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Editorial

As you may have noticed, our illustrious Editor-In-Chief, Ragna Boerma, has stepped down from the position she has held for the past two years to pursue other interests. I am honoured and flattered to be passed the reins of editorial direction here at Global Medicine, and I am excited for what is to come. Over the past years, I have had the privilege of learning the ins and outs of medical journalism and I am eager to expand my skills as the new Editor-in-Chief. I can assure our readers, most of them medical students and junior doctors, that we will continue to bring you accessible and readable analyses of global health issues relevant to you, as well as interviews with key opinion leaders, columns and more. The website has been renewed and the printed edition of GM has another, more practical format. We have welcomed a new project coordinator, Merve Ulubas, and also the editorial team has welcomed new members. I am honoured to introduce you to Daniël Korevaar, our new Senior Editor, and to Sanne Jongma as fairly new editor.

Also the lay-out and public relations teams have welcomed enthusiastic new members. Please see the colophon for further details on the people involved in this magazine.

In this 16th edition of GM you can read an in-depth article by Rocío Acuña Hidalgo about the financial aspects of orphan and neglected diseases, and why they are (or are not) of interest to the pharmaceutical industry. I myself discovered that rare diseases are rare, but rare disease patients are numerous. Furthermore, you can read about another neglected problem, the “medical brain drain” (the emigration of people with technical skills or knowledge). In his article, Paul Yonga proposes some solutions to tackle this pressing problem. Finally, you will find out how it feels to be a patient as a medical student in a low-resource hospital, far, far away from home. Enjoy reading!

Benjamin Jelle Visser, Editor-in-chief

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✝ **78 per 1 000**
under-5 mortality rate in Ghana (2008)

35%
of tested anti-malarials are of
poor quality in Asia



COUNTERFEIT ANTIMALARIAL DRUGS

Malaria still constitutes a major threat to global public health. In 106 countries, 3.3 billion people are at risk. Between 665,000 and 1.2 million people die every year from a *P. falciparum* infection. Therefore, antimalarial drugs are widely distributed and often prescribed (correctly and incorrectly) for the many febrile episodes attributed to malaria in endemic areas. However, over the past few years, reports of poor-quality and counterfeit antimalarial drugs have increased. Recently, a study in *The Lancet* reported that 36% of antimalarial drugs are falsified in South-East Asia. Furthermore, in Sub-Saharan Africa 35% of antimalarial drugs failed chemical analysis. These numbers are disturbing. Poor-quality antimalarials not only have many public health consequences among vulnerable populations, but also drug resistance becomes more and more prevalent. **BJV**

GHANA'S ATTEMPT TO REDUCE CHILD MORTALITY

Last year, Ghana was the first developing country ever to successfully start two immunization programs concomitantly. They introduced a vaccination program for both Pneumococcal bacteria and Rotaviruses. This greatly contributed to Millennium Goal number four which aims to reduce child mortality by two thirds between 1990 and 2015. In 2008, worldwide 28% of all deaths in children under the age of five were caused by pneumonia or diarrhea. Hence the urgent need for low-cost prevention measures. The planning of this major investment started three years ago by initiating fundraising, educating the population, training health workers, and fine-tuning the cooperation of all involved organizations involved. The next country planning to initiate the same program is Tanzania. Let's hope for the best. **SJ**



~2.5 million
people suffer from Yaws worldwide

GMNews

SLOWDOWN IN ACHIEVEMENTS IN MALARIA

In the past decade, many countries made efforts to lower the number of malarial infections by several prevention and control interventions. Of the 1.1 million patients surviving malaria after treatment, 58% come from one of the ten countries with the highest malaria burden. Most of these are in sub-Saharan Africa, for example, the Democratic Republic of Congo and Nigeria. Unfortunately, according to the World Malaria Report 2012, international funding for malaria prevention and treatment has been lowered and the progress of delivery of some life-saving commodities has slowed down. The report also indicates that funding for malaria appears to have reached a plateau below the level required to reach the health-related Millennium Development Goals and other malaria targets. For example, millions of people still live in endemic areas without effective prevention and diagnostics available. What will this hold for the future? **MU**



YAWS ERADICATION: RENEWED EFFORTS

In January 2012, a study in Papua New Guinea showed that a single dose of oral azithromycin is as effective as injectable penicillin in curing yaws, highly facilitating large-scale treatment of affected populations. In response, the World Health Organization (WHO) has announced that it now targets the eradication of yaws by 2020. A new strategy for eradication was developed, based on a more aggressive approach in dealing with cases and contacts. This will ensure less disease transmission. Additional technical support will be provided to 14 endemic countries.

Yaws is a chronic bacterial infection caused by *Treponema pallidum pertenuis*, and is found in poor tropical regions in Africa, Oceania, Asia and South America. The disease is transmitted by skin-to-skin contact, through pre-existing skin-lesions. Clinically, Yaws presents as lesions of the skin, bone and cartilage which may lead to gross deformities and disabilities due to bone, joint and soft tissue destruction. It has its greatest incidence among children 6-10 years of age. Global mass treatment campaigns from 1952 to 1964 reduced its prevalence from an estimated 50 million cases to 2.5 million. Yaws was included on the WHO's list of neglected tropical diseases in 2007. **DK**

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Medical brain drain among doctors in Africa

A neglected global health component

Paul O. Yonga

Introduction

Human resources are pivotal among the requirements needed for delivery of services in any sector, both in low, middle, and high-income countries. In 2002, the World Health Organization (WHO) equally affirmed that Human Resources for Health (HRH) are essential managing and delivering health services. It has also been recognized that insufficient Human Resources for Health in low and middle-income countries are currently one of the main constraints limiting initiatives towards the achievement of the Millennium Development Goals (MDGs).

Most countries in the WHO African Region (most of them Sub-Saharan) continue to experience the loss of a considerable number of doctors due to their migration to high-income countries and other countries which, though not high-income, have better terms of service and remuneration packages for doctors. This so called “brain drain” has now become one of the challenging healthcare problems facing the African continent. The Commonwealth’s

countries (which were part of the colonial British Empire) are particularly hard hit because their health professionals

Brain drain has become a major healthcare problem in the African continent

speak English and have therefore many job opportunities in Western English speaking countries. A closer look at the pros and cons of the medical brain drain stresses the potential gains in managing medical migration to produce outcomes that are beneficial to individuals, households, and the society as a whole.

Globally, imbalances in the healthcare workforce, partly influenced by the decision of these health professionals to migrate to parts of the world where incentives are better, tend to be influenced by a broad range of political, social, economic, and professional factors, several of which are beyond the control of policy makers within the health sector.



Kenya



40 513 000
inhabitants



♂ 58yrs ♀ 62yrs
life expectancy



4.8 %
of GDP for health



1.4
doctors/10 000 people



As a result, the health worker population ratio is better in the urban and the high-income countries as compared to the rural and low-income countries where health services are needed more in view of their poorer health indices.

