MTb

BULLETIN of the NETHERLANDS SOCIETY for TROPICAL MEDICINE and INTERNATIONAL HEALTH

PHOTO HANNEKE DE VRIES

Nº 04 / December 2013 - volume 51

SCIENCE AND RESEARCH IN A TROPICAL ENVIRONMENT

CURRENT ISSUES

CONTENT

RESEARCH IN TROPICAL MEDICINE

Traditionally, research in tropical medicine has received much less attention compared with western conditions such as cancer and cardiovascular diseases. Ironically, while HIV originated in Africa and where it has its most devastating impact, research efforts were intensified manifold when it also appeared to affect western populations. As a result new anti-HIV treatments have now also been introduced in developing countries and millions of lives in the tropics are saved because of this spread to the west. To a certain extent this also applies tuberculosis and malaria (affects travellers and US military personnel). Other conditions have not been so lucky and these have been branded as the Neglected Tropical Diseases (NTDs). Recently the non-communicable diseases are becoming more important.

The field of tropical medicine research has changed. Because of their "exposure" to the whole spectrum of tropical medicine, Médecins sans Frontières (MSF) has increasingly responded to the need to address pressing issues in research and the Drugs for Neglected Diseases initiative (DNDi) was founded as a result of this.

Obtaining a PhD at a university in the Netherlands is popular among students from low- and middle income countries (LMICs) because of its unique and open system with focus on publishing high quality research papers on the selected topic. However, how useful is the PhD degree in pursuing a further career in the country of origin, in research or otherwise? In the Netherlands having a PhD can be a prerequisite for certain academic positions but the subject of the thesis does not seem to matter much; it is mainly seen as a training exercise in research at a high level. Is this basically the same for successful PhD students from LMICs? How many are able to pursue and continue a career in research?

Translation of research into practice is the most difficult issue and universities offering a PhD position have an important responsibility here. A PhD program in a Dutch university should never stand on its own just for the sake of adding another PhD thesis to the universities' scientific output. Long term collaboration with universities and ministries of health in LMICs is the best guarantee for meaningful research and this is not always the case.

Immediate access to research publications is of course essential. Free online access should be the standard and fortunately this is more and more the case. It comes at a cost as these open access journals charge a fee; while this should not pose a problem for the western countries these fees should be waived for contributions from LMICs. Some journals stubbornly fail to adjust or still apply restrictions to recent publications for a year or so. There is already a drive to publish research by preference in open access journals and some funding agencies such as the Wellcome Trust require this and rightly so. The HINARI initiative supported by WHO offers access to many journals if you are working in a LMIC, but there are still restrictions.

The field of tropical medicine research is changing with different priorities and new players. Intensive collaboration between institutions has not been pursued with great zeal in the Netherlands in the past decades; various new programmes are started because of personal interest, political reasons or relations while in other areas years of (internationally acclaimed) experience is lost. A more in-depth analysis of activities aimed at better coordination may very well be in the mandate of the Netherlands Society of Tropical Medicine and International Health.

ED ZIJLSTRA
ROTTERDAM CENTRE FOR TROPICAL MEDICINE
E.E.ZIJLSTRA@ROCTM.COM

Research developments and international collaboration in tropical medicine and international health: the example of tuberculosis

What useful contribution can Dutch researchers make to tropical medicine and international health? In recent years an increasing role is being played by researchers from low- and middle-income countries (LMIC), while research funding in many industrialized countries is being reduced. Yet, the research infrastructure is most developed in industrialized countries and human and financial resources in low- and middle-income countries are still limited. The most successful field research in tropical medicine and international health is the result of international collaboration between research institutes in low- and middle-income countries and industrialized countries. Technological developments (new diagnostics, drugs, vaccines) mainly arise in industrialized countries, although an increasing role of emerging economies is taking shape. Field trials take place primarily in high burden countries. Tuberculosis (TB) is used as an example to demonstrate these developments.

