*Disease, Poverty, Biologists and NGOs –*

# Ways of Changing the World Outside the Lab

AIDS/HIV, tuberculosis and malaria kill millions of people per year in sub-Saharan Africa. But also the so called 'neglected diseases' like, for example, leprosia or the African sleeping sickness take their toll. Biologists often just know the pathogens from the bench but they can also work on site.

As university-educated scientists working in Europe, most of us live fairly comfortably. But many of us are also more-or-less aware that the rest of the world isn't so well-off and occasionally wonder what we can do about it. Around 20% of the world population lives in extreme poverty, suffering from the disastrous effects of infectious disease and poor health. This is especially true for sub-Saharan (formerly 'Black') Africa, where up to 50% live on less than €1 a day and extensive health problems present major obstacles to development.

However, since our professional lives are frequently tied up in specialised institutions focussing on long-term goals, our contributions towards alleviating the effects of disease and poverty are usually restricted to financial donations. But what happens if you want to become more involved? Welcome, reports Jeremy Garwood, to the colourful world of non-governmental organisations, where, if you can't find a group for your voluntary time and expertise, you can always start your own!

Non-governmental organisations (NGOs) account for most of the organised efforts by ordinary citizens to bring about change in the world. However, the term NGO is a fairly loose one, which simply refers to legally constituted organisations that don't have government participation in their organisation. Their legal status, e.g. as a registered charity in the UK, allows them to receive tax-deductible donations and to avoid commercial taxes. At a national level, there are literally millions of NGOs but only around 40,000 operate internationally or 'transnationally'.

Some NGOs are politicised lobbying organisations; others have specific programmes and activities. Despite their non-governmental tag, NGOs can receive government funds, e.g. it accounts for almost half of the funding for Médecins Sans Frontières, winner of the 1999 Nobel Peace Prize. In many cases, this is because governments recognise that NGOs have a great public utility, identifying problems and providing solutions, often at a lower cost than governments. Most NGOs are fairly small and they frequently interact in networks to improve their chances of success on particular projects, reducing their overheads and presenting a larger public profile.

## The major infectious diseases

The Big Three diseases: AIDS, tuberculosis and malaria, have attracted a lot of media attention and funding during the last decade, and for a good reason – they kill a lot of people. In 2005, it was estimated that 6% of the adult population of sub-Saharan Africa (25 million people) was infected with HIV/AIDS, killing two million people a year. Tuberculosis (TB) kills somebody every 15 seconds. Malaria infects some 500 million people worldwide, killing up to three million a year, the majority of whom are young children in sub-Saharan Africa. Furthermore, cures, therapies and preventive treatments already exist – if only they could be better administered.

## Neglected tropical diseases

However, the WHO has also drawn attention to the so-called 'neglected tropical diseases', caused by a group of 14 pathogens that have a severe impact on public health but are relatively ignored in terms of intervention or research. In sub-Saharan Africa, the impact of these diseases as a group is comparable to malaria and tuberculosis. They include parasites like roundworm, which affects around a billion people worldwide, hookworm, with around 800 million sufferers, snail fever (schistosomiasis) about 200 million, elephantiasis, trachoma, Kala-azar black fever, leprosy and African sleeping sickness. Overall, they affect more than 1.4 billion of the world's poorest people.

British parasitologist, Mark Booth, started research during his BSc studies in Zoology at the Imperial College, London. He looked at the distribution over a local play-

ing area of dog muck samples containing *Toxocara canis* eggs. For his PhD, he moved from dog to human parasites, trying to understand patterns of co-infection with multiple species of parasite, initially in rural China, then in East Africa.

But the idea of conducting charity work in addition to his research took a long while to emerge. "I've always been aware of working for the public good but never considered that I was capable of organising something charitable until I promised to raise money for a borehole in one school in Kenya."

## From Cambridge to Kenya

For five years, he had been visiting East Africa as part of the Schistosomiasis Research Group at the University of Cambridge's Department of Pathology, studying parasitic infections including malaria and schistosomiasis. One day, he asked the headmaster of a local primary school if there was something useful he could do for the school. The headmaster asked for a source of clean water. So in 2005, Mark set up an NGO, the Matangini Project, named after this Kenyan village school.