Experiences from Kenya

So far, Kenya has experienced 3 national doctors' strikes, at least since its independence in 1963. The first strike was in 1994, resulting in a substantial number of doctors migrating to other countries after the Kenyan Government showed insensitivity to their demands which included, among others, increase in their salaries and allowances, and better working conditions. In fact, the authorities dared them to look for jobs elsewhere if they were not satisfied with their current working conditions, and so they did. It was almost certain that these doctors would not have met their demands unless they came together and formed a union. This had been contemplated in the past but because of the autocracy the Government used to practice, no doctors' union would be allowed under their reign. But with the subsequent political changes and new leaders in 2002, hopes of forming a doctors' union were revived. Finally, with careful planning and strategizing, a union was formed and registered in August

2011, which consisted of young doctors, pharmacists, and dentists, of whom a majority worked in the public health-care sector. After this huge milestone, it was time to push the current government to listen to their grievances which included improvement of working conditions, increase in salaries and allowances, increased staff training and payment of registrars/residents. This last grievance is quite important because in Kenya, registrars/residents (doctors in specialty training) are not remunerated for their services. Considering that apart from their hectic study schedule, they are subjected to at least 80 hours per week offering services in the Government tertiary health facilities, this highly reduces the morale of other doctors with the intent of specializing. As a result, many of them opt to specialize abroad and do not come back, while others do not specialize at all. A following strike was scheduled for December 2011, barely 3 months after the creation of the union. However, after intense negotiations between the union and the Government, the strike was cancelled. An agreement was made to form a taskforce to look into the doctors' grievances and to implement an immediate increase in doctors' basic salaries. Within the subsequent month, the taskforce had come up with a draft of recommendations which included formation

of a Health Services Commission (HSC), a complete overhaul of postgraduate medical training in Kenya, creating additional referral hospitals, and modalities of remunerating registrars/residents. Nonetheless, six months down the line, there was still no commitment to implement each of these recommendations, thus setting the stage for a third strike which started with registrars/residents at Kenyatta National Hospital, the largest national referral hospital in Kenya. Two weeks later, all doctors in Kenya working in public services joined the strike. The government then responded by sacking the 3,500 doctors and placing adverts to recruit new doctors. Nevertheless, they realized that the doctors that they fired were the only doctors available in the country and recruiting new doctors would be an unfeasible task so finally they had to pander to the doctors' demands and the strike was once again cancelled.

Discussion

Very few studies into the medical brain drain problem have been carried out as far as Human Resources for Health (HRH) in Africa are concerned, leave alone Kenya. In a study performed by the WHO African Regional Office regarding the cost of healthcare professionals' brain drain in Kenya, it was found that the total education costs per medical doctor from primary school to undergraduate medical studies is USD 65,997. Coupled with the cumulative dollar value of the investment made by the Kenyan society in producing a medical doctor, the cost per medical doctor escalates to USD 517,931. In a cross-sectional survey carried out by Yonga et al in 2012 regarding the perceptions of medical brain drain among young doctors in Kenya, 244 of the 288 participating young doctors (85%) were thinking of seeking employment outside Kenya. Therefore if this was to be translated mathematically into the costs of the

medical brain drain, Kenya would stand to lose about USD 126,375,164, which of course is a phenomenal amount of money.

As regarding the Health Service Commission (HSC), the low wages of the Kenyan doctors are partly explained by their lumping together with other public servants who are not doctors. This means that a doctor working a 48 hours weekend shift is remunerated the same amount of benefits, if not lower, as a government departmental secretary who works 8 hours a day, 5 days a week. Other unique cadres of professionals, for example, doctors and judges, have commissions that draw their budget, formulate their terms of service, and handle other welfare-related issues, which is why a HSC could come in handy to solve the majority of problems faced by doctors.

Conclusion

Whereas human resources for health (HRH) is a key component of global health, it is one of the most neglected components with more emphasis being focused on diseases and not the workforce which actually treats and contributes to advisory issues on preventing these diseases, keeping in mind that Africa bears the biggest brunt to medical brain drain. Thus, the time has come for the international community to play a more proactive role in addressing this phenomenon as far as pressuring African governments to prioritize health is concerned.

About the author

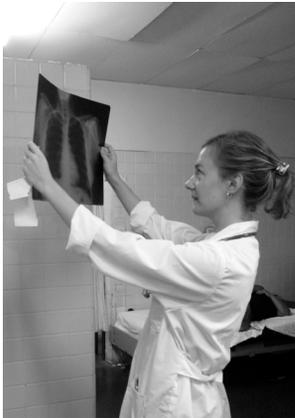
Paul O. Yonga serves as the National Focal Point (NFP) for Kenya to the World Young Doctors' Organization (WYDO).



Column

Doctor and Patient: Surviving Dengue in Nicaragua

Caroline Canté



Caroline Canté has recently finished her medical studies at the Academic Medical Centre (Amsterdam, the Netherlands).

Sweat drips down my back. All my muscles are aching. I feel restless and try to move my body while my muscles keep on tightening. Then the headache kicks back in, it feels as if my eyeballs are pushed out of my head. As I try to focus on the Spanish speaking voices next to me, I see two soft eyes staring at me through my mosquito net. I must be dreaming. Then I realize I am not. I have dengue hemorrhagic fever and I am in the middle of Nicaragua, one of the poorest countries in Central America.

My internship of tropical medicine in León was starting to get more interesting day by day. For four weeks I had been working at the emergency department of internal medicine at a public hospital with 400 beds in the centre of an old colonial city. Every day I would interview patients in my best Spanish and after working I enjoyed the city and the rest of Nicaragua with my friend, another intern from the Netherlands. After withstanding some macho-behaviour and kind remarks about my appearance ('Can we trade eyes? You have the most beautiful eyes I have ever seen.') my colleagues finally got used to the blonde girl from Europe. Meaning that they took me seriously and taught me everything about being a doctor in Nicaragua.

In the end it turned out I would learn much more than that. After the first shock of being admitted at the same hospital I had been working at all these weeks, still wondering how it was even possible people got better instead of worse, I found myself in a bed at one of the wards of internal medicine. Every morning I woke up with more than ten residents and interns at my bedside making their round. While staring at me with dead serious faces they mentioned the results of my blood exams in Spanish so fast I got completely lost and had to struggle to find out what my blood platelets were doing. Providing understandable information to their patients was surely not the best quality of these doctors. It felt like I gave more blood than I collected

