of an outbreak.

Safe water, good hygiene and sanitation go a long way to control the spread of many infections, including the Ebola virus, which is transmitted via secretions and excretions from infectious patients.

The power of education and communication in the control of NTDs is often not fully appreciated. Effective interventions rely not only on treatment and care facilities, but also on an integrated strategy of information dissemination, education and continual communication.

This is well illustrated by the Ebola epidemic where mistrust of local governance and absence of effective communication have resulted in key messages not getting through to the majority at risk.

A greatly enhanced international response in the next few weeks is vital to bring the Ebola epidemic under control.

Let us hope that placing an emphasis on greatly strengthening healthcare infrastructure also serves to lay an enduring foundation for the better control of the NTDs that cause so much morbidity and mortality in the poorest regions of the world.

Sir Roy Anderson is director of the London Centre for Neglected Tropical Disease Research, Imperial College London, and a non-executive director of GlaxoSmithKline

The Liverpool command post in the global fight against suffering

Research

This centre of expertise is developing techniques that range from genome mapping to computer games, reports *Andrew Bounds*

The war on neglected tropical diseases (NTDs) is being fought by "boots on the ground" in the jungles of Africa and Asia. But a key command centre of this war lies thousands of miles from those front lines, in northwest England.

The Liverpool School of Tropical Medicine (LSTM) is one of the biggest recipients of funds from the Gates Foundation and other charities to tackle the scourges that ravage poor countries.

The weapons it is developing range from insecticides to computer games, from bed nets to thermal imaging cameras. LSTM has just hired Lorenzo Savioli as a senior fellow; Mr Savioli recently retired from the post of director of the department of control of neglected tropical diseases at the World Health Organisation. Mr Savioli will work alongside Professor David Molyneux in the parasitology department to expand its work in NTDs and attract new funding.

The school was founded in 1898 by shipowners worried by their crews' exposure to diseases when trading around the British empire. Ronald Ross, the British army doctor who won a Nobel Prize for demonstrating that malaria was spread by mosquitoes, was one of its first lecturers.

The school leads 12 international consortiums and product development partnerships aimed at reducing or eliminating the impact of diseases upon the world's poorest people. Its Centre for NTDs leads the Anti-Wolbachia Consortium, which works with AstraZeneca to develop antibiotics to cure conditions caused by parasitic worms: river blindness and elephantiasis.

"I don't know that there is anywhere else in the world that has quite that breadth of activity going on," says Janet Hemingway, director of the school. Her expertise is in vector control – the insects are the vectors that carry infections such as malaria, dengue fever and river blindness.

The school has a number of UK and international PhD students, but its main role is research, not just on drugs but how to use genetics, IT and social policy to fight diseases. It advises many governments, works with industry to develop insecticides and other drugs, and also undertakes field trials for vaccines through its field stations. The school now employs about 650 people and has a £58m budget.

Its scientists are mapping the extent of elephantiasis in Ethiopia and DR Congo in preparation for a UK government-funded control programme. They are also assessing the attitude of local populations to mass drug administration to prevent the disease – drugs that can cost as little as 50 cents a day.

The school has also found that vector control can be as important as preventive drug use in controlling the spread of infection in many diseases. However, this struggle is getting considerably harder, because of insecticide-resistant mosquitoes.

"In the short term, we need to do something to stem the tide of resistance," says Ms Hemingway. "In the medium term, we need to speed the rate at which we can obtain new insecticides. We do not have 15 years to wait."

Martin Donnelly, professor of evolutionary genetics at Liverpool, believes that genes hold the key. He is studying the most insecticide-resistant mosquitoes to see what genetic pattern they have in common, work funded by the Wellcome Trust foundation. He dubs it the "mosquito genome project" to match the human genome project, which was concluded in 2003.

"If we find what causes the resistance, we can find ways to tackle it," says Mr Donnelly. "We know there is resistance in those populations. How has it evolved? I believe genetics holds the key."

Another area of work is improving bed nets, the standard tool to protect people from mosquitoes. Phillip McCall at LSTM aims to track mosquito behaviour. "Where exactly do they enter rooms? Why do they bite certain people and what are their flying patterns? We actually know very little about what mosquitoes do."