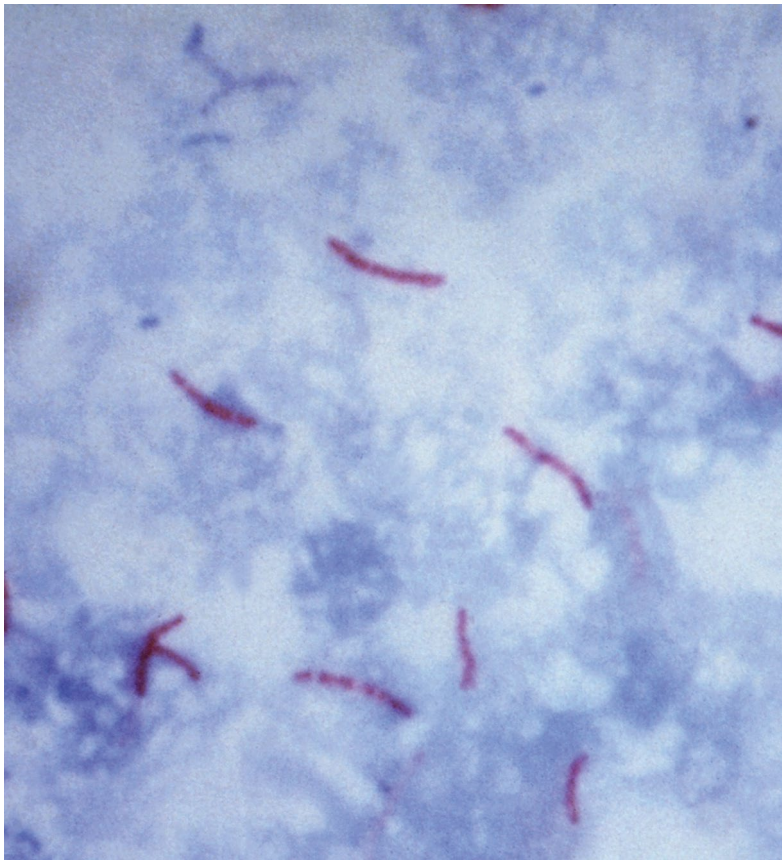
ENDING NEGLECT

In the 1970s and 1980s TB control had reached a stage of neglect in industrialized countries based on the wrong assumption that lasting control had been achieved [1]. From 1990 TB control and research received increasing attention and funding through a combination of factors. In New York a large outbreak of TB was brought under control with difficulty [2]. The first Global Burden of Disease study showed that, worldwide, TB was in the top ten causes of mortality [3]. The World Bank released a report in 1993 showing that TB control through diagnosis and treatment was among the most cost-effective interventions [4]. The impact of the HIV epidemic on TB incidence in Africa was tremendous [5], and the emergence of multidrug resistant , followed by extensively resistant TB was considered a major threat [6]. More recently, the impact of the Global Stop TB Strategy was shown to lag far behind the projections, despite great progress in coverage and treatment success [7]. While over the past two decades many tuberculosis deaths have been averted, the 'treatment as prevention' approach of tuberculosis control with currently available tools is clearly not sufficient to achieve tuberculosis elimination in the foreseeable future.

RESEARCH AND DEVELOPMENT

Over the past two decades, major progress has been made in tuberculosis research as well. The genome of M. tuberculosis has been deciphered [8], bringing tuberculosis biology research back into mainline biological research, and providing an additional basis for the development of new diagnostics, drugs, and vaccines. Moreover, molecular markers were identified, leading to major progress in the molecular epidemiology of tuberculosis [9].

Mycobacterium tuberculosis Ziehl-Neelsen stain



The diagnosis of tuberculosis relies heavily on sputum smear microscopy which has limited sensitivity, and culture, which is technically demanding and slow. The recent introduction of GeneXpert is a major step forward, allowing more sensitive and faster TB diagnosis, as well as rapidly identifying drug resistance [10]. Prior to that, the introduction of line probe assays was a major step forward in drug susceptibility testing. The diagnosis of latent infection (LTBI) relied on the tuberculin skin test. Interferon-gamma release assays represent a major advance as they are more specific and can be performed in vitro and are logistically simpler. The current standard drug regimen takes 6 months of treatment, while treatment for drug resistant tuberculosis takes much longer and is associated with poor outcomes. This year, bedaquilin, the discovery of which was reported less than a decade ago [11], was recommended by the World Health Organization for the treatment of multidrug resistant tuberculosis. New candidate drugs in the pipeline such as PA824 and delamanid are well advanced in clinical trials. The BCG vaccine is widely used, provides good protection against serious childhood TB, but variable protection against pulmonary TB among adults. Given our lack of knowledge on correlates of protection, and limitations of animal models, vaccine candidates need to be tested in human trials. A trial in South Africa of one of these vaccine candidates (MVA85A) showed that in infants this vaccine provided no benefit if given after BCG, in comparison with infants who had received BCG only [12]. This disappointing result confirmed vaccine research is high risk. Yet, if successful, vaccines would have huge public health benefits and thus research needs to continue.

WHERE TO GO NEXT?

Clearly, much more work is needed in the coming years to identify immunological correlates of progression to disease [13], to identify individuals who would benefit most from preventive therapy, or early TB treatment in candidates for cART. This knowledge would also be very helpful for vaccine development. Further development of point of care diagnostics is important to improve TB case finding in the general population and the early identification of (multi)drug resistance. New, shorter, drug regimens would be of enormous help to improve treatment outcomes in challenging circumstances [14]. And finally, an effective vaccine against pulmonary tuberculosis in adolescents and adults would be a game changer in tuberculosis control.

The evaluation of new tools will primarily be conducted in high burden, low- and middle- income countries. In these countries the need is greatest and evaluations can be performed in the most cost-effective way. However, there are constraints to such studies, such as limited clinical trials capacity, both in terms of human resources and laboratory capacity. Therefore, international collaboration is important to help overcome these constraints, provide technical and financial inputs, as well as links to centres of excellence in industrialized countries. In the Netherlands, even though financial resources for TB research are becoming more and more limited, an important contribution to international TB research is made through international collaboration in a range of areas, including immunology, genetics, microbiology, clinical medicine, pharmacology, and epidemiology. Given the nature of TB epidemiology in industrialized countries, including the Netherlands, with 70% of TB patients having been born abroad, additional funding for international TB research would not only be of global benefit, but also serve the interests of the population of high-income countries directly.

MARTIEN W. BORGDORFF, MD, PHD
PUBLIC HEALTH SERVICE AMSTERDAM AND ACADEMIC MEDICAL CENTRE,
UNIVERSITY OF AMSTERDAM
MBORGDORFF@GGD.AMSTERDAM.NL