In effect, lack of clean water is a big problem in Kenya. Around 24 million Kenyans live in rural areas and only half have access to safe drinking water, let alone clean water for washing. Many infectious and parasitic diseases are waterborn. For example, schistosomiasis is caused by parasitic flatworms of the *Schistosoma* genus – 80% of the 200 million people infected globally live in sub-Saharan Africa.

**Many diseases can easily be cured with apropriate medication. For Schistosomiasis treatment for example a single dose of praziquantel is sufficient.**

The natural host of the *Schistosoma* flatworm is a species of water snail and the parasite is most commonly contracted by wading or swimming in water infested with the infected snails. Parasite larvae emerge from snails daily and have specialised mechanisms for penetrating human skin.

Once inside the human body, the parasite is passively transferred from the blood to the lungs and then to the liver, where the worm feeds on red blood cells, maturing into its adult form. Adult worms live in the mesenteric veins connecting the gut to the liver. Here, they produce eggs that cause a strong immune response in the human host resulting in the disease pathology, with symptoms ranging from diarrhoea and fever to long-term liver and intestinal damage or severe cystitis that can progress to blad-

Volunteers often work with simple lab equipment.

der cancer. The worms live in the body for up to 20 years. Even though there is a low mortality rate, Schistosomiasis is seriously debilitating. A drug, praziquantel, can cure the disease with a single dose but it cannot prevent reinfection by the parasite, which means that people living with infected water are always at risk.

The original goal of Mark Booth's Matangini Project was simple – raising money to install a borehole in the grounds of a rural primary school. The cost was around €1,200 and, to avoid extra costs, overseeing the borehole's construction would be incorporated within his existing research visits to the field sites.

Fundraising ventures for his project included sponsored runs and selling 'photo gift' calendars. However, the most original involved donating profits from sales of his novel about an accident-prone parasitologist, "The Wonderful World of Joseph McCrumble", in which Dr McCrumble is expelled from his village having accidentally poisoning all the pet rabbits with an experimental anti-parasite drug.

## Water for schools-project

"The first borehole was completed in July 2006 and now provides a lifeline for the whole school. About 400 students and their teachers have clean, safe water to drink. They can also use the water to irrigate the school vegetable patch, which is a vital source of nutritious food for the children."

Mark wanted to provide more rural boreholes and chose to join forces with a larger British NGO, Stand Up For Africa, to form the Water for Schools Project. This long-term programme works in association with a local NGO, the Kenya Water for Health Organisation (KWAHO). "We install boreholes in the grounds of primary schools that are most affected by parasitic diseases. The local community provides manual labour to dig the boreholes and we train them to maintain the pump so that there will be safe, clean water for the school for many years to come. We also improve sanitation facilities and provide hygiene education to help the children avoid infection from water-borne parasitic diseases."

Sickle cell anaemia (drepanocytosis) was the first human genetic disease shown to be due to an amino acid abnormality. It is also the world's most prevalent genetic disease affecting over 50 million people, mostly in sub-Saharan Africa. In Central and West Africa, sickle cell anaemia (SCA) homozygotes account for up to three percent of births. It is also quite common in countries with large populations of African origin, representing the number one genetic disease in France (>10,000 cases) and the US (>70,000).

## Against sickle cell anaemia

Neurobiologist Corinne Mbebi-Liegeois came to France from Cameroun as a teenager. Her PhD research in Paris on inflammatory disease was followed by a decade of research on neurodegenerative diseases in Paris and Strasbourg. Since 2008, she has been developing a diagnostic test for Alzheimer's disease at a start-up company within the CNRS' Centre de Neurochimie, Strasbourg. In 2004, Corinne was brutally reminded of the effects of SCA when her sister died from its effects.

Corinne's sister had been living in a small rural town in Eastern France where the local hospital staff lacked knowledge of this "exotic disease" and didn't know how to treat it. "Responding to the symptoms, they even sent her to oncology, thinking she had cancer". Shocked to discover that the French medics weren't properly trained, Corinne was furious they hadn't even bothered to contact the national SCA centre in Paris to learn more. In response, she set up her own NGO, Drepavie (Drepanocytosis for Life), to provide more information about the disease to the concerned populations, health professionals, and the general public.