Janet Hemingway, director of LSTM

Mr McCall has a three-year grant to work on developing a camera-tracking system provided by AvecNet, an EU-financed vector control consortium working in Africa. LSTM has even developed an online computer game to help field workers 'role-play' disease outbreaks. The WHO's standard handbook on dealing with malaria, for example, had been read by only half those fighting the disease; 92 per cent found it hard to understand.

While Ms Hemingway believes more developing countries will build their own research institutes, there will always be a role for the school. "The demand for what we are doing is only increasing. As long as we do the right thing in the right way, we will be here in 100 years," she says.

Snake bite anti-venom remains crude and expensive

Research Fear and stigma is hampering progress on treatment for a killer condition. By *Andrew Jack*

On a farm at an undisclosed location in Utah, a British company milks venom from 500 carefully nurtured snakes every month. It ships the venom to Australia to inject into thousands of cosseted sheep, then processes in Wales the immunoglobulin that the sheep produce, before sending it on to the US for distribution to doctors.

"Those sheep are the biggest and happiest you'll ever meet," jokes Andy Burrows, vice-president of corporate and investor relations at BTG, the company which produces CroFab anti-venom to treat more than 5,000 potentially lethal pit-viper bites every year in North America. "Lambs are usually slaughtered before they are 18 months old. Ours are euthanised after nine or 10 years, when they have tooth decay so they can no longer eat."

On paper, the business sounds lucrative. CroFab sells for $2,000 a vial – and a course of treatment can require more than 24 vials. Yet BTG, which generates $100m a year from the product, is investing little in diversifying into treatments for other poisonous snake bites or expanding its existing treatment to other countries.

This complicated chain reflects the difficulties of producing affordable, effective and innovative treatments around the world for snake bites, one of the more neglected medical conditions of the poor, and estimated to cause 100,000 deaths globally each year. Amputation and psychological trauma is a consequence for many more.

"For every death, there are possibly four times more left handicapped," says David Warrell, emeritus professor of tropical medicine at Oxford, who is hosting an international conference next year to draw wider attention to the problem. "There is not just mortality and morbidity but psycho-morbidity. The experience of being bitten as a child often leaves a lasting impression."

He describes being "laughed out of court" by experts for years when he raised concerns over snake bites – by donors, academics and clinicians in the west and even in countries such as India, where snake bites are common. "People find it very difficult to take seriously."

He suggests the reasons include "a primal, biblical, morbid fear of snakes" and stigma, as most snake bites occur in poor, rural areas. Only a handful of authorities, including Myanmar, have given the problem significant political attention.

Dr Robert Harrison, head of the Alistair Reid venom research unit at the Liverpool School of Tropical Medicine, says that most funders have failed to show interest – from the Gates Foundation to the European Commission, which recently inadvertently excluded snake bites by unveiling programmes earmarked specifically for "infectious" diseases.

"Snake bites have no epidemic potential," he says. "They have been treated in the [World Health Organisation] statistics alongside road traffic accidents as injuries – something you can do very little about. It's very difficult to change that perception."

Hooded menace: a cobra about to strike — Dreamstime

Snake bite incidence and mortality rate

Tropical disease	Incidence ('000)	Deaths ('000)
Chagas disease	217	14
Cholera	178	4
Dengue Haemorrhagic fever	73	19
Leishmaniasis	1,691	51
Japanese encephalitis	44	14
Schistosomiasis	5,733	15
Snake bite envenoming	420-2,682	20-125
Yellow fever	0.1-2.1	0.06-0.1

Source: www.thelancet.com

Both researchers are cautiously optimistic, as they point to recent developments in prevention, diagnosis and treatment that could help reduce the burden. The launch of the Global Snakebite Initiative, an NGO, in 2008 and the decision of the WHO to add the condition to its list of "neglected tropical diseases" in 2009 have provided boosts.

Simple, cost effective prevention has considerable potential: from clever repellents and bed-nets to redesigning houses to deter snakes. Basic education and support, to encourage lightweight boots for farmers, and gloves for those collecting fruit, could substantially help reduce the burden. So could cheap torches to help ensure safe passage when walking at night.