REFERENCES

1. Institute of Medicine. Ending Neglect. Washington DC: National Academy Press, 2000.
2. Frieden TR, Fujiwara PI, Washko RM, Hamburg MA. Tuberculosis in New York City--turning the tide. N Engl J Med. 1995 Jul 27;333(4):229-33.
3. Murray CJ, Lopez AD. Mortality by cause for eight regions of the world: Global Burden of Disease Study. Lancet. 1997 May 3;349(9061):1269-76.
4. World Bank. Investing in Health. World Development Report 1993. New York: Oxford University Press, 1993.
5. Corbett EL, Watt CJ, Walker N, Maher D, Williams BG, Raviglione MC, Dye C. The growing burden of tuberculosis: global trends and interactions with the HIV epidemic. Arch Intern Med. 2003 May 12;163(9):1009-21.
6. Gandhi NR, Nunn P, Dheda K, Schaaf HS, Zignol M, van Soolingen D, Jensen P, Bayona J. Multidrug-resistant and extensively drug-resistant tuberculosis: a threat to global control of tuberculosis. Lancet. 2010 May 22;375(9728):1830-43.
7. Dye C, Lönnroth K, Jaramillo E, Williams BG, Raviglione M. Trends in tuberculosis incidence and their determinants in 134 countries. Bull World Health Organ. 2009 Sep;87(9):683-91.
8. Cole ST, Brosch R, Parkhill J, Garnier T, Churcher C, Harris D, et al. Deciphering the biology of Mycobacterium tuberculosis from the complete genome sequence. Nature. 1998 Jun 11;393(6685):537-44.
9. Borgdorff MW, van Soolingen D. The re-emergence of tuberculosis: what have we learnt from molecular epidemiology? Clin Microbiol Infect. 2013 May 8. [Epub ahead of print]
10. Boehme CC, Nabeta P, Hillemann D, Nicol MP, Shenai S, Krapp F, et al. Rapid molecular detection of tuberculosis and rifampin resistance. N Engl J Med. 2010 Sep 9;363(11):1005-15.
11. Andries K, Verhasselt P, Guillemont J, Göhlmann HW, Neefs JM, Winkler H, et al. A diarylquinoline drug active on the ATP synthase of Mycobacterium tuberculosis. Science. 2005 Jan 14;307(5707):223-7.
12. Tameris MD, Hatherill M, Landry BS, Scriba TJ, Snowden MA, Lockhart S, et al. Safety and efficacy of MVA85A, a new tuberculosis vaccine, in infants previously vaccinated with BCG: a randomised, placebo-controlled phase 2b trial. Lancet. 2013 Mar 23;381(9871):1021-8.
13. Maertzdorf J, Weiner J 3rd, Kaufmann SH. Enabling biomarkers for tuberculosis control. Int J Tuberc Lung Dis. 2012 Sep;16(9):1140-8.
14. Salomon JA, Lloyd-Smith JO, Getz WM, Resch S, Sánchez MS, Porco TC, Borgdorff MW. Prospects for advancing tuberculosis control efforts through novel therapies. PLoS Med. 2006 Aug;3(8):e273.

Neglected Tropical Diseases

INTRODUCTION

The Neglected Tropical Diseases (NTDs) were introduced as a new entity in tropical medicine in 2005 in response to all the attention the "big three": malaria, tuberculosis and HIV/AIDS received in particular after the creation of the Global Fund to Fight AIDS, tuberculosis and malaria, in 2002. This has caused these important diseases to receive and attract funds, and resulted in an enormous drive to develop new tools for their control in particular drugs; numerous private-public partnerships and multiple large scale interventions have saved millions of lives.

However, a long list of other diseases have received even less attention than before as a result of this diversion and concentration of efforts and funds. The NTDs that affect 1 billion people include classical tropical diseases such as Human African Trypanosomiasis (HAT) and leishmaniasis that were still treated with old and toxic drugs containing heavy metals including arsenic (melarsoprol in HAT) and antimony (stibogluconate in leishmaniasis) and that were developed decades ago. A systemic review covering a 25-year period showed virtually no new chemical entities for tropical diseases in contrast to drugs for cancer and neurological diseases [1]. Similarly diagnostic tools remained inadequate. The list is of course much longer and the current list includes 40 diseases including helminthic, parasitic, bacterial, ectoparasitic and fungal diseases (Table 1). Common characteristics are that they are chronic, debilitating and stigmatizing diseases that affect the poorest segment of populations that live in remote areas. They have a profound effect on poverty and social and intellectual development thus causing a vicious circle. Lack of access to safe water, poor sanitation and poor housing are important contributing factors. There are major difficulties in estimating the global burden of the NTDs in DALYs; recent estimates are 56.6 million DALYs for NTDs compared with 46.5 million for malaria and 34.7 million for tuberculosis. Actual estimates for NTDS may be much higher and currently new estimates are being collected.

IMPORTANT PLAYERS AND DEVELOPMENTS

Médecins sans Frontières (MSF) was among the pioneers to draw attention to the lack of drugs for the neglected diseases and brought together 7 partners [among these: the Pasteur Institute, the Kenya Medical Research Institute (KEMRI) and WHO/TDR (special programme for Research and Training in Tropical Diseases)] to establish the Drugs for Neglected Diseases *initiative* (DND*i*), based in Geneva, in 2003. On a similar note, the Bill and Melinda Gates Foundation (BMGF) provided a grant to establish the Foundation for Innovative and New Diagnostics (FIND), also in Geneva, in 2003. While initially focussing on new diagnostics for tuberculosis, FIND now addresses neglected conditions such as HAT, Chagas' disease and leishmaniasis.

The World Health Organization (WHO) has also adapted to these developments and a Neglected Tropical Diseases department was established; on their website now feature 17 diseases and another 4 that are recognized as NTDs but that receive limited though important support such as collection of epidemiological data and production of guidelines [3]. Mycetoma was the last addition to this list in July 2013. To qualify as an NTD the WHO has published a number of criteria that should be met:

- A proxy for poverty and disadvantage
- Affect populations with low visibility and little political voice
- Do not travel widely
- Cause stigma and discrimination, especially of girls and women
- Have an important impact on morbidity and mortality
- Are relatively neglected by research
- Can be controlled, prevented and possibly eliminated using effective and feasible solutions

The WHO-TDR (special programme for Research and Training in Tropical Diseases) has a new 10-year strategic plan. Funding is increasingly available from BMGF, Wellcome Trust, the NIH and US and UK governments. Neglected diseases are in their portfolio.

A number of public – private partnerships provide free drugs such as for onchocerciasis (ivermectin), filariasis (albendazole) and azithromycin (trachoma).

International journals have also increasingly embraced NTDs and more than 1600 papers had been published by September 2012 [2]. The Public Library of Science launched the PLoS Neglected Tropical Diseases journal as one of its open access journals.