SCA results from a single amino acid change in the beta-globin subunit of the oxygen-carrying haemoglobin protein. Unlike wild-type haemoglobin-A, this haemoglobin-S tends to aggregate when deoxygenated, only slowly dissociating upon reoxygenation. Red blood cells, packed full of haemoglobin, are drastically affected by polymerisation of haemoglobin-S – they lose their elasticity, an essential property for circulation through the finest blood capillaries.

AS heterozygotes do not suffer, indeed a mixture of haemoglobin-S and normal haemoglobin actually confers resistance to malaria. However, SCA is inevitable in homozygotes with two copies of the recessive allele (SS). They have defective red blood cells that can collapse from the normal doughnut into a sickle shape at low oxygen levels. When this happens, the cells can block blood flow through narrow capillaries causing tissue damage, notably to the lungs, spleen, kidney and liver, and severe, debilitating pain. Damage to the spleen also makes sufferers, especially young children, highly vulnerable to infections. Anaemia results when the bone marrow fails to generate enough new cells to match the higher rate of destruction in SCA – sickled red blood cells are destroyed after 10-20 days compared to the normal 90-120 days.

Corinne knows that she is a heterozygote carrier for the haemoglobin-S form, yet millions of people around the world are not aware that they are carriers nor that, should they have children with another AS heterozygote, they run a one in four risk of having a 'SS' baby with sickle cell anaemia and all of its complications. Drepavie organises information days for the concerned

British parasitologist, Mark Booth, runs a project in Kenya to install boreholes for fresh water to prevent water-born diseases. Cameroonian/French neurobiologist Corinne Mbebi-Liegeois informs people about sickle cell anaemia and gives seminars to local health professionals.

populations, encouraging them to have a simple diagnostic blood test to determine their status and, if necessary, to seek genetic counselling.

But the larger problem is in Africa itself. People need to be informed in these countries. "When my own sister was ill, I cared for her, rather than learning more about the problems associated with chronic anaemia and how to prevent them."

Most of Corinne's holidays are spent in Africa on Drepavie missions in the company of volunteers from other NGOs. Typically, they inform local populations through lectures and press interviews, organise seminars so that local health professionals can better understand the disease and the blood detection test. Parents of SCA children are advised to come to hospitals for preventive treatment before their children are already "virtually dead" – the average life expectancy for an SCA sufferer in Africa is just five years. It is nearer 50 in France and the US.

## Travelling around Africa

For the 2008 mission to Madagascar, she was accompanied by biologist Danielle Lena-Russo, whose own NGO, the Mediterranean Haemoglobin Association, sets up neonatal screening programmes in Africa. The mission also succeeded in getting Madagascar's health authorities to finally recognise SCA as a public health problem. In 2009, she went to rural zones in Cameroun accompanied by Jacques Cheminet, a pharmacologist from another NGO, Douleur Sans Frontières (Pain without borders), that seeks to minimise pain. In 2010, Corinne will go to Mali and Burkina Faso.

"Drepavie missions also interact with education ministries to promote education in schools." The essential information is presented in a brochure, "Bobby and his 12 guidelines for drepanocytosis". Bobby advises on hygiene (clean teeth, washing the hands and body); getting medical treatment in case of high fever or yellowing of the eyes or red-brown urine or sudden fatigue or severe pain; drinking lots of water – three litres a day; avoiding heat, high altitudes, poorly ventilated areas, eating well, sleeping well and avoiding physical effort.

Although their means are modest, Drepavie also provides some medical supplies, buying drugs in Europe and taking them directly to the medical doctors that coordinate their use with the patients' families and rural pharmacies.

"The medicine is not free, but is sold for a symbolic 'one franc' to ensure that it is valued. It includes antibiotics against frequent infections and painkillers to relieve the agonies associated with blocked arteries." They also provide the vaccine, 'Pneumo 23' from Pasteur Merrieux, against pneumococcal infections, particularly pneumonia. Drepavie receives funds from both private donations and French local government.

From volunteer to professional: Spanish immunologist Carola Vinuesa first did voluntary work on leprosy and TB patinents in India and Africa, in 2008 she became Australia's 'Life Scientist of the Year'.