Snake venoms are highly complex and vary widely around the world, even among related species. Many products manufactured in one region are unsuitable elsewhere.

Anti-venoms – most still developed from immunoglobulin in horses and sheep – remain crude and expensive.

Dr Harrison expresses hope that research funding to his unit will help develop a fresh generation of treatments effective for a wide variety of snakes, in lower doses and with fewer side effects.

'Snake bite statistics are gathered alongside road accidents – it's difficult to change perceptions'

Hookworm Shoes, sanitation and culture are key in Kenya

Kapalo Wenslaus grew up in western Kenya where perfect conditions exist for hookworm to flourish. The weather is hot and humid; the region has loamy and sandy soil and poverty is widespread. The 35-year old gardener believes he had hookworm intermittently for eight years. He has no idea how he became infected, and why the hookworm suddenly disappeared.

"The lack of energy and feeling so often miserable caused me to miss school very frequently. My parents were poor, and when my school results were bad they refused to pay for my secondary education. I was told to look for a job when I was 16."

He feels his sickly youth prevented him from receiving a good education and from creating a better life for himself. "I stayed in the same poverty level as my parents," says Mr Wenslaus.

Hookworm, or helminthiasis, belongs to a group of soil transmitted helminths which have, says the World Health Organisation, infected almost a quarter of the world's population, mainly in tropical regions. They are just a quarter of an inch long. Hundreds of them can live in the body, sucking the blood and laying thousands of eggs.

The prevalence rate in Kenya is estimated at 20 per cent and those mostly affected are children aged between eight and 14.

Hookworm is widespread in the west, east and coastal regions, and Kenyans consider it a poor person's condition.

"The larvae penetrate humans through the skin and get into the blood vessel to find their way to the smaller intestines," says Dr Jimmy Kihara, a medical parasitologist at the Ministry of Health. "The most common point of entry is the feet because people don't wear shoes. Another problem is lack of toilets and people defecating in the open."

Once a person is infected with hookworm, the eggs leave the body with the faeces, which are often disposed of behind bushes, because toilets are not available.

Children in poor communities often do not have shoes until they are almost adults. They play and run around barefoot, without paying attention to whether areas have been used for faeces disposal.

"The cognitive abilities of children are affected, and the school performances in regions with hookworm are frequently low," says Dr Kihara, who had hookworm as a child.

Treatment is simple, requiring one cheap pill. In 2009 the Kenyan government started a deworming project in schools in regions with high incidents of hookworm.

"The medicine is very effective and kills the worms instantly," says Dr Kihara. "But as long as the children walk around barefoot and there are no proper toilets, they get reinfected."

The government wants hookworm to be eradicated by 2020. There are, however, social obstacles to overcome.

Teachers explain to pupils how to prevent hookworm and children go home and tell their parents. But "in rural and traditional societies, the culture does not allow children to teach adults anything", says Dr Kihara. "We should get the elders to explain that shoes and toilets are a must."

Ilona Eveleens

Environmental and educational efforts lead assault on trachoma

Case study

The disease was once endemic in Ethiopia, even seen as a way of life. Now a multi-agency approach offers hope, says *Rose Jacobs*

Some diseases are devastating because of their symptoms, some because of their outcome. Blinding trachoma is both: transferred to humans from flies that feed on human faeces, the microorganism inflames an infected person's upper eyelid, causing it to turn inward. In doing so, the lid brings the lashes into contact with the cornea, scratching it and leading to blindness. It is a painful process, disfiguring and disruptive to individuals and communities.

And yet as recently as 15 years ago, most people in the Amhara region of Ethiopia, a zone stretching from the country's centre to the Sudanese border in the west, "viewed trachoma as a way of life", says Dr Tebebe Berhan, a medical doctor and businessman. Some saw it as a curse rather than an infectious disease, and few connected it with their community's tradition of open defecation, their lack of access to clean water, or their high population density.

The prevalence of trachoma there was the highest in the world. The World Health Organisation says that for blinding trachoma to be eliminated from a population, fewer than 5 per cent of children under age 10 should be infected with a case of active trachoma; in the Amhara region in 2000, 53 per cent of children had it. The number of adults with the most advanced stage of the disease before vision loss was 200 times what WHO called acceptable.