Table 1 **Neglected Tropical Diseases**

Fungal diseases	
	Mycetoma
	Paracoccidioidomycosis
Viral diseases	
	Dengue
	Japanese encephalitis
	Yellow fever
	Rabies
	Rift Valley fever
	Viral haemorrhagic fevers
Bacterial infections	
	Bartonellosis
	Bovine tuberculosis in humans
	Buruli ulcer
	Enteric bacterial infections: cholera, ETEC, shigellosis, salmonellosis
	Leprosy
	Leptospirosis
	Relapsing fever
	Trachoma
	Treponematosis
Ectoparasitic infections	
	Myiasis
	Scabies
Helminthic infections	
	Cysticercosis
	Dracunculiasis
	Echinococcosis
	Enterobiasis
	Food-borne trematodiasis: Clonorchiasis, Fascioliasis, intestinal flukes infections, Opisthorchiasis, Paragonimiasis
	Loiasis
	Lymphatic filariasis
	Mansonellosis
	Onchocerciasis
	Schistosomiasis
Soil-transmitted helminthiasis	
	Ascariasis, hookworm infection, Strongyloides,Trichuriasis
	Toxocariasis
Protozoal infections	
	Chagas' disease
	Human African Trypanosomiasis (HAT)
	Intestinal protozoan infections: Amoebiasis, Balantidiasis, Giardiasis
	Leishmaniasis

RESEARCH IN NEGLECTED TROPICAL DISEASES

Who are working in neglected diseases research? A complete overview of research activities in NTDs in the Netherlands is beyond the scope of this article. Traditionally, schistosomiasis research has been strong in Leiden University Medical Center (LUMC), while the Erasmus MC continues to play a leading role in basic science research in mycetoma. More recently a much needed research line has been introduced in the field of pharmacokinetics and pharmacodynamics of drugs used in leishmaniasis, supported by DNDi, first in the AMC in Amsterdam and now in the University Medical Center in Utrecht.

In the past decade the face of tropical medicine has changed. While classically this was the business of some universities and tropical medicine schools, non-governmental organizations such as MSF have taken an important role. By nature of their mandate they are working in the field and in remote areas and as such they have exposure to a whole range of tropical, infectious and non-infectious conditions. While 20 years ago research was not felt by many MSF workers to be part of their mandate this fortunately changed as there was a need for improved diagnosis, treatment etc. for better management of the conditions they encountered. In addition it was felt that the organization had a moral duty to make optimal use of their strong presence in the field and carry out research with or without other partners. Now we have numerous examples of excellent contributions to the management of a variety of conditions. Indeed MSF is now a leading player in the whole field of tropical medicine research.

Another good example is DNDi that was founded by MSF (and other partners) to address the issue of lack of drugs for the neglected diseases. DNDi has developed new treatments for leishmaniasis that are easier to administer, with shorter duration and fewer side-effects. In East Africa a combination therapy of SSG and paromomycin for 17 days has now replaced monotherapy with stibogluconate for 30 days. New compounds are in the pipeline such as fexinidazole. Another example is the introduction of nifurtimox - eflornithine combination therapy (NECT) for HAT reducing the duration of monotherapy with eflornithine infusions from 14 days (4 times per day) to 10 days (twice per day only), in combination with nifurtimox as an oral treatment, with similar efficacy. Other conditions in the research agenda are paediatric HIV treatment, filarial diseases and Chagas' disease [4].

In January 2013, a collaborative disease eradication programme was launched that is committed to eradicate, eliminate or control 10 NTDs. This so-called London Declaration on Tropical diseases was endorsed by, among others, the WHO, the World Bank, DNDi, USAID, leading pharmaceutical companies and the BMGF [5].

THE FUTURE

While the advocacy for NTDs has been successful and already a lot has been achieved, a new set of conditions are now more and more coming into the picture: the non-communicable diseases that have been more seriously neglected and for much longer than any other group of conditions. Hypertension, diabetes mellitus, and heart failure (from whatever cause) are common throughout the tropics and may become even more important as urbanization increases with changes in dietary habits, etc. A different approach is needed here; for example, for diabetes the drugs needed are largely there; the problem lies in patient education, improved nursing care and ensuring uninterrupted drug delivery. This also applies to hypertension and heart failure, but here there is a pressing need to carry out research studies as the tremendous amount of knowledge on hypertension and heart failure comes from studies in western populations. These do not necessarily apply to non-Caucasian populations as was shown in studies in the USA when comparing results in white and black Americans.

The advance of neglected diseases will be unstoppable; they are fashionable and attract attention in the media and therefore donors are more and more interested. This may be at the expense of other conditions; some already fear that the big three (malaria, HIV/AIDS and TB) are now at risk of becoming neglected. And now the non-communicable conditions are starting to compete for the limited funds available, the principal reason for this unnecessary dividing up of tropical medicine in categories.

ED ZIJLSTRA
INTERNIST-INFECTIOUS DISEASES SPECIALIST
ROTTERDAM CENTER FOR TROPICAL MEDICINE
E.E.ZIJLSTRA@ROCTM.COM

LITERATURE

1. Trouiller P, Olliaro P, Torreele E, Orbinski J, Laing R, Ford N. Drug development for neglected diseases: a deficient market and a public-health policy failure. Lancet 2002; 359:2188-94.
2. Utzinger J, Becker SL, Knoppa S, Blum J, Neumayr AL, Keiser J, Hatz CF. Neglected tropical diseases: diagnosis, clinical management, treatment and control. Swiss Med Wkly. 2012;142:w13727.
3. www.who.int/neglected_diseases/en
4. www.dndi.org
5. www.UnitingToCombatNTDs.org

Research capacity development for Africa: consolidation, ownership and independence

AFRICAN INSTITUTES NEED TO GET MORE ACTIVELY ENGAGED IN RESEARCH PROGRAMMES CONDUCTED IN THEIR COUNTRIES AND THE OWNERSHIP OF THESE RESEARCH PROGRAMMES SHOULD BE SHIFTED FROM THE NORTHERN PARTNERS TO THESE AFRICAN INSTITUTES