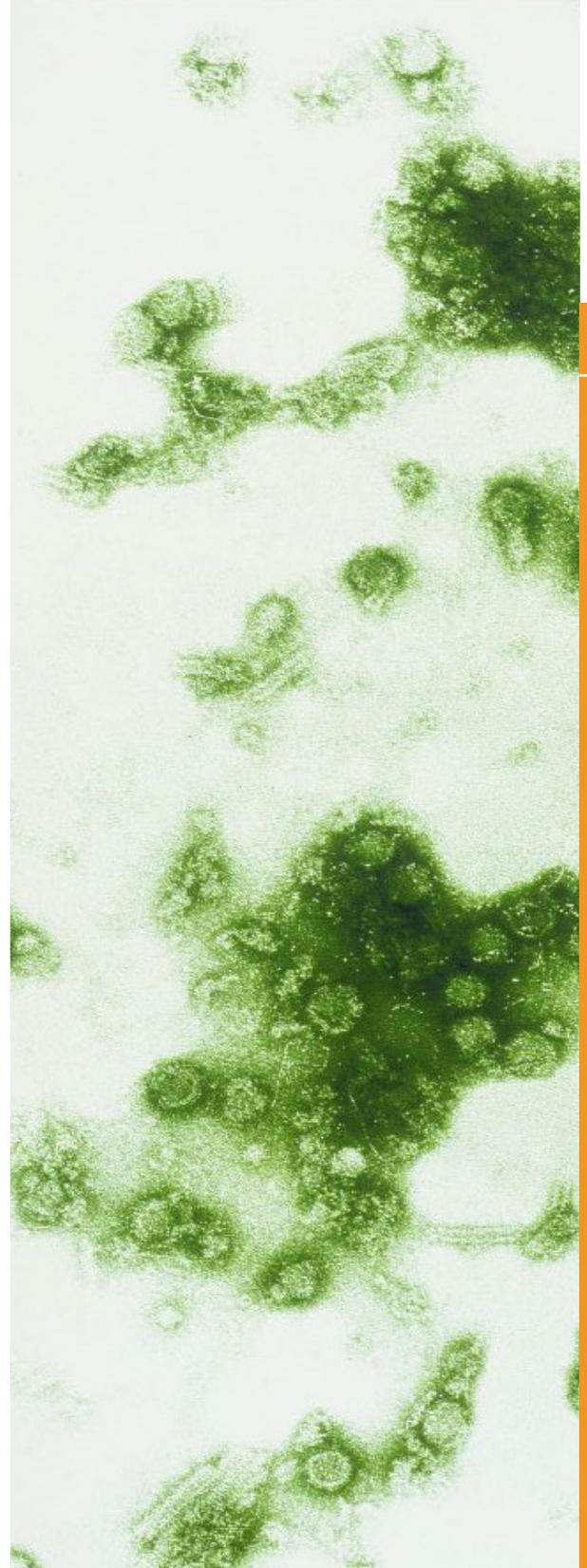
during all my previous internships, while the blood platelets kept lowering and almost reached the transfusion limit.

I tried to grow accustomed to my new role as a patient, but during the day my former colleagues kept on lecturing me until the bitter end. 'Can I please have some ibuprofen?' 'No, you can't, and what would be the reason for that you think?'. It was bedside teaching to the max.

However, what I still remember most are the ludicrous moments my friend and I experienced during my admission. Every day we had to struggle to make our way to the toilet in a wheelchair with only three properly working wheels, trying to avoid vomit, spit and urine on the floor. All patients were laughing at us, as we stumbled our way to the permanently clogged toilet. Back at the ward my new roommates, 7 patients including their entire families, preferred vomiting on the floor instead of using the bin in front of them. I liked to think this was to make the differential diagnosis of vomiting easier for their doctors.

Three times a day the male 'chief' nurse and his army would march into the room, commanding the families to leave. All the nurses did was checking the infusions and handing out the medication. I started to understand why patients needed their families so much to take care of them; the nurses simply didn't.

Slowly the fever disappeared and I started to feel better. But because it took the laboratory a long time to process the blood results, the fear of a blood transfusion kept



threatening me longer than necessary. After seven exhausting days I could finally leave the hospital. In the cab ride home I felt I had learned a lot more about the hospital I had worked in back home.

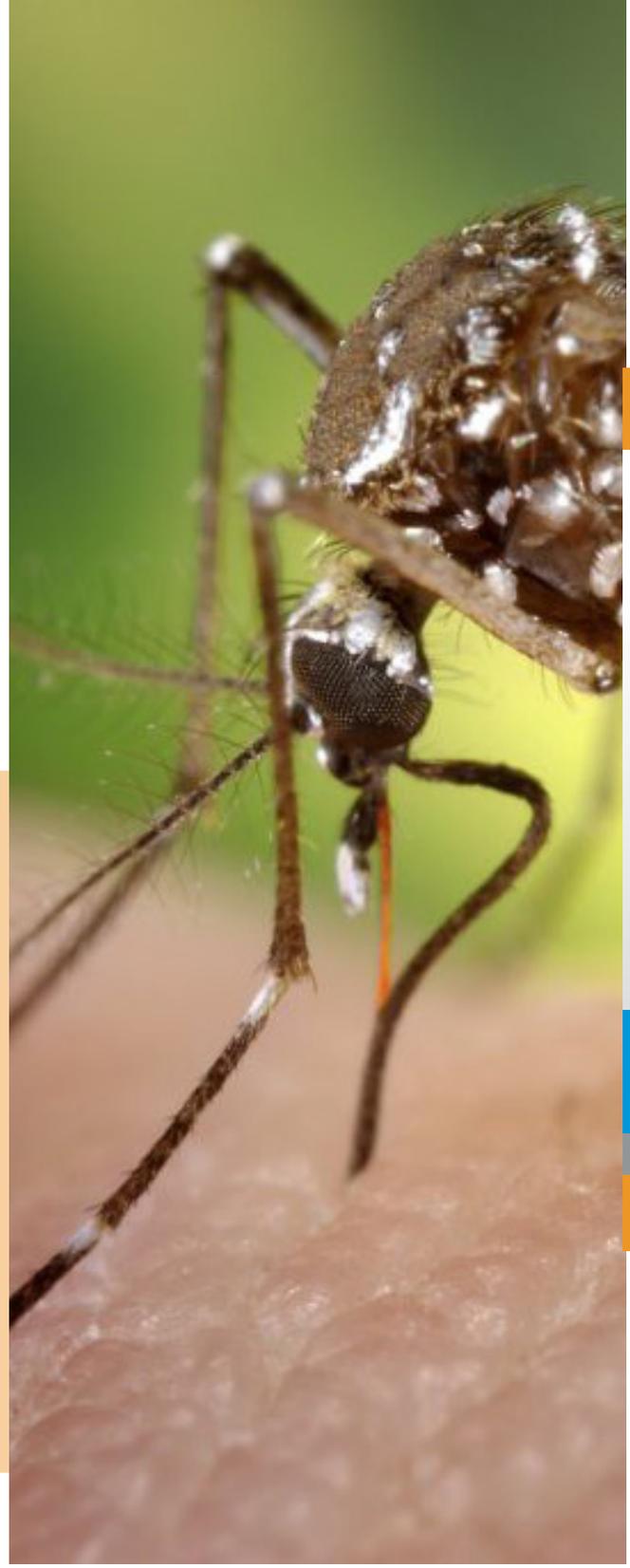
When I returned working at the emergency room I was no longer the blonde doctor from Europe but 'el sobreviviente del dengue', the survivor of dengue. While finishing my internship I realized wherever you are, doctors try the best they can, and make do with what they have. Although cockroaches were part of daily protocol more than cleaning your hands with alcohol, this was still a place to get better instead of worse.