At the time, the Carter Center, among other agencies, was in the region combating Guinea worm (*as described on page 3*). Jimmy Carter wanted to expand its efforts to trachoma; moreover, he had a personal connection as he remembered his mother treating people suffering from the condition in his native Georgia. The push in the Amhara region came when the Lions Club agreed to fund the drive, and both the national and regional governments gave full support to the project.

The emphasis at the start, says Kelly Callahan, director of the Carter Center's trachoma control programme, was on

Let there be light: a woman receives treatment in Vietnam

improving the environment and on education; teaching villagers to wash their hands and faces, since the flies are attracted to mucous round the nose and eyes which can travel from person to person when a mother, for example, touches a child's face. Schoolteachers played an important role here, encouraging best practice among students who took that home to show their families.

As for the environment, the priority was building pit latrines in order to minimise the fly population. Local materials were used to reinforce the pits, fashion covers and build vestibules around them. Families were encouraged take ownership of their own latrines – an important point, given the refurbishment the structure would require after each rainy season.

You have to explain to people how you are going to solve their multiple problems – not just focus on trachoma

Other advantages of the latrines helped win over the Ethiopians, points out Dr Berhan, a Lions member who has played a key role in the trachoma elimination drive. Women, for example, used to wait until after dark to defecate out of modesty and had long been exposed to dangers such as rape. Now, they had an option for daylight hours. "You have to explain to people how you are going to solve their problems, their multiple problems – not just focus on trachoma," he says.

Between 2000 and 2006, 300,000 latrines were built and significant portions of the population educated about sanitation and hygiene. But prevalence among children under 10 remained stubbornly high, at 40.1 per cent. "We realised we needed to scale up our efforts," says Ms Callahan.

The team decided that two elements in the fight needed more attention: surgery and antibiotics. Pfizer had agreed to donate Zithromax, a highly effective antibiotic that proved popular with people not just because it knocked out trachoma, but other lingering illnesses as well. The Lions Club, the Ethiopian Ministry of Health and regional government then put huge efforts into creating an army of health workers who today administer doses to the entire population once a year, in two rounds.

The federal government, meanwhile, set out to train eyecare workers capable of performing surgery on trachoma victims – funded by the Lions. An estimated 300,000 procedures must be completed to achieve elimination, and surgeons are currently managing about 66,000 a year. That is a far cry from the situation in 2000, when about 50 ophthalmologists struggled to serve a population of 60m.

As for scaling up latrine building, whereas 300,000 were built in the first seven years of the programme, another 2.6m have been built since – helped by public health innovations developed by the Lions Club, such as competitions between neighbouring farming associations. The goal of 4.1m latrines no longer seems impossible.

Wider targets are more intimidating. The WHO aims for the elimination of trachoma worldwide by 2020. Ms Callahan admits this is a tall order, not least because funding remains an issue.

But she believes there are valuable lessons to be drawn from Amhara – from the importance of balancing the approach (not neglecting medical intervention in favour of behavioural change, or vice versa) to the importance of scaling up successful operations. Most of all, she emphasises the necessity of evaluation and measurement – done early and done often.

"What gets measured," she says, "gets done."

#HEALTHYEU CONFERENCE
15 OCTOBER 2014 - BRUSSELS

On 15 October 2014, EFPIA will host a public conference to discuss the best path towards a stronger, healthier and more prosperous EU. **#HealthyEU – Health Driving Growth in Europe** will bring together a diversity of representatives – from healthcare leaders to policymakers – to discuss the future of European health policy, at what is a critical juncture with the start of a new Parliament and Commission.

Health has the potential to serve as a key enabler of a productive economy in Europe. If we get it right, quality healthcare can help keep people in work longer, can reduce absenteeism and, since Europe is one of the world's leading regions in healthcare industries, directly generate economic value.

EFPIA believes in a new generation of multi-stakeholder partnerships and collaborative solutions to target the EU's health and competitiveness challenges. We invite you to join us on 15 October as we spark a discussion towards this end. Registration: **http://healthandgrowth.eu/**

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