CURRENT SITUATION

Currently, African institutes often depend on international collaborators for conceptualization and development of research ideas, technical support and funding. As a consequence, the bulk of research activities focuses on specific diseases selected by the international communities which may not necessarily feature highly on local national health research agendas. Furthermore, long-term visions on regional health problems that are likely to emerge, due to, for example demographic and ecological shifts, are in most cases not adequately developed. In the North, universities play a central role in health research and in maintaining health research capacity through attracting and supporting undergraduate biomedical students and postgraduates to a research career, and providing career opportunities to senior researchers. In sub-Saharan Africa, medical faculties are primarily geared towards practical training of doctors and conduct of research projects is marginal. This being the case, students are not stimulated to seek a research career, and academic institutes are not attractive employers for senior researchers. This is partly due to lack of funding, but also due to a lack of institutional capacity to conduct and promote health research as part of, and in addition to, biomedical teaching curricula. Strengthening the role of universities in health research should therefore start by building local research capacity. However, due to brain drain and social instability in the region it is often difficult for universities to develop and maintain local research capacity. A combination of limited career opportunities, poor working environment and remuneration has been identified by talented African academics as being the main reasons not to return to their home country after completing their training (MSc, PhD and specialist training) overseas. As a consequence the research pyramid in African universities often has a narrow top of a few internationally active researchers and a weak but relatively large base of research-inactive staff.

QUALITY OF RESEARCH

Due to the above described problems, research conducted at African institutes has not always been of high quality, neither has it been driven by local agendas. However, with the recent introduction of international research standards (e.g. Good Clinical Practice in accordance with the International Conference on Harmonization [ICH-GCP]), the quality of research being conducted in African institutes has generally improved, but it has further increased their dependence on international collaborators due to the increase in complexity and costs of conducting clinical research.

THE ARISE CONSORTIUM INITIATIVE

In 2012 the ARISE (Africa Research Initiative and Support – Network) consortium was founded as a joint venture of the existing COMMAL (College of Medicine - Malawi Amsterdam Liverpool) and INTERACT (Infectious diseases Network for Treatment and Research in Africa) programmes. These programmes, funded by the Ministry of Foreign affairs of the Netherlands, were initiated in 2005 with the general objective to strengthen the sub-Saharan African research and development capacity in the field of poverty-related diseases (HIV, TB and malaria).

Recently, the Ministry decided to extend the funding for a period of four years (2012-2015) with the prime focus on consolidation of capacity built under the first phase of the programme.

The objective of the ARISE consortium is to develop and consolidate a network of Research Support & Training Centres (RSTCs) in sub-Saharan Africa. These centres will be embedded in the local universities, will have ownership of the conducted research and will be working according to ICH-GCP research standards.

RESEARCH SUPPORT & TRAINING CENTRES

As mentioned in Table 1 the key characteristics of the RSTCs are local ownership, independence and coordination.

The main focus of the ARISE consortium is:

1. To consolidate and improve research capacity within four regional RSTCs at universities in Malawi, Rwanda, Zimbabwe and Uganda by synchronizing and twinning the success models for training and research capacity strengthening of the COMMAL and INTERACT programmes.

2. To develop a coherent functional capacity building network of RSTCs

with harmonized training methodology, international accreditation and a standardized evaluation system. This includes capacity sharing of PhD training and supervision.

3. To further develop the individual RSTCs into units capable of addressing national health problems as they emerge and delivering a service portfolio based on research disciplines. This includes the establishment of necessary infrastructure for the individual RSCTs to house the different ingredients of the RSTC model.

4. To further strengthen capacity in the field of grants & administration, data and IT management and improve communication strategies with the aim of increased know-how, income and visibility, ultimately resulting in financial independence not enforced by donor funding.

The above focal areas are captured in three key elements and nine functions (Table 2). Using these elements and functions, a scoring system has been developed to facilitate standardization and structured progress assessment of RSTC output and achievements.
A strong RSTC network for southern Africa will offer important opportunities for mutual support (South-South) in research projects and thereby advantages of scale. For example, specialist laboratory or analytical expertise available in one institute may be put to use, through collaborative grant proposals, in research projects primarily run at another institute and vice versa. Making use of the strongest areas in the different institutes to develop these areas in the other institutes will have a synergistic effect benefiting each partner institute and the RSTC network as a whole.

An (sub-Saharan) African network will help focusing and forwarding research agendas of regional relevance. While many health problems seem local at first glance, several of their elements are essentially of a regional nature (e.g. disease epidemiology, organization of the health sector, rapid urbanization). Addressing these in a structured manner in different African settings will improve comparability between sites and a better understanding of the overarching questions. African research networks will not only be essential for formulating research agendas in this respect, but also for attracting the funds necessary to carry out such projects.

STUDENTS ARE NOT STIMULATED TO SEEK A RESEARCH CAREER, AND ACADEMIC INSTITUTES ARE NOT ATTRACTIVE EMPLOYERS FOR SENIOR RESEARCHERS

TIME WILL TELL

Critical for the success (sustainability) of the RSTC-network will be the buy-in of the host institutes (universities) by recognizing the individual RSTCs as essential part of their research infrastructure. This should also include a contribution towards the basic running costs of the RSTC. It is expected that the remaining costs will be generated by the RSTCs through income generating activities (course fees, monitoring- and grant management services). Once established, the RSTC network is anticipated to make a significant contribution towards research capacity building in Africa and towards a shift of research ownership from western to local institutions. Time will tell.

TABLE 1 Key characteristics of the Research Support and Training Centre (RSTC)

Characteristic	Details
Locally owned	Universities will fully own their RSTCs, and allow them to take ownership of the new research projects generated and of the research policy.
Independent	The RSTCs will be independent of the 'North' relying on the expertise of their own staff to provide research support and training.
Coordinated	The support, training and research infrastructural activities of the institute are coordinated by the RSTC.