Dengue

Dengue or “breakbone fever” is the most important arbovirus infection in humans. It is caused by an RNA flavivirus which is spread by the *Aedes aegypti* mosquito. Annually, there are an estimated 50 million cases. A dengue virus infection may present as a non-specific febrile illness or asymptomatic infection. Symptomatic patients often have high temperature, vomiting, headache with retro-orbital pain, arthralgia and myalgia. Furthermore a transient macular rash, mild hemorrhagic manifestations and hepatosplenomegaly are frequently present. Most cases of dengue are self-limiting, making treatment a mere supportive necessity. In the case of dengue hemorrhagic fever, the more serious manifestation of dengue, close monitoring of vital signs and prompt admission of intravenous fluids are recommended to prevent circulatory failure and shock.

Further reading:

Simmons CP, Farrar JJ, Vinh Chau N, Wills B. Dengue. *N Engl J Med* 2012;366: 1423-32



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Lymphatic Filariasis

A neglected disease

Sanne Jongma

A 30-year-old man is admitted to a local hospital in rural Kenya. His right leg is extremely swollen up to his knee, the skin cracked. People ignore him as they walk by. His leg hurts so much he is unable to walk, let alone that he can work as a farmer. The doctors told him worms had invaded his body and nothing could be done to improve his condition. He is now permanently disabled, unable to look after his six children. Recently, the pain got worse and he got a fever. He decided to head back to the hospital to ask for medicine once again.

Introduction

Lymphatic filariasis, also known as “elephantiasis” in the advanced stage, is a parasitic tropical disease caused by thread-like nematodes (roundworms). It is thought to have affected humans since approximately 2000 BC as artefacts from ancient Egypt show possible elephantiasis symptoms. The first reference to the disease is found in ancient Greek literature, where scholars differentiated the often similar symptoms of lymphatic filariasis from those of leprosy. Three species of filarial worms are known to cause lymphatic filariasis, of which *Wuchereria Bancrofti* is the most significant. The other two are *Brugia malayi* and *Brugia timori*. Lymphatic filariasis is a communicable disease transmitted by many different mosquito vectors, including Anopheles, Culex and Mansonia species, with humans as definitive hosts.

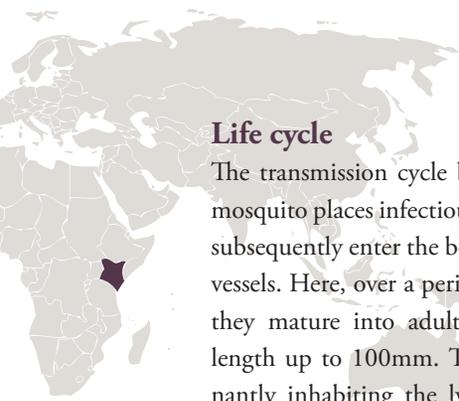
Epidemiology

Lymphatic filariasis is endemic in tropical regions of South-east Asia, sub-Saharan Africa, Central and South America,

and many Pacific islands, where 90% of the infections are caused by the *Wuchereria Bancrofti* parasite. Estimations suggest that of the more than 120 million people currently infected, over 30% live in Africa and 60% in Asia. India alone accounts for 40% of the global infection prevalence. Worldwide, more than 40 million people are disfigured and severely incapacitated by the disease, many of them living with social stigmatization. This causes a high burden of disease, both on the individual as on the community. Approximately 15 million people live with the characteristic severe lymphedema also known as elephantiasis.

In endemic areas, the occurrence of microfilaremia increases with the age of individuals, as nearly everyone has been exposed by their forties. The adult worms however, only subsist when somebody stays in an endemic area, as these worms do not replicate inside the human host, and demand exposure to new infective larvae to increase the worm burden. The mosquitoes are relatively ineffective transmission vectors, hence the acquired prolonged stay before symptomatic infection occurs.





Life cycle

The transmission cycle begins when a bite of an infected mosquito places infectious larvae on the human skin, which subsequently enter the body and migrate to local lymphatic vessels. Here, over a period of approximately nine months, they mature into adult threadlike worms, some with a length up to 100mm. These full-grown worms, predominantly inhabiting the lymphatic vessels of the lower extremities or scrotum, remain in the human body for 5 to 10 years. Male and female worms mate and produce thousands of so-called microfilariae daily. The microfilariae circulate in the bloodstream and generally have a lifespan of one year. Subsequently, a vector bites an infected person once again, engorging the microfilariae. Inside the mosquito they develop into 'third stage' larvae within two weeks and the cycle starts all over again.

Clinical features

Most people in endemic areas are infected early in life, but the disease onset usually starts from the adolescence onwards once worms have accumulated in the lymphatic ducts. About one third of the patients go through periods of acute adenolymphangitis with self-limiting fever and pulmonary eosinophilia provoking nocturnal wheezing and shortness of breath.

Most infected people stay asymptomatic but do develop subclinical lymphatic dilation and dysfunction. In 30% of all patients the affected limbs, predominantly the lower extremities, eventually start to swell, over time transforming from pitting to irreversible non-pitting lymphedema. Hyperpigmentation and hyperkeratosis finally create the image of an elephant skin, hence the name elephantiasis. In males there might be scrotal involvement where serous fluid accumulates and a hydrocele forms. Regularly, the skin

cracks and secondary infections occur in the affected limb causing severe pain, fever and chills. Additional nutritional deficiencies and anaemia, mainly caused by chyluria due to renal involvement, weakens the patients severely. Elephantiasis is seen as the leading cause of permanent disability in the world.



Diagnosis

There are several tools to diagnose lymphatic filariasis. In the clinical setting, the disease is usually diagnosed based on clinical findings and detection of microfilaria in the peripheral blood. The parasites are detectable after a latent period of twelve months after infection. Blood is drawn around midnight, in the nocturnal periodicity, when the number of microfilariae in the bloodstream is greatest. This corresponds to the peak biting period of the mosquito vector. A Giemsa stained blood smear is then examined under the microscope. Serologic techniques, such as enzyme immune assay tests have very high sensitivity and specificity results but cannot be used for follow up, as the antigens stay present after the parasites have perished. Furthermore, filarial specific antibodies and PCR based assays are available. Ultimately, the ultrasound can show the filarial dance sign, their distinctive pattern of movement, detecting where in lymphatic duct the adult worm has its residence. This non-invasive technique is particularly used in the scrotal area where the worms in 80% of the infected men abide in the lymphatic vessels of the spermatic cord.