In regular contact with the SCA biomedical research community, Corinne says progress is being made – June 19th, 2009 saw the first UN-recognised Sickle Cell Disease World Day.

## From volunteer to professional

For Spanish immunologist Carola Vinuesa, voluntary work in Africa changed her professional outlook. Named Australia's 'Life Scientist of the Year' in 2008, she revealed that her research motivation dated back to volunteer work she had performed in India and Africa. In 1990, as a medical student in Madrid, she had taken time out to join the Calcutta Rescue NGO in India, providing medical assistance to leprosy and TB patients. Then, in 1991, she joined the Village Concept Project in Ghana, as a volunteer with the International Federation of Medical Students' Associations. This experience showed her directly how infectious diseases operate at epidemic scales but Carola realised there was limited understanding of the diseases she was treating. She felt she could save more lives by researching the diseases rather than treating them.

She returned to Europe and completed her medical studies in England, before making the fateful switch to science. In 1997, she began research in Immunology at the University of Birmingham, obtaining her PhD in 2000. Carola proceeded to do post-doctoral research in Australia where, in Professor Chris Goodnow's group at the Australian National University, she began work on the mechanisms underlying autoimmune diseases. Goodnow's laboratory had generated mouse "libraries" by introducing multiple random gene variants throughout the genome in order to discover novel immunoregulatory genes. Carola screened these libraries for autoimmune diseases, adapting a test normally used in the clinic for the identification of autoantibodies in patients with lupus, an autoimmune disease that causes women of childbearing age to suffer swollen lymph nodes, sore joints, rashes and kidney trouble.

## A passionate researcher

By examining the genetic makeup of these mice with lupus, she traced the cause to a single point mutation in a single, previously unknown, gene. Carola named the gene 'roquin' after St Roch (Roque in Spanish), the patron saint of plague victims, epidemics and skin diseases. Roquin regulates the quality control of antibodies. It stops the production of poor quality or rogue antibodies that would attack 'self', preventing T-cells from displaying a stimulatory receptor, ICOS, that may cause the cells to attack normal body tissues. Her subsequent research has shown that roquin's activities are orchestrated by micro RNAs. Previously considered to be 'genetic junk', micro RNAs can induce decay of mRNAs, regulating expression of proteins like ICOS. Up to 30% of the genome might be regulated by microRNAs.

Carola thinks micro RNAs are the fundamental regulators of autoimmunity, opening up novel strategies for the development of therapies using small RNA molecules. "If we manage to detect what makes the immune system supply the signals to produce these amazing, good quality antibodies, the work would have similarly important implications for vaccine development, for protection against infectious diseases. At the moment there are no effective vaccines for HIV and malaria, for example."

What is the best strategy to adopt when dealing with the enormous scale of poverty and disease in sub-Saharan Africa? This ongoing debate usually divides into two camps: humanitarian NGOs who want to save as many people as possible as quickly as possible, often relying on the presence of foreign staff and volunteers who administer the donation of food and medical supplies. On the other hand, there are development-

oriented NGOs who support the long-term development of infrastructures that will enable African countries to manage their own health and food problems.

Médecins Sans Frontières (MSF, doctors without borders) tends to exemplify the former situation. This NGO was founded in 1971 by a group of French medical doctors to respond to humanitarian disasters in war-torn regions and developing countries facing endemic disease. It sends volunteers, both medical and non-medical, to operate the medical and nutrition components of short-term field missions. Sometimes they take charge of groups of local medical staff. In 2005, of the estimated 5,000 international health volunteers in sub-Saharan Africa, over 2,000 were sent by MSF.

## Not always the best choice

However, as Geert Laleman from Antwerp's Institute of Tropical Medicine has found, "Country experts express more negative views about international health volunteers than positive ones" (*Human Resources for Health* 2007; 5:19). Often, volunteers aren't prepared to work in poverty-stricken countries, don't value local knowledge and generate tensions by creating parallel systems and procedures. Also, at an annual cost of €29,000-€40,000, they aren't very cost effective, especially when there are local unemployed health workers. Nevertheless, their role in emergencies and crisis situations can be vital.

Biologie Sans Frontières (BSF, biology without borders) is a French development-oriented NGO. Headed by microbiologist Yves Gille and pharmacologist Christian Collombel from Lyon's University Hospital, BSF was founded in 1991 to create and equip laboratories in developing countries. They had spent their French military service on civil missions in developing countries and were dismayed when laboratory restructuring in Lyon resulted in the senseless loss of operational biological equipment that could have been used elsewhere.

"We form people on the terrain, put in place, from scratch, small laboratories or make improvements to existing labs, we perform audits, either for our accounts (to know what aid we need to provide) or for those of our partners," says Yves Gille. BSF intends to provide help in developing long-term, reliable medical biology services, notably in rural zones of sub-Saharan Africa.

"Medical biology is an integral part of any health strategy since it permits the medical doctor to confirm his diagnoses, to use simple and inexpensive tests in order to detect the start of disease epidemics and to help in the correct prescription of drug treatments for AIDS, TB, malaria, etc."

In the spirit of the 1987 Bamako Initiative (when African health ministers agreed to implement strategies to increase availability of essential drugs and other healthcare services), it aims to create long-term development rather than short-term interventions in response to crisis situations, to work in cooperation with the local health authorities and only to intervene if a real need exists.

BSF organises short missions of two to three weeks (>100 since 1992), preferably of two volunteers, e.g. a senior professional, possibly in retirement, and a junior, from the hospital laboratory or pharmaceutical staff. These missions can either help an existing laboratory that is struggling or can create a mini-laboratory from scratch.

To achieve their aims, they recuperate used, but still serviceable equipment from French laboratories, including microscopes, centrifuges, visible and UV spectrometers, etc. and dispatch this to their mission sites. From their donations they pay for the transport, insurance and anti-malarial treatment of their volunteers. In general, the food and accommodation of their volunteers ("sometimes very spartiate") is covered by the local organisations they're helping.

Yves Gille spoke of BSF's experiences at the Institut Pasteur in Paris, "It's essential to always act with the accord of the local authorities, who are often very jealous of their own status. We only intervene directly in response to motivated and justified requests. We refuse to provide consumable materials, except for samples. Often, the real needs are more for training than equipment but this training isn't so much technical (the technicians often have a good technical knowledge) as it essentially concerns organisation, rigour and quality control in the laboratory. Unfortunately, it isn't so easy to provide this kind of training since those concerned are rarely conscious of their failings and the required habits of organisation and control are often alien to the culture of the countries where we intervene." Furthermore, "Training periods, that last only a few days, are quickly forgotten if there are no follow-up visits."

**The NGO "Médecins Sans Frontières" send medical and non-medical volunteers for short missions. They also work together with local staff.**

ReMeD (Réseau Médicaments et Développement; Medicinal Network and Development) is an NGO concerned with the quality, availability and accessibility of pharmaceutical drugs in developing countries. Created in 1993, it represents a network of 2,000 health professionals worldwide, working in 22 countries of sub-Saharan Africa. ReMeD coordinates the exchange of information on medicines between health professionals in developed and developing countries, organises information campaigns on the issues of reliable

pharmaceutically active drugs and helps train health professionals in developing countries. Their website provides an extensive documentation on the provision, management and storage of the essential drugs for health treatment, together with the latest guidelines on pharmaceutical therapy for TB, AIDS, and malaria.

Parasitologist Pascal Millet, at the University of Bordeaux, is an active member of ReMeD. His French military service from 1981-82 was spent doing civic work at a research institute in the Ivory Coast. He campaigns for improvements in the pharmaceutical systems of African countries, citing examples of unnecessary waste and misdirected aid.

## Not only pharmaceuticals

In 2009, he wrote in *Libération*, "The major funding agencies like Unitaid and the Global Fund to Fight AIDS, tuberculosis and malaria concentrate their actions on providing the planet's poorest countries with drugs directed against these three priority illnesses. However, although AIDS, TB and malaria effectively represent a considerable weight in terms of morbidity and mortality, their treatment can only be effective if each country has the resources that permit each patient to have access to diagnosis, treatment and appropriate medical care. These international programmes evaluate the success of their actions in terms of the number of treatments delivered to the health authorities of the concerned countries. They directly associate this figure to the number of lives that can be saved based on the principle that 100% of these treatments will get to the patients. However, studies realised by several university groups and the observations of both local and foreign health workers in the field clearly show the inaccuracy of this association (the number of patients and cures is far inferior to the number of treatments donated)."

**Bill Gates, one of the richest people in the world, committed €8.1 billion over the next ten years for research, development and delivery of vaccines for the poorest countries in the world.**

For example, in January 2006, Senegal received 3.3 million doses of the anti-malarial ACT treatment (based on artemisinin). ReMeD says this was too much to be rapidly absorbed by the existing health system – some got as far as outlying dispensaries but a large proportion remained in storage and had to be destroyed since its effective shelf-life is only two years and the ACT was already six months old when it arrived in Dakar.

"There is no point giving medicines to countries if the drugs are not getting to the sick people who need them. To do this it is necessary that the public health and pharmaceutical systems function. It is imperative that our intervention provides technical support and training of health professionals."

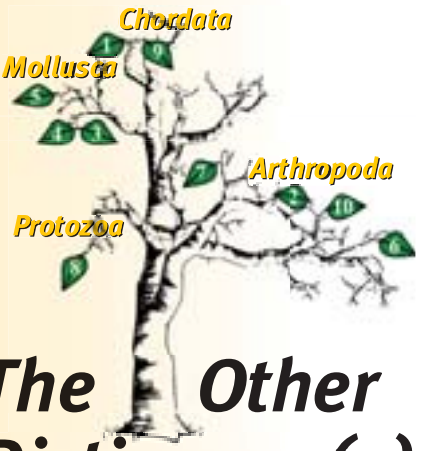
## Hope for the future

Given the scale and complexity of the problems involved, NGOs and their volunteers can only make a modest overall contribution. However, the progressive activities of NGOs continue to define the issues and publicise the enormous challenges involved.

The last decade has seen some notable initiatives – the Global Fund for AIDS, TB and Malaria, and the Bill and Melinda Gates Foundation. In January, Bill Gates committed a further €8.1 billion over the next ten years to help research, develop and deliver vaccines for the world's poorest countries. And, through the Global Health Initiative, the US government proposes to invest €51 billion over six years to help partner countries "improve health outcomes through strengthened health systems".

Even industry is changing its attitude. The health editor of the *Guardian* described her contrasting interviews with successive chief executives of GlaxoSmithKline (the world's second largest pharmaceutical company). In 2003, the GSK line was that if donor governments provided enough money to buy anti-HIV drugs, it would offer them a discount price. In 2010, the new head of GSK said that multinational companies like GSK have a duty to society to help the poorest people on the planet get the drugs they need – he has cut prices, waived patent rights on any potential drugs that might work against neglected diseases and is now releasing details of 13,500 compounds in GSK's library that might be active against malaria.

JEREMY GARWOOD




# The Other Dictionary (3)

The hidden meaning behind real species names. By Jörn Glökler

***1) Ara ararauna***
the distinct noise produced by a vortexer with worn rubber feet on a stony lab bench.

***2) Crematogaster bingo***
when all quadruplicate samples yield the same value. This indicates that the experiment is either highly reproducible or, more likely, that the instrument is broken.

***3) Monodonta confusa***
the one colony more comparable with the negative control after transformation.

***4) Monodonta perplexa***
the one colony less comparable with the negative control after transformation.

***5) Periploma papyratium***
all failed experiments that don't make it into the final thesis. Periploma usually exceeds the final version by orders of magnitude, resulting in environment-friendly thesis hardcopies.

***6) Pipiza quadrimaculata***
the carefully balanced minimal medium some of your colleagues seem to live on every lunchtime.

***7) Porcellia transmutatus***
the petrified plasticware sometimes found in less frequented storage compartments in the lab. A still unknown, probably light-sensitive mechanism slowly turns petri dishes, syringes, pipettes and small receptacles into glass or stoneware. Extant date markings on the retrieved material indicate that the process may have taken more than 20 years.

***8) Quinqueloculina arctica***
the one glycerol stock culture that refuses to grow, despite several attempts to revive it.

***9) Surnia ulula ulula***
the wailing sound that tells you when the centrifuge is definitely out of balance.

***10) Tetraponera demens***
the fourth time in a row you forgot where you put your sample. Time to go home and get a good night's sleep.