CONTINUE READING »

TABLE 2 **Details on the essential elements of the Research Support and Training Centre**

Element	Functions	Details
Support services and consultation	Scientific support	Consultation on study design, protocol writing, data analysis and manuscript writing.
	Data management support	Database programming. Data entry and validation for medium-sized databases. Advanced system suitable for complex (multicentre) databases.
	Grants and Research project management	Support with trial design, ethics and project finance. Support with writing grant applications and negotiating research contracts (legal and financial matters).
	Clinical trial support and Quality assurance	Support with monitoring of research data against source documents, clinical trial management and other clinical trial support services. Quality assurance of study procedures and reporting.
Training & Courses	Applied training	Short modules providing basic knowledge and skills. Training in GCP, GCLP, data collection, data management.
	Academic courses	The basic package includes: research methodology, biostatistics, research ethics, evidence-based medicine, and protocol writing. Allows Institutes to train their own future researchers (MSc, MPH or PhD level).
Research governance and institutional infrastructure	Ethical review	Establishment of an ethical review board in accordance with national policy. In second instance, to upgrade the board to adhere to international standards (with respect to modus operandi and composition).
	Research information and communication	Communication (newsletter, website etc.) focusing on activities, policy issues and research results. Information (grants, training opportunities, conferences, etc).
	Research coordination and management	Central coordination of research support, training and governance activities. Executive committee guidance for institutional research policy through research management information system, assessments and prioritization.
	Research agenda	Developing an institutional research agenda based on local/national needs and research interests. RSC positioned directly under the responsibility of university rector or college dean in order to improve its coordination capacity.

NADINE PAKKER, MSC, PHD
EPIDEMIOLOGIST; MANAGER CLINICAL OPERATIONS, AMC-AMSTERDAM INSTITUTE FOR GLOBAL HEALTH AND DEVELOPMENT (AIGHD) / MANAGING DIRECTOR HEALTH[E] FOUNDATION, THE NETHERLANDS
N.PAKKER@AIGHD.ORG

EXNEVIA GOMO
DIRECTOR RESEARCH, UNIVERSITY OF ZIMBABWE, COLLEGE OF HEALTH SCIENCE, ZIMBABWE

PATRICK KYAMANYWA
DEAN FACULTY OF MEDICINE, COLLEGE OF HEALTH SCIENCE, UNIVERSITY OF RWANDA

WILSON MANDALA
DIRECTOR RESEARCH SUPPORT CENTRE, COLLEGE OF MEDICINE, UNIVERSITY OF MALAWI

ELLY KATABIRA
PROFESSOR, COLLEGE OF HEALTH SCIENCE, MAKERERE UNIVERSITY, UGANDA

PAUL KLATSER
PROFESSOR UNIVERSITY OF AMSTERDAM, DEPARTMENT HEAD BIOMEDICAL RESEARCH, ROYAL TROPICAL INSTITUTE, AMSTERDAM, THE NETHERLANDS

MICHAEL BOELE VAN HENSBROEK, MD, PHD
PAEDIATRICIAN-INFECTIOLOGIST / GLOBAL CHILD HEALTH GROUP/EMMA CHILDREN'S HOSPITAL AMC/ AMC-AMSTERDAM INSTITUTE FOR GLOBAL HEALTH AND DEVELOPMENT (AIGHD), THE NETHERLANDS
MBVH04@GMAIL.COM

LITERATURE

1. Gomo E, Kalilani L, Mwapasa V, Trigu C, Phiri K, Schmidt J, Boele van Hensbroek M. Towards Sustainable Research Capacity Development and Research Ownership for Academic Institutes in Developing Countries: The Malawian Research Support Centre Model. Journal of Research Administration, 2011, Vol XLII, Nr 1.
2. NACCAP/NWO grants awarded website. Retrieved July 5, 2010, from http://www.nwo.nl/nwohome.nsf/pages/NWOA_6LMKB5_Eng.
3. Research Support Centre website. http://www.medcol.mw/rsc/index.htm.
4. Sawyerr, A. (2004). African universities and the challenge of research capacity development. JHEA/RESA, 2(1), 213–242.
5. University of Malawi (2004). Partnership in capacity building for community and public health and biomedical research in Malawi. Report of proceedings of a meeting of 30-31 May 2003. Cameron Bowie, College of Medicine.
6. Forland F, Rohwer AC, Klatser P, Boer K, Mayanja-Kizza H. Strengthening evidence-based healthcare in Africa. BMJ Evid Based Med 2013, Feb 21.

ENUMERATOR EVALUATION OF A POPULATION BASED SURVEY OF SURGICAL NEED IN SIERRA LEONE: LESSONS FOR FURTHER USE

In November 2013 Reinou S. Groen succesfully defended her thesis on surgical needs in low and middle income countries. Not included in this thesis, but summarized here, is an evaluation that was conducted into the use of a survey tool. The Surgeons OverSeas Assessment of Surgical need (SOSAS) is developed to evaluate the prevalence of surgically treatable diseases at community level. In a cross-sectional evaluation SOSAS enumerators were asked to anonymously complete a questionnaire about their opinion on the survey questions and execution. The objective was to determine improvements for further use of SOSAS and to solicit information on their experiences during the survey execution. Responses indicated that SOSAS and the iPad were well explained. The greatest difficulty was listing the ages of household members and questions related to the groin, genitalia and menstruation. Explanation of random sampling of household members and real-time translation were the most difficult aspects of survey execution. In conclusion, SOSAS was successfully used during a countrywide assessment of surgical need in Sierra Leone. Although there were issues with translation and implementation of the survey, on the whole, enumerators found the tool adequate and easily adopted the use of iPads in data collection. Translation into local languages is recommended if feasible.