Global Medicine presents

Neglected Diseases

About one billion people in the world are affected by one or more neglected tropical diseases (NTDs). Neglected, because these diseases persist exclusively in the poorest and the most marginalized communities, and have been largely eliminated and thus forgotten in wealthier places.
www.who.int/neglected_diseases

This is the ninth article in a series on neglected diseases. For more information check www.globalmedicine.nl

Treatment and prevention

There are two main treatment goals, namely bringing the disease to a halt by trying to reverse the progress of the parasite, and interrupting its transmission. Until recently, all infected people living in endemic areas received intense Diethylcarbamazine (DEC, an antiparasitic chemotherapeutic) courses as this has a profound micro- and macro-filaricidal working.

Unfortunately, DEC has a lot of side effects most probably triggered by the dying parasites sourcing local and systemic adverse effects such as fever, malaise, abdominal pain, arthralgia, diarrhea, dizziness, nausea, vomiting and chest pain. Another drug available is albendazole. Different studies showed that albendazole is as effective as DEC (alone or combined with albendazole) and has proven to have the same amount of adverse effects. In addition, ivermectin is used, mainly to reduce the microfilariae intensity.

A global program to eliminate lymphatic filariasis was launched in 1997 by the WHO. A mass drug administration was initiated, providing the endemic population with yearly doses of DEC, co-administrating albendazole for 5 to 6 years, and mass distribution of diethylcarbamazine-fortified salt. The outcome of the ongoing mass administration strongly depends on three main factors, namely (A) the pre-treatment endemicity microfilariae level, (B) the proportion of the population treated per round and (C) the efficiency of the applied drugs regimen. Besides killing the adult worms, the administered drugs reduces the blood borne reservoir of microfilariae, making it less likely the vector will ingest a parasite during a blood meal, diminishing the overall infection risk.

The eradication-program of the *Wucheria Bancrofti* is showing positive progression towards elimination of the disease. Hopefully it will become a successful objective in the future.

Most affected countries completed mapping the endemic foci and 80% of these have started mass drug administration covering over 500 million endemic individuals. So far only China and South Korea have managed to complete elimination, but it is expected that soon more countries will follow.

Conclusion

Although neglected by the western world, the *Wuchereria Bancroft* parasite causes a high burden of disease amongst people living in the endemic areas. Global eradication of lymphatic filariasis is possible but will require much effort from policy makers worldwide.

About the author

Sanne Jongma is a fifth year medical student at the VUmc in Amsterdam and editor at Global Medicine.

Further reading

- Lymphatic Filariasis: Transmission, Treatment and Elimination – Thesis by W.A. Stolk; Erasmus MC; 2005



Column

Homeless in Hollywood

Anne-Lotte van der Kooi



Moving around by bus in Los Angeles, California, is not a recommended way of transportation but, for a student on a limited budget, not always avoidable.

On a late Friday night, a friend and I were brave and broke enough to face the challenge and decided to take the bus home. It soon became clear that the average passenger did not travel light: all of them were carrying a garbage bag with, presumably, all their belongings. Knowing that a bus ride can easily take several hours and costs only 50 cents, we figured out the reason for the popularity of the bus: the opportunity of being comfortable and warm for a few hours for many homeless people.

Los Angeles is widely known for its sunny beaches and rich and famous movie stars. However, recently it has also become the homeless capital of the United States of America. We all know the “American Dream” and the sturdiness of the low and middle classes who always seem to believe in themselves and their possibilities to succeed in life. Yet, since the economic recession started in 2008, many people have lost these dreams. In the USA, an estimated 7 million jobs have been lost since then, resulting in an unemployment rate of 9.6% in 2010 and 8.9 in 2011. With their jobs, people also lost their health insurance. This means they are now saddled with unaffordable medical expenses and many of them do not dare to seek medical care if they would need any. The Obama-care (officially, the “Patient Protection and Affordable Care Act”) is not a quick fix for these people since it will only provide them “Medicaid” starting in 2014 and it will not pay the bills from prior medical care. Education, food, mortgages, everything becomes priceless. Hence, foreclosure can be a harbinger for homelessness. In the USA, in 2009 and 2010 1 out of every 45 homes were foreclosed.

Anne-Lotte van der Kooi is a sixth year medical student currently enrolled in her clinical rotations at the Academic Medical Center (AMC), Amsterdam, The Netherlands. During her research internship at the University of California, Los Angeles (UCLA), she lived in Los Angeles.

The situation is particularly worrying since an estimated 20 to 25% of the homeless population in the USA suffers from severe and persistent mental illness, such as depression and schizophrenia, compared to only 6% of Americans in general. This has partly been attributed to the closure of many mental hospitals in the 1950s and 1960s as part of a wide call for de-institutionalization. However, insufficient money was devoted to the alternative, community-based care. This became especially a problem in the 1980s when relatively cheap housing options started to diminish.

In the Netherlands, there has recently been a fierce debate about the desirability to further introduce deductibles in mental health care. Opponents fear that this will increase the homelessness rate considerably and warn us with examples of the American streets. Fortunately, foreclosure is relatively seldom a problem in the Netherlands. Only around 2000 homes a year are foreclosed, out of 4.2 million property owned houses. This is mainly due to the extended welfare system the Dutch handle. Job losses do not mean immediate bankruptcy or a less accessible health care system.

My friend and I get in a conversation with one of the homeless bus travelers. He tells us about his life. He went to college, had a house, a family and a good job. He lost everything due to the economic recession. He is now resiliently making plans to go up north where there may be better job opportunities. There are many reasons to be happy with our social welfare system in the Netherlands. It is widely believed that the smaller the social gap and the stronger the solidarity in a given country is, the happier a population on average is. But maybe decades of social security and imbedding of the tall poppy syndrome, a social phenomenon in which people of merit are resented or criticized because their achievements distinguish them from their peers, also has its disadvantages. My fellow bus traveler is an illustration of the perseverance of many of the American homeless people. After all, although they lost everything, many are still capable of believing in their dreams.



When treating a disease is bad business: orphan and neglected diseases

Rocío Acuña Hidalgo

Introduction

Over the past decades, the development of thousands of new drugs to treat diseases has improved the lives of people with medical conditions all around the world. However, not every disease has received the same amount of attention from the pharmaceutical industry and many conditions still lack a satisfactory medical treatment.

Creating a new drug to treat a disease is not only a long and arduous process, but also an expensive one. Although the release of a new drug may generate exorbitant profits, 30% of all drugs still fail in Phase III of clinical trials (one of the final steps in drug development, in which the product is tested on patients at a large scale). This means that expensive projects to develop new drugs often reach a dead end without generating any revenue. As a consequence, drug companies are reluctant to invest large amounts of money in drug development unless they can be assured that they will receive a return on their investment. Business (and regrettably, even the business of treating diseases and saving human lives) is about earning as much money as possible.

Drug development for orphan diseases is like financial Russian roulette

And sometimes, investing money in curing a certain disease may not seem profitable enough to be considered “good business”.

Orphan diseases

Orphan diseases are medical conditions with a very low prevalence in the population (less than 5 per 10.000 persons, according to regulations from the European Union). Most of the diseases considered as “orphan” are rare genetic disorders, such as Gaucher’s disease, a lysosomal storage disorder, or rare forms of cancer, for example, chronic myeloid leukemia. However, also other infrequent non-genetic medical conditions requiring medical attention and treatment, such as botulism or intoxication with digitalis, are included in this category.

Drug development for orphan diseases may seem like financial Russian roulette for pharmaceutical companies. The low prevalence of orphan diseases implies that the market for treatments is small. When compared to conditions such as high blood pressure or depression, which affect millions of people around the world, developing treatments for rare disorders could seem unappealing to investors looking for a project likely to generate profit. The small number of people affected by a disease also represents an obstacle at the

level of drug development as patients are not only scarce, but often also geographically dispersed. This complicates the organization of clinical trials logistically as many





medical centres may be required to collaborate in order to have a large enough sample of patients, which is, of course, also more expensive.

In an attempt to neutralize the financial risk of drug research for orphan diseases and promote the development of treatments, special “Orphan Drug legislations” and government agencies have been created in the European Union, United States and other countries. The aim of these legal frames is to make the development of orphan drugs profitable and therefore more attractive for investors.

one third of the drugs currently released being intended for rare diseases. Since the approval of the Orphan Drug Act in the United States in 1983, over 350 treatments for orphan diseases have reached the market, compared to only ten in the decade prior to 1983. However, these benefits have occasionally been abused by pharmaceutical companies, for instance, by extending the total duration of the drug’s patent to maintain market exclusivity. “Evergreening”, a practice in which a compound is slightly modified, and applying for sequential patents of the same drug for different

30% of all drugs still fail in Phase III clinical trials

According to these Orphan Drug legislations, pharmaceutical companies working on treatments for orphan diseases can benefit from public research grants, assistance in protocol design, tax benefits, fast tracking for drug approval by health authorities, and longer patents guaranteeing extended exclusivity in the market. The implementation of these legislations has led to a huge increase in the efforts invested in the development of treatments for orphan diseases, with

conditions, can be both used to renew and extend the life of a patent. For example, Imatinib (marketed as “Gleevec” or “Glivec”), originally developed for the treatment of chronic myeloid leukemia, has undergone modifications since its first release and has been gradually approved for seven separate rare blood malignancies. Novartis, the drug company that developed Imatinib, has been accused of abusing the benefits derived from Orphan Drug legislations by

There is a lot of pressure from NGOs to bypass some of the patents and laws for protection of intellectual property so that affordable drugs can be provided to people in need

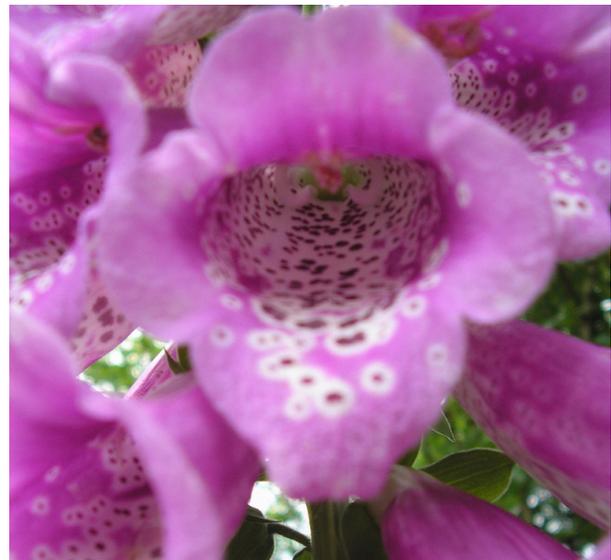
obtaining sequential patents and through “evergreening”. Another way through which drug companies neutralize the risk of investing in research and development of orphan drugs is by offering the treatments at very high prices. Because a patient with a serious medical condition would pay virtually anything to receive treatment, pharmaceutical companies can take advantage of the situation. For instance, the majority of the world’s most expensive drugs are designated to treat orphan diseases, with treatment prices soaring over €100.000 per patient per year. Although the high costs of orphan drugs are usually covered by insurance companies, one might argue that it is unethical to offer these treatments at high prices, which heavily increase the cost of health insurance policies for all other users.

Neglected diseases

In contrast to orphan diseases, neglected diseases are disorders that may affect over one billion people living in precarious conditions and with limited access to medical attention. Neglected diseases consist of infectious diseases, such as onchocerciasis (river blindness) or human African trypanosomiasis (sleeping sickness), which rarely occur in developed countries. Orphan diseases have mostly escaped the scope of pharmaceutical companies due to their rarity but neglected diseases, despite the millions of people affected, have been genuinely neglected.

Drug patents and protection of intellectual property rights are still a big point of debate for drug development for neglected diseases. For instance, until recently, India did not grant patents on medicines and a number of local pharmaceutical companies were producing generics for a fraction of the price of the original drug. Medical organizations such as Médecins Sans Frontières (Doctors without Borders or

MSF) rely heavily on these affordable drugs to treat people who otherwise would not be able to afford the treatment in developing countries. Therefore, there is a lot of pressure from such non-governmental organizations (NGO’s) to bypass some of the patents and laws for protection of intellectual property so that affordable drugs can be provided to people in need. This generates a climate of uncertainty among pharmaceutical companies about whether the patent of a drug developed almost exclusively for use by poor people in developing countries will be respected and, as a consequence, whether the investment in the development of this drug will be profitable. In addition, financial interests are not the only obstacle to drug development for neglected diseases. It is difficult to organize and carry out clinical trials in underdeveloped areas due to the lack of healthcare infrastructure and its association with a high rate of patient loss to follow-up during the trial.



Lessons and hopes for the future

High hopes have been put on large pharmaceutical companies to develop new drugs for neglected diseases in developing countries. However, the solution may lie in smaller pharmaceutical or biotechnological start-up companies, universities and NGO's. Over 35 years ago, the World Health Organization (WHO) created the "Special Programme for Research and Training in Tropical Diseases" (TDR). Its aim was to improve the treatment of tropical and neglected diseases by creating new tools for disease control and by boosting research in developing countries. Nowadays, organizations such as the "Bill and Melinda Gates Foundation" are joining the TDR to support developing countries in establishing their own research activities and contribute to the control of diseases affecting the area. MSF has also set up the "Drugs for Neglected Diseases" initiative with the object of increasing the cooperation between public and private sectors to enhance discovery and development of new drugs. Perhaps a legal framework similar to the one created for

drugs against orphan diseases should be adapted to protect and support the development of drugs against neglected diseases. Similar to the "Orphan Disease legislations", a "Neglected Disease legislation" could help provide smaller companies or research groups with assistance in their research as well as financial support in the form of funding, tax benefits, prioritization in drug approval and prolonged patent. Although the orphan drug designation by itself may not be sufficient to boost the development of drugs for neglected diseases, it should be considered as a useful tool to support and reward these efforts.

About the author:

After finishing her medical studies in Mexico, Rocío Acuña decided to change tracks and work in research. She moved to the Netherlands and earned a master's degree in Molecular Mechanisms of Disease in Nijmegen and is currently a PhD student at the Radboud University Nijmegen Medical Centre.

Pharmaceutical companies facts:



Average costs of an innovative new drug approximately \$400 million over 8-12 years.



The combined wealth of the top 5 pharmaceutical companies outweighs the GNP of sub-Saharan Africa.



Pharmaceutical industry spent 24% of their budget on promotion, versus 13.4% for research and development.



Market leaders in terms of sales: 1) Pfizer 2) GlaxoSmithKline 3) Novartis.

World Health Summit

Young Professionals at the WHS 2013

Tobias Gerder

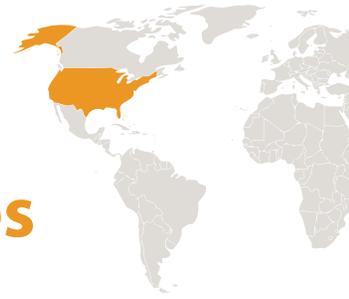
The outcome document of the Rio+20 United Nations Conference on Sustainable Development gives health a central place as a precondition for, and an outcome and indicator of, all three dimensions of sustainable development: economic growth, social improvement and environmental protection. Health is the central angle for addressing tomorrow's challenges and taking care of a better future worldwide.

Since its inauguration in 2009, this has been the credo of the World Health Summit (www.worldhealthsummit.org) as well. The World Health Summit brings together representatives from civil society, academia, the private sector, governments and international health and development agencies to foster approaches for successfully addressing future health challenges. But the success of this unique initiative can only endure if the future leaders of global health are included too: students, young doctors and professionals from all health-related fields. What ideas will they bring in? How will they spar with the international academic elite? And how well are they prepared to take responsibility for the future global health?

The fruitful collaboration with the next generation of health professionals so far culminated in the satellite event "Rethinking Global Health – A Student Perspective" at the World Health Summit 2012. This included a series of

activities for students, that emphasized the important role of students in the vast area of global health. This course will be continued at the World Health Summit 2013 through further cooperation with student organizations and research groups. In addition, there is the "Young Physician Leaders" meeting of the InterAcademy Medical Panel, and the well-established competitive abstract submission and selection program "New Voices in Global Health" in cooperation with The Lancet, designed to highlight important research, policy and advocacy initiatives of new and future leaders in global health. And finally, there will be a special track focusing on "Education and Leadership" in the main-program of 2013, which further consists of "Global Health for Development", "Evidence to Policy", and "Research and Innovation".

The world needs well-trained leaders to build high-performing and sustainable health systems. They will be change agents who will better serve the needs identified by their communities. The World Health Summit invites these young professionals with a special student rate to join the meeting. The fifth World Health Summit will be held from October 20th – 22nd at the Federal Foreign Office in Berlin, under the high patronage of Chancellor Angela Merkel (Germany), President François Hollande (France) and President Jose Manuel Barroso (European Commission).



West Nile Virus in the United States

Coincidence or fate?

Merve Ulubas

In January this year, health officials reported 1118 cases of West Nile Disease and 41 deaths across 38 states in the United States(US), almost half of which occurred in Texas. The Centers for Disease Control and Prevention (CDC) speak of the largest outbreak in the US in years (1). Every year, several states are invaded by symptomatic presentations of disease caused by this virus. How did the virus get to the US in the first place? And more importantly, can it be prevented?

West Nile Virus

The West Nile Virus (WNV) is a RNA arbovirus, part of the Japanese encephalitis virus group. The virus resides in African, Asian and European regions. Generally, viral initiation in humans leads to silent infection. The primary vector of WNV in the US is the *Culex pipiens L.* mosquito, of which the females' blood feed on birds and humans. Other vectors are *Aedes* and *Anopheles* mosquitoes. Once infection in an individual mosquito has been established, transmission occurs vertically. The cycle includes mosquito-bird-mosquito transmission, although birds as natural hosts are usually not symptomatic. Transmission to humans occurs through mosquito bites, and the peak period of virus transmission to humans in the US is between (mid)summer and autumn. During the winter months, the virus is assumed to survive through hibernation of mosquitoes. To date, the exact survival mechanism has not been resolved.

Presentation of disease

During infection, WNV is symptomatic in approximately 20 to 40 percent of people. The incubation period, the period between infection and manifestation of symptoms, ranges from 2 to 14 days. It usually presents as West Nile fever and encephalitis, or as meningitis. The degree of symptoms range from an uncomplicated fever to fatal neuro-invasive disease. This may lead to symptoms such as lowered consciousness and lethargy. Furthermore, acute flaccid paralysis and movement disorders may occur. The definitive diagnosis is made through the detection of IgM in serum or cerebrospinal fluid, which can be found during the first 10 to 28 days of infection, as well as polymerase chain reaction (PCR) tests.



United States



315.743.000
inhabitants



♂ 75yrs ♀ 81yrs
life expectancy



17.6 %
of GDP for health



2.3
doctors/10000 people



United States

Interestingly, WNV causes the most prevalent neuro-invasive disease in humans in the northern states of the US. But how did the virus come to the US and why did it progress in the following years? Up until now, the mode of introduction in the US is speculative. To gain a better understanding, knowledge of WNV's history is essential. WNV was isolated for the first time in 1937 in a patient in Uganda near the West Nile, hence the name. Migration of infected birds may have led to cases of WNV in Asia and Europe in the 1950s and 1960s. WNV was introduced in the US in 1999, when an epidemic of meningo-encephalitis was reported in New York City (NYC), leading to 59 hospitalized cases and 7 deaths. From there on, the virus extended to Ontario, Canada and several other eastern states in the US. The spreading trend developed during the following years, when 142 cases of the neuro-invasive WNV disease, including 18 deaths, occurred in the US. In 2011, out of 107 registered patients in New York state, 60 of them had neuro-invasive disease, 7 of which proved fatal. In addition an estimated 785 patients with neuro-invasive disease were diagnosed with WNV in Texas that same year.

NYC outbreak: source of introduction to USA?

It turned out that the two first cases described in the outbreak of 1999 in NYC lived within a radius of 3.2 kilometres of each other and in the proximity of two major international airports in NYC. It is believed that transmission may have been caused by the importation of infected vectors, such as birds. Interestingly, during this epidemic, an increased number of deaths among birds were reported in the same region

Prevention

No vaccine against the West Nile presentations has been developed to date, although governmental and medical agencies are working on it. Currently, the emphasis of policy lies on prevention. Any form of disease by WNV can be prevented through public education about avoidance of mosquito bites. For example, this is achieved by advocating long sleeved clothing, gazed screens on doors and windows and insect repellents. Another advice is to avoid breeding spots for mosquitoes, such as stagnant water. Furthermore, organised centre vector mosquito control plays a vital role in prevention. This can be implemented by exploring mosquito breeding sites and controlling their larvae spread.

Conclusion

Although the West Nile Virus usually resides in Asian, African and European countries, the spread of the virus to parts of the US is thought to be caused by introduction of mosquito and bird vectors. Various outbreaks have occurred in different cities and states across the US, of which NYC was the first in the late 1990s. An important task at hand is public education about prevention of WNV and multi-centred vector control, since vaccination is not possible yet.

Further reading

Campbell GL et al. West Nile Virus. *Lancet Infect Dis* 2002;2:519-29.

About the author

Merve Ulubas is a fifth year medical student at the Radboud University in Nijmegen and editorial member of Global Medicine.

Going abroad?

Take your healthcare precautions!

Nupur Kohli

When you travel, remember that a foreign country is not designed to make you comfortable. It is designed to make its own people comfortable - Clifton Fadiman

When travelling abroad for an internship, work or a long holiday, it is important to prepare yourself for emergency situations. Especially when travelling to resource-poor countries where healthcare systems show very few similarities with our own, proper healthcare precautions should always be taken. Here are seven tips that will help you prepare medical-wise for your amazing trip!

1. Get familiar with healthcare system basics

In case of a medical emergency, it is essential to have some basic knowledge about how the healthcare system works. For example, in some countries a medical specialist is directly accessible, while in others you have to consult a General Practitioner (GP) first. Furthermore, it may be useful to know some basic medical words in the local language, if hospitals are private or governmental, and what role hierarchy plays in these hospitals. Additionally, the latter information could also contribute to your work or internship

2. Get all the required vaccinations

It is important to check which vaccinations are recommended for the country you are travelling to. Many travellers forget that some vaccinations need to be given several weeks before departure. Others are not aware of the fact

that a previous vaccination may have expired. Furthermore, some hospitals abroad may require special vaccinations for their employees. If your insurance does not cover the costs of your vaccinations, a discount is usually possible for students or groups at your hospital.

3. Know where the nearest medical centre is

In case of an emergency you may be too stressed out to even follow your GPS properly. In a foreign country all roads and small streets can feel like a maze. Therefore, it is important to know how to reach the place beforehand. Ask a local to write down the name of the hospital in their foreign language and keep it in your wallet. It will help a non-English-speaking cabdriver bring you to the doctor in your moment of despair.

4. Know how to find the nearest pharmacy

An often heard remark among people exploring foreign cuisines is: "If you can't pronounce it, don't eat it". However, even when applying this rule, many travellers suffer from gastro-intestinal problems. This is one of the reasons why it is important to be able to find the nearest pharmacy. In most countries pharmacies not only sell drugs, but also other useful medical equipment, such as bandages and

Health is like money, we never have a true idea of its value until we lose it Josh Billings (1818-1885, American writer)

tick removers. If you already know that you will need certain medication, bring your prescriptions with you. When asking for medication, use the generic names since brand names vary widely throughout the world. Even better is to find out local brand names of often used medication such as Loperamide.

5. Health insurance: check

Always take your insurance card with you. In some countries healthcare is very expensive and showing your health insurance card may be required. Find out exactly what your insurance covers, especially when you are staying abroad for a longer period. Ultimately you can call the insurance company for advice, provided you are in possession of a working phone. are estimated to exceed US\$ 200 million in lost productivity and medical costs.

6. Have easy access to your medical history

If you have a relevant medical history, you should know how to access it. It will save you a lot of time and fuss when visiting a doctor in a foreign country. An even better option is to take copies of it in English with you.

7. Put emergency numbers in your phone

It will only take a couple of minutes to do this and when you need them the most, you will be very glad to have them. Think of the country's emergency numbers and a number to call when you lie on the floor unconscious. In the latter case, the internationally known abbreviation "ICE" In Case of Emergency, followed by the phone number of your contact person.

About the author

Nupur Kohli obtained her Masters degree in Medicine from University of Amsterdam and is currently doing clinical rotations.





50 133 000
inhabitants



♂ 54 yrs ♀ 55 yrs
life expectancy



9.2 %
of GDP for health



7.7
doctors/10 000 people

STUDYING MEDICINE IN...

Pretoria, South Africa

Amy Chapman (22) is a third year medical student at the University of Pretoria (fondly known as Tuks to its students), South Africa

How is university life in South Africa?

South Africa presents many unique challenges when it comes to the health care environment. South African medicine and teaching is very practically focused as students need to become adept quickly due to the fact that each and every health care practitioner will be needed. As students, we are exposed to much more risky situations in comparison to students from other countries. Simply put, it is because the incidence of infectious diseases, such as HIV/AIDS and tuberculosis co-infection, is much higher than in other countries. Overall, studying in South Africa prepares a student for any eventuality. Our doctors are capable, resourceful and able to cope under immense pressure.

What do you think is the best part of medical education in South Africa?

Our practical experience is the best part of our education. At Tuks, students already move into the clinical field in their first year. This consists of visiting clinics and performing skills such as injections and drawing blood. The patient interaction and opportunity to see first-hand medicine in action is invaluable in later years.

If you could change one thing in the medical education in South Africa, what would that be?

In order for the medical degree to be internationally recognized, all students have to complete a basic sciences component. Subjects

include physics, chemistry, philosophy and sociology. I didn't really enjoy it and couldn't wait to get into the "real" work of medicine – physiology, anatomy, histology, pathology etc. I think that this is how the degree is structured and so students have to take the bad with the good.

What is the biggest difference between studying medicine in South Africa and other countries?

The importance placed on your responsibility to the community. When studying in South Africa, all the lecturers make clear how important it is that we do something back for our country and how it will be up to us to make a change in what could be seen as our ailing health-care system.

Is it financially possible for everyone to study medicine in South Africa?

Yes. Many universities offer bursaries to outstanding students. In addition, respective health departments from various provinces offer bursaries, based on students working to pay back the bursary after completing the degree. There is ample support from government and university sides. We also have a student financial aid program.

What are your plans after graduating?

After graduating, I will work as an intern for 2 years and complete my one year of obligatory community service after that. Currently, I have no other plans yet due to the fact that the first three years of my degree have not given me a specialty of interest. I am interested in working with "Doctors Without Borders" or on the Health train perhaps. I know that I will continue to work in South Africa as I love it with all my heart!

Next issue **Global Medicine 17** December 2013 at your faculty

Deadline for article submissions (GM 18): 5th of January 2014

Deadline for photo gallery: 1st of February 2014

Send your submissions to editor@globalmedicine.nl

Colophon

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Editor in chief Benjamin Jelle Visser

Senior editor Daniël Korevaar

Project coordinator Merve Ulubas

Editors Sanne Jongma, Merve Ulubas

Art Directors Esra Dede, Anne Marye de Jong, Sándor Öry,
Anne Prins, Lynne Rumping

Logistics and Distribution Simone Cornelisse

Public Relations Stijntje Dijk

Webmaster Simone van Grieken

Proof-reader Johan van Breda, Beatrice Clarke, Magda
Maarleveld

Contact coordinator@globalmedicine.nl

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