GATHERING STORM: THE RISE OF DRUG-RESISTANT TB
HUMANITARIAN SPACE

Not long ago, when people asked me to cite a success story, I would talk about Sri Lanka. After 19 years of brutal and ethnically charged civil war, the Liberation Tigers of Tamil Eelam (LTTE) and the Sri Lankan government were able to reach a ceasefire in February 2002. The following year, as the Sri Lankan health system reestablished itself in the north and east—the areas that bore the brunt of the war—Doctors Without Borders/Médecins Sans Frontières (MSF) was able to close all of its emergency programs that had provided surgical and medical care to victims of the conflict.

Just three years later, the situation is much different. As the Norway-brokered ceasefire has collapsed and both government and LTTE forces have ratcheted up their attacks against each other, MSF is struggling to regain a foothold inside the country.

In October, after three months of providing support inside Point Pedro Hospital on the Jaffna Peninsula, MSF was forced to suspend its medical activities in light of false allegations brought against it in the Sri Lankan media. MSF was cited as a “threat to national security” and was accused of actively supporting the Tamil Tigers. Though MSF has not been officially charged, these allegations, combined with a lack of clear support from the government for our humanitarian work in war-affected areas made the risk for our staff unacceptably high. In August, 17 staff members of Action Contre la Faim (ACF) were assassinated in the eastern town of Muttur, illustrating how dangerous the situation can be for humanitarian workers.

These allegations came against the backdrop of heightened mistrust in Sri Lanka of nongovernmental organizations (NGOs), stemming, in part, from frustration with slow and wasteful reconstruction efforts following the Indian Ocean tsunami. There is also strong opposition to the involvement of foreign organizations in the conflict. Many foreign entities, whether international organizations, states, or international NGOs, are grouped together and perceived as being pro-LTTE or as profiting from the war. This is why it is extremely important for MSF to explain our medical action and to be publicly and officially recognized as independent, neutral, and impartial. Finally, it may be that belligerents do not want an international presence in the areas where war is being waged.

The decision to pull our medical team out of Point Pedro was not taken lightly. It was especially hard to leave the patients and to stop collaborating with our colleagues in the hospital. The situation on the peninsula continues to deteriorate, and currently there is heavy bombing in the area. We have grave concerns for the population living in the war-affected areas. Fighting is increasing. Heavy bombing has displaced tens of thousands of people who are in need of assistance. Hospitals are in need of support to meet the demands. It is deplorable that population living in areas where heavy fighting is underway is being deprived of medical assistance.

MSF representatives, including me, have met with Sri Lankan officials in Colombo and in capitals around the world to make our case for greater access to the war-affected populations. Promises have been made, but until medical teams can effectively do their work, we will continue to advocate for independent humanitarian assistance for Sri Lanka’s forgotten victims.

Nicolas de Torrenté, PhD
Executive Director
US Section of Doctors Without Borders/Médecins Sans Frontières (MSF)
OPERATIONAL OUTLOOK:
The Gathering Storm of Drug-Resistant TB

"After I take the medicine, I feel very tired, sometimes I vomit, and I feel very sleepy during the day. I can’t even work because there are a lot of tablets in my body," says Silus.

Silus is one of nearly 400 Kenyan patients receiving treatment for tuberculosis at the “Blue House,” the Doctors Without Borders/Médecins Sans Frontières (MSF) TB treatment program in Nairobi’s notorious Mathare slum. Around the world, TB kills nearly two million people every year, and more than 450,000 people contract drug-resistant tuberculosis. This year, MSF has treated more than 17,000 living with TB in 44 countries and has seen an increasing number of cases of multidrug-resistant TB, or MDR-TB.

Dr. Liesbert Ohler, an MSF physician working at the “Blue House,” sees firsthand the toll on patients who no longer respond to first-line TB drugs. “Every morning they have to take nine tablets and get one injection. And they have to take granules (anti-TB medication),” says Dr. Ohler. “Every afternoon they have to take the granules again and three extra tablets. These medications have many more side effects than the first-line TB treatment, which doesn’t make it easy for patients to continue taking them.”

The devastating toll taken by TB around the world shows how the approach spearheaded by the World Health Organization (WHO) to control TB has failed on several fronts, says Dr. Jean-Hervé Bradol, president of MSF in France.

"The strategy of the WHO and of other national and international health agencies, in place for some 20 years, has failed to control the disease or prevent the emergence of more threatening strains that are extremely resistant to the antibiotics available today," says Dr. Bradol.

Above: At MSF’s “Blue House” health center in the Mathare slum, Nairobi, one laboratory is dedicated to the detection of tuberculosis. Sputum smear tests are conducted, and TB bacteria are cultured. Kenya, 2006 © Matthew Smeal
The standard drugs for TB were developed in the 1950s and 1960s. Moreover, the most commonly used TB test was developed over a century ago and detects TB in only about half of the cases. Treating TB in people living with HIV/AIDS can be much more complex. It can take weeks of testing to confirm TB drug resistance, further complicating efforts to treat TB-HIV coinfection. Using standard drugs to treat resistant forms of TB, even for those patients who are not coinfected, can be a death sentence.

“The pace of research is not keeping up with the progression of the disease,” says Dr. Jean-Hervé Bradol, president of MSF in France.

A new analysis released by MSF at the 37th Union World Conference on Lung Health in Paris shows that none of the TB drugs currently in development—however promising they may be—will be able to drastically improve TB treatment in the near future.

“We are convinced that the strategy has to be changed so that we can incorporate more powerful tools in the battle against TB, whether in diagnostic or treatment terms,” says Dr. Bradol. “I’m talking about tools that can be read more quickly and that simplify doctors’ and patients’ lives. Today, those tools are incredibly complex. Complexity is not what we are after, given the seriousness, urgency, and worsening of the situation.”

DANGEROUS STRAIN

More recently a dangerous form of extremely drug resistant TB—known in medical circles as XDR-TB—has begun to intensify. Some drug resistance in MSF patients has proven to be XDR-TB. People living with XDR-TB no longer respond to either one of the first-line antibiotics used to treat the disease or to either of two classes of second-line drugs. They have little hope of survival. A recent study of TB patients in South Africa’s rural district of KwaZulu Natal found that one in 10 had XDR-TB.

XDR-TB is not a new problem. Cases have been documented in Eastern Europe and Central Asia. What is alarming about this latest outbreak of XDR-TB is that it is occurring in the country with the largest number of people living with HIV/AIDS. It can take weeks of testing to confirm TB drug resistance, so starting to treat a potential MDR-TB patient with standard drugs can effectively condemn him or her to death.

“THE TIP OF THE ICEBERG”

“What we’ve identified as a problem may be the tip of the iceberg,” says Dr. Juliet Melzer, who has treated TB in MSF programs in Africa, Asia, and Europe. “This is a particular concern for Africa, where there’s a large burden of HIV. There are already many TB cases and many more that have not been identified yet because of the difficulty in diagnosing the disease. So we need to be vigilant for resistant TB—including our diagnostics and treatments—or else we may find that what we see is just the beginning of a growing epidemic of resistant TB in HIV-prevalent areas.”

CALLING FOR AN EMERGENCY RESPONSE

The situation will not improve unless the WHO takes the lead in pushing for more effective drugs and in accelerating the development of easy-to-use tests. Dr. Bradol says the WHO should avoid the temptation to delegate this responsibility to drug and diagnostic development partnerships.
“MSF is calling for the adoption of a multipart emergency plan,” says Dr. Bradol. “One part of that plan would strengthen the ability to diagnose the disease—particularly its most dangerous, difficult-to-treat strains. Today, that process is extremely complicated, whether we’re dealing with the simple or complicated form of the disease. We are calling for accelerated testing of new drugs because we know that, although research is under way, it seems that its pace is not keeping up with the progression of the disease.”

“We may find that what we see now is just the beginning of a growing epidemic of resistant TB in HIV-prevalent areas,” says MSF physician Juliet Melzer.

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Page 4, left to right:
An MSF pharmacist dispenses life-extending anti-retroviral drugs to a patient at MSF’s “Blue House” in the Mathare slum, Nairobi, Kenya, 2006 © Jun Aoki/MSF

In Takeo, MSF is working to improve treatment for TB patients by offering training to Ministry of Health staff and building or renovating wards where patients, including those with multidrug-resistant TB, can be properly isolated and treated. Cambodia, 2006 © Petrana Ford/MSF

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A child sits on her mother’s bed in the infection-disease ward of a Siem Reap hospital, where MSF administers care for patients with TB and with HIV/AIDS. Cambodia, 2006 © Justin Mott/World Press Association

An MSF physician reviews the x-ray of a multidrug-resistant TB patient undergoing treatment in the TB clinic at Gulprish Hospital. Abkhazia, 2005 © Alexander Glyadelov
The first Doctors Without Borders/Médecins Sans Frontières (MSF) team entered Lebanon on July 20, one week after the conflict began. Within a few weeks, more than 100 MSF staff were working in nine areas of Lebanon and Syria. The teams distributed 300 tons of relief and medical supplies but struggled to reach the most war-affected areas of southern Lebanon.

Until a ceasefire between Hezbollah and Israel took hold on August 14, much of southern Lebanon was cut off from assistance. Roads were under near constant threat of bombardment, and bridges had been destroyed, preventing aid supplies from reaching cities in the Bekaa Valley and south of the Litani River. At one point, MSF teams created a human chain to pass relief items across the Litani River.

As the fighting raged in southern Lebanon, MSF’s operations focused on providing relief items, medical care, and water and sanitation to hundreds of thousands of displaced people who sought refuge in Beirut, Saïda, Sour, Jezzine, Nabatiye, the West Bekaa districts, and the Aley region, and to refugees in neighboring Syria. MSF also sought access to populations trapped in combat areas, mainly in the Bekaa Valley and south of the Litani River.

After the August 14 ceasefire, the majority of displaced people wanted to return home. Within two days of the truce, most displaced-persons centers were empty. MSF refocused its activities on assessing needs in areas that had been previously inaccessible; bringing support—medical and non-medical—to returnees and to those who had stayed behind; and providing medical supplies to health facilities in the most affected areas. MSF also pre-positioned emergency surgical kits in case of a resumption in fighting.
Misery in the Palestinian Territories

The war in Lebanon diverted much of the world’s attention away from the conflict in the Palestinian Territories. In the weeks preceding the Hezbollah-Israeli conflict in Lebanon, Palestinians endured increased Israeli military operations. Those incursions continued even as hostilities ceased in Lebanon. From the period of June 25 through November 8, following the Israeli military operations known as “Summer Rain” and “Autumn Clouds,” more than 350 Palestinians died and 1,000 people were wounded in the Palestinian Territories, according to the U.N. “Summer Rain” was initiated following the kidnapping of an Israeli soldier, and “Autumn Clouds” came after a surge of qassam rocket launches into Israel. From January until November 8, qassam rockets fired from the Palestinian Territories had injured 41 Israelis.

These two Israeli offensives, combined with the cut-off of aid to the Palestinian Authority from major donor governments (the US, European Union, Japan, and Canada), have resulted in significant shortages of essential medicines and supplies, and have begun to disrupt the Palestinians’ health services. MSF has made periodic donations to hospitals in Hebron and the Gaza Strip while maintaining its mental health programs there.

Since August 29, 90 percent of West Bank Ministry of Health employees have been on strike because they have not received their salaries since February (with the exception of EU allowances), causing a marked deterioration in medical services for the people in the West Bank: almost all primary health care centers have closed, and, in the hospitals, maternity wards and all non-emergency services have closed. Since November 6, even the emergency rooms of public hospitals have been closed. In Hebron district, MSF has opened two clinics for severe chronic diseases and for serious primary health disease concerns.
EPICENTER: Fighting African Sleeping Sickness

Human African trypanosomiasis, also known as sleeping sickness, is a fatal and much neglected disease that plagues parts of Africa. It is transmitted by the tsetse fly, which harbors the trypanosome parasite. Tsetse flies are found in 36 countries in sub-Saharan Africa, near stretches of water or forest. According to World Health Organization (WHO) figures, trypanosomiasis affects 50,000 to 70,000 people each year.

The drug used most often to treat the disease is so toxic that it kills one in 20 patients. Although a better drug exists, it is too complex to administer in impoverished areas. In the Democratic Republic of Congo (DRC), sleeping sickness has made a disturbing comeback over the past few decades. Doctors Without Borders/ Médecins Sans Frontières (MSF) runs programs to treat sleeping sickness in the DRC and Sudan, and has transferred its treatment programs to national health authorities in Angola and the Republic of Congo. Last year alone, MSF treated one out of every five patients treated for the disease.

Three years ago, Isidor’s village, in the remote territory of Isangi in the DRC’s Eastern province, was hit by a mysterious disease. Villagers began losing sleep at night and were overcome by an irresistible fatigue during the day. Some would wander incoherently, sometimes becoming violent; others slipped into deep comas and died.

“People became tired, apathetic. They would go to hospital but could not be diagnosed. Superstition replaced medical knowledge and people started thinking it had something to do with their neighbors, child witches, and so on. Even the older generation had forgotten the symptoms and thought it was a new disease,” says Isidor, an MSF patient.

“The strange illness actually was not new. Transmitted by the bite of an infected tsetse fly, sleeping sickness had plagued the area when it was a Belgian colony. Faced with waves of epidemics that ravaged entire villages and decimated the workforce, the colonial administration launched huge campaigns to combat the disease. These efforts were largely successful and, by the end of the 1960s, sleeping sickness had been brought under control.

But years of civil war combined with poor public-health management have ruined the country’s health care infrastructure and trypanosomiasis has come back with a vengeance.

During an emergency intervention in 2003, MSF found that the Isangi area—where the Congo and Lomami Rivers meet—was suffering from an extremely high incidence of the disease. MSF opened a program in August 2004 to try to bring the prevalence down from an alarming peak of 14 percent to less than one percent, largely through screening people for the disease and providing treatment.

HUNTING THE TSETSE FLY

A cornerstone of MSF’s operations in Isangi is an “anti-vector campaign.” Its objective is to catch the tsetse flies and reduce the spread of the disease.

“We place floating traps,” says Dr. Bertrand Draguez, medical coordinator for the Isangi program. “The tsetse is the only insect to be attracted by these traps. The trapping operation is backed up with screening activities to help interrupt the disease-transmission cycle.”

“HIDDEN KILLER”

MSF’s in-depth information and awareness-raising campaign is a vital component for the success of the program. “Because fairly common symptoms develop over a period of several years, many sufferers die before they even know they have contracted trypanosomiasis,” says Dr. Draguez. This is undoubtedly why the disease is sometimes called the “hidden killer.”

“FIRE IN THE VEINS”

In the DRC, the most commonly available treatment—melarsoprol—has serious drawbacks. The national protocol continues to call for the use of this drug, an arsenic derivative developed more than 50 years ago, for the advanced stage of the disease. Described as “fire in the veins,” the injected drug is excruciatingly painful. Some five percent of those treated die from complications, and in some areas, treatment failure has increased to 30 percent of cases.

A better drug does exist: Eflornithine—dubbed the “resurrection” drug for spectacularly waking patients from a coma—has demonstrated its effectiveness in many of the places where MSF has used it. It is far less toxic than melarsoprol.
But in many countries, including the DRC, eflornithine treatment is extremely difficult to implement. “It requires significant human resources with four infusions per day for 14 days. You need nurses 24 hours a day. There is a lot of fluid, and you need catheters, not to mention the transport of all the materials to areas that are likely to be remote. National programs may be unable to afford the treatment even if they are given the drug for free,” says Els Torreele, project manager for the Drugs for Neglected Diseases initiative (DNDi), a product-development partnership established by MSF and a number of other organizations.

Current developments offer some hope. MSF is encouraging Sanofi-Aventis, eflornithine’s manufacturer, and the WHO to make available to national programs “eflornithine kits” containing ready-to-use equipment. “We hope that this option will convince national programs to use eflornithine,” says Unni Karunakara, medical director for MSF’s Campaign for Access to Essential Medicines.

In a parallel development, preliminary results from a clinical trial carried out by MSF and several partner organizations, including DNDi, Epicentre, and the WHO/TDR (a program for research and training in tropical diseases) in the Republic of Congo found that a combination of eflornithine and nifurtimox is a safe and effective alternative to currently used monotherapies. In addition, when eflornithine is combined with nifurtimox tablets for 10 days, the study shows that patients require only one week of infusions twice a day. Therefore, treatment is significantly simplified. Use of eflornithine in combination with nifurtimox would also lessen the danger of resistance developing.

Sanofi-Aventis recently signed an agreement with WHO to ensure the production and free availability of eflornithine for the next five years. Bayer, the maker of nifurtimox, needs to provide similar guarantees to make combination therapy a reality for patients in Africa.

"We have now shown that combining eflornithine with nifurtimox makes it possible to simplify and make safer the treatment of sleeping sickness. Countries should not settle for a drug that kills one out of every 20 patients," says Dr. Gerardo Priotto, principal investigator of the study.
Southern Sudan is an isolated region with few resources. To maintain its network of Primary Health Care Units, MSF must bring water by plane on a regular basis.

In Banashawa, our PHCU carries out about 1,000 consultations per month, treating everything from basic health problems to malnutrition, and providing treatment and referral services for major tropical diseases such as kala azar, malaria, river blindness, tuberculosis, meningitis, measles, whooping cough, sexually transmitted diseases, and diarrhea. As an outreach nurse, I helped to open the PHCU in Banashawa. By the end of my nine-month assignment, a cargo airplane will have dropped me off at five of such units.

In this impoverished area, devastated by decades of civil war, formal education, infrastructure, and health facilities are minimal to nonexistent. This region faces continuing insecurity and is virtually devoid of roads, bridges, or transportation. And so, where the Sudanese people cannot access health care, MSF has responded by setting up remote Primary Health Care Units (PHCUs), spread among various villages of the Upper Nile. Medical services would otherwise be unavailable for the people here.

As we await the arrival of Matthew, our Sudanese community health worker, our eager young staff uses this time to conduct health-education talks. Today’s topics include the importance of washing hands after using the latrine, how to properly boil water for safe drinking, and why all pregnant women should come to the clinic at least once for a thorough exam by the community health worker.

When Matthew arrives and the patients have begun being triaged, the clinic is open. Remke (my Dutch nurse colleague) and I take turns supervising the activities of the staff. I spend most of the morning sitting beside Matthew monitoring and evaluating his assessments, diagnoses, and treatments.

As the clinic becomes busier, Stephen, one of the Sudanese staff, comes to me concerned about the health of one of the infants in the home-based therapeutic feeding program. Just two weeks ago,
Baboya was admitted to the program with a weight-for-height ratio of less than 67 percent of the normal ratio for her age. She had been frail and sickly, but since joining our program had made significant gains in body mass and strength. Since last night, Baboya has had high fever, fast-breathing, chest indrawing, and nasal flaring. Stephen suspects pneumonia and I quickly come over to investigate. He is correct and together we treat this emergency case with an intramuscular injection of a strong antibiotic. Baboya will have to return for the next few days for additional injections and follow-up care.

Remke is hidden away in the storeroom *tukul* with Peter, our most experienced paramedic. They have until noon to complete a stock inventory before Remke has to radio our base in Lokichoggio, Kenya, with a list of needed medical supplies to be delivered on the next flight to Banashawa, in a few days. The order must be placed today because if the medicine does not make the next flight, it could be delayed for several months. Such is the inconsistency of the flight schedule to this isolated location.

Remke and Peter find that, in addition to our running dangerously low on amoxicillin tablets, rats have eaten their way through all the “water-for-injection” plastic vials. This is such a harsh and dry environment that even the rats must steal sterile water from plastic vials to survive. All the water for drinking, swallowing pills, preparing oral-rehydration salts, and hand-washing has been flown to the PHCUs in large empty jet-fuel canisters via chartered MSF airplanes that pass through every 10 days or so. Remke and I have calculated that we will have just enough water to get us through until the next flight is scheduled to pick us up and drop off supplies for the clinic.

For Remke and me, clinical nursing care is only the beginning of our responsibilities. We often oversee water and sanitation, building construction, communication and radio operations, and security, as well as maintain good working relations with community leaders and authorities. We have had to learn to deal with tropical diseases we had neither heard of nor seen. We are constantly learning how to adapt to stressful and harsh conditions, analyze an airstrip for its safe “landability,” and develop negotiation skills for dealing with people of various tribes and clans. We have learned to say “hello” in five different languages. We have reluctantly learned how to

As a nurse back home in Chicago, where would I have had the opportunity to hike through some of the most beautiful African landscapes and call it work? Where would a typical “day at the office” consist of sharing cups of tea among tribal chiefs while discussing how to feed the refugees returning from neighboring Ethiopia? And where else but here in southern Sudan would the cries of “cawaja” (foreigner), joined by the handshakes of dozens of children, be my daily reminder of how much I love this job and how much I love these people?
A Refugee Camp in the Heart of the City

Doctors Without Borders/Médecins Sans Frontières (MSF) has re-launched its outdoor educational exhibit, “A Refugee Camp in the Heart of the City.” Created by MSF, the internationally touring exhibit sheds light on the plight of more than 33 million people around the world who have been uprooted by war. During the exhibit’s fall 2006 tour of the US, more than 20,000 visitors, including 6,000 middle school, high school, and university students, experienced the exhibit at four locations: Central Park and Prospect Park in New York City, Piedmont Park in Atlanta, and Centennial Park in Nashville. Plans are under way to bring the exhibit to more US cities. Please visit doctorswithoutborders.org for more information.