For the full article and references of the study please visit: www.nvtg.org

The PhD thesis can be uploaded at: http://dare.uva.nl/record/456716

REINOU S. GROEN, MD, MIH, PHD
DEPT. OF GYNAECOLOGY AND OBSTETRICS, JOHNS HOPKINS HOSPITAL, BALTIMORE, USA
SURGEONS OVERSEAS (SOS), NEW YORK, USA

MOHAMED SAMAI, MBBS, PHD
COLLEGE OF MEDICINE AND ALLIED HEALTH SCIENCE (COMAHS), FREETOWN, SIERRA LEONE

KERRY-ANN STEWART, PHD
SCHOOL OF MEDICINE, STANFORD UNIVERSITY, STANFORD, CALIFORNIA, USA

THAIM B. KAMARA, MD
DEPARTMENT OF SURGERY, CONNAUGHT HOSPITAL, FREETOWN, SIERRA LEONE

ANDREW JOHNNEY
STATISTICS SIERRA LEONE (SSL), SECTION HEAD OF THE CENSUS, FREETOWN, SIERRA LEONE

ADAM L. KUSHNER, MD, MPH
DEPARTMENT OF SURGERY, COLUMBIA UNIVERSITY, NEW YORK, NEW YORK, USA
DEPT. INTERNATIONAL HEALTH, JOHNS HOPKINS HOSPITAL, BALTIMORE, USA
SURGEONS OVERSEAS (SOS), NEW YORK, USA

LUCIE BLOK MD, MPH
ROYAL TROPICAL INSTITUTE, AMSTERDAM, THE NETHERLANDS

Corresponding author:
Reinou S. Groen, MD, MIH, PhD
rsgroen@hotmail.com
rgroen1@jhmi.edu

PhD theses 2007–2013

PHD THESES IN THE NETHERLANDS IN THE FIELD OF TROPICAL MEDICINE & INTERNATIONAL HEALTH (2007–2013)

INTRODUCTION

PhD theses can be seen as the highlights in academic research and as a reflection of the main scientific activities. This is also the case in the field of Tropical Medicine & International Health. By showing what is happening, this field can make their mark. In this paper the results are presented of an analysis of theses defended at Dutch universities between 2007-2013.

Tropical Medicine and International Health is not a precisely defined area. Therefore it was decided to include theses with subjects which are discussed regularly at the biannual European Congresses on Tropical Medicine and International Health (ECTMIH). In general theses have been excluded when data collection was not done in a low- or middle-income country or among multi-ethnic populations in high-income countries.

METHOD

The scientific agendas of the Dutch universities from 2007-2013 have been scrutinized regarding titles and advisors (promotores) that could be relevant to our goal. Controls were performed through searching PhD databases (Alba Promotorum) with keywords like chairholders in this field of research, country names, or diseases. For this analysis the theses themselves were not studied. The selected theses can be found on http://www.nvtg.org/index.php?id=117. Because of the search strategy, laboratory studies performed in the Netherlands e.g in the field of molecular biology and immunology may be underrepresented.

RESULTS

A total of 239 theses was found. (Table 1) The majority has as subject infectious diseases and parasitology (52.3%). Theses in the field of anthropology are well-represented with 7.9%.

Over the years the number of theses has increased. The University of Amsterdam and Radboud University together produced almost 60% of all theses. (Table 2) The majority of the PhD students were women (52.3 %, data not shown).

Table 1 **Overview main subjects of theses Tropical Medicine & International Health 2007 – 2013 (N= 239)**

Subject	n	%
Infectious diseases[1]		
• HIV/AIDS, incl. HIV in pregnancy	27	11.3
• HIV co-infection	11	4.6
• Malaria, incl. malaria in pregnancy	24	10.0
• Tuberculosis[2]	22	9.2
• Leprosy	8	3.3
• Dengue	3	1.3
• Schistosomiasis	2	0.8
• Leptospirosis	2	0.8
• Other	16	6.7
• Parasitology	10	4.2
Obstetrics and gynaecology	11	4.6
Pediatric diseases	11	4.6
Dermatological diseases[3]	6	2.5
Mental health	4	1.7
Non-communicable diseases	2	0.8
Nutrition	5	2.1
Health of migrants/refugees in Europe	10	4.2
Travel medicine	3	1.3
Health economics	11	4.6
Health policy	4	1.7
Public health/health systems	13	5.4
Reproductive health	10	4.2
Medical education	2	0.8
Anthropology	19	7.9
Other	3	1.3

[1]epidemiology, control and prevention included; laboratory research in the Netherlands with referral to populations in low-income countries included; parasitology, nutrition, health economics excluded; [2]non-tuberculous mycobacteria included; [3]leprosy excluded.

Table 2 **Number of theses Tropical Medicine and International Health 2007-2013 by university and year**

	2007	2008	2009	2010	2011	2012	2013[1]	Total
Leiden		1	3	3		4	6	17
Groningen		2	5	1	2	5	2	17
UvA	11	11	8	12	19	18	25	104
Utrecht	3			1		5	1	10
VU		1	1		1	2	1	6
Rotterdam	4		4	3	4		2	17
Nijmegen	5	2	7	3	4	8	8	37
Maastricht				1	4	3	5	13
Wageningen			3	3	6	3	2	17
Tilburg		1						1
Total	23	18	31	27	40	48	52	239

[1]from January until October

DISCUSSION

These basic facts about the theses in tropical medicine and international health are not surprising. Over the years the number of theses has increased; the University of Amsterdam is the most important producer and infectious diseases are the most common topics.

But these facts leave many questions unanswered. They only describe, but do not explain. No information was collected about the selection of research projects, the selection of PhD candidates or the motivation of PhD candidates. Obviously these are important factors to fully understand the process.

Research projects are often part of a wider study or research programme and initiated by universities or research-related organizations. They also take the initiative to get these projects funded. Only a small part is initiated by an individual candidate. That is a difficult track and also difficult to fund.

The selection of PhD candidates is generally speaking done by the future PhD advisor (promotor).

One can expect that the advisor is interested in capable and motivated candidates with an interest in research. But in case of twinned projects the candidates may be selected on different grounds.

And finally the motivation of the candidate. It is known that a PhD often offers more career opportunities (application for medical specialist training position or partnership, academic career).

But the motivation can also be very personal (family, partner).

These questions can only be answered by studying the research programmes, questioning PhD advisors and candidates.

It is certain that experience from PhD thesis research is unique. The candidate is not only trained in many aspects of research, but has also gone through a personal development process. With this experience the candidates enter a new phase in their career. Since only 30% of all PhD candidates can stay at a university or in research-related activities (www.ru.nl/promovendi) it is clear that the majority continues with a clinical carreer or other positions in health care. At the last ECTMIH in Copenhagen it was discussed at a session organized by the German Society for Tropical Medicine and International Health, that for PhD candidates from low- and middle-income countries it is much more difficult to stay in science because of lack of funding and lack of a proper post-doc infrastructure.

In the strategic plan (2012-2016) of the Netherlands Society for Tropical Medicine & International Health (NVTG) a vision has been formulated on promoting research in this field. This overview can offer tools for a more active cooperation of the Society with certain research areas which up to now have not been well covered. Maybe doctors and tropical doctors in residence who are interested in a PhD track will be encouraged to see that annually around 40 candidates take this step.

HANS WENDTE, MD, PHD
RETIRED PUBLIC HEALTH SPECIALIST
HANSWENDTE45@GMAIL.COM

PhD theses obstetrics and gynaecology and the influence of endowed chairs (1945–2013)

INTRODUCTION

During the period 1945-2013, 56 theses in the field of obstetrics and gynaecology in low-income countries, were defended at Dutch universities. These theses will be described by numbers and subjects, by continent, by university, and by departments of their PhD-supervisor. In that period two endowed chairs were established which are related to this field. First the chair of International and National Aspects of Safe Motherhood at the VUmc (2007- 2012) and second the chair of Tropical Child Health at the AMC (1998-2013). The question is how these endowed chairs have contributed to the production of PhD theses.

METHOD

The theses were defined as having as subjects obstetrics and/or gynaecology or subjects closely related to these, mainly researched in low-income countries between 1945-2013 and defended at Dutch universities.

Obstetric and gynaecology subjects were defined according to the contents of current textbooks on the subject or well-known textbooks especially focused on the tropical environment.

A search has been done on subject and chairholder of the departments of obstetrics/gynaecology in existing databases of Dutch universities. Controls were performed through the registration of PhD-dissertations by Zuidema (NvTG 1958-1981), Wendte (NvTG-site 2007-2013) and the database of the NVOG (1945-2013).

Table 1 **Some characteristics of obstetric/gynaecology theses defended at Dutch universities 1945 – 2013 (N=56)**

	1945 – 1982	1983 –2013	Total
Gynaecology	4	14	18
Subtopics[1]			
• reproductive health	3	9	
• HIV/AIDS	-	3	
• urinary tract fistulae/surgery	-	2	
• malignancy	-	1	
• abnormal sexual development	-	1	
• endocrinology	1	1	
Obstetrics	8	30	38
Subtopics[1]			
• traditional maternal health care	-	2	
• antenatal/maternal health care	3	7	
• perinatal health and health care	1	2	
• HIV/AIDS	-	1	
• malaria in pregnancy	1	10	
• obstetrical complications	3	8	
• haematology	-	1	
Universities			
University of Amsterdam	7	18	25
Leiden	1	6	7
Nijmegen	1	5	6
Free University Amsterdam	–	6	6
Utrecht	2	3	5
Groningen	–	2	2
Rotterdam	1	1	2
Maastricht	–	2	2
Wageningen	–	1	1
Departments responsible			
Obstetrics and gynaecology	6	19	25
Paediatrics	1	11	12
Tropical medicine/infectious diseases	1	6	7
Other (e.g. public health, nutrition)	4	8	12

[1] Since some theses cover more subjects the total of subtopics is > 56.

It was decided to start the analysis in 1945 as being the end of the colonial period and the beginning of the period of development aid. This period has been divided in 1945-1982 and 1983-2013. The reason is that generally speaking in the first period a PhD-project and the subject was often initiated by a PhD-candidate her-/himself, often at their own expense. In the second period PhD-projects have often been part of a wider and officially approved research programme and projects with application procedures for funding.

RESULTS

The findings are presented in Table 1.

The majority of the theses refer to research projects carried out in Africa (40/56, 70.1 %, data not shown); the remaining research has been carried out in Asia, Central America/the Caribbean and Europe.

DISCUSSION

The period 1983-2013 clearly has more dissertations probably due to an improved PhD structure.

The gynaecological subjects mainly deal with reproductive health issues; the majority of the obstetrical theses cover an obstetrical subject with roughly the contents as shown in the overview. In general more often health care issues have been chosen than the health of mother and child itself.

The University of Amsterdam hosted most of the defences like Wendte has already shown in his paper. It is tempting to suggest that PhD infrastructure in Amsterdam with the Royal Tropical Institute and the Departments of Tropical Medicine and the Global Child Health Group has stimulated this. The establishment of endowed Chairs in International and National Aspects of Safe Motherhood at the Free University of Amsterdam (2007) and in Tropical Child Health at the University of Amsterdam (1998) has clearly been successful in contributing to quite a few of the theses.

Many questions are still unanswered. In particular the question how obs.gyn PhD-candidates continued their career. An interesting question is also what happened with their recommendations.

CONCLUSION

Preparing and subsequently defending a thesis is not an easy thing to do. Especially for young tropical doctors. The workload in hospitals does not leave the doctor much time. The circumstances are difficult and resources limited. It is therefore highly commendable that quite a few have succeeded in doing so. This analysis shows that it has been possible in the past, but also to date.

FUTURE TROPICAL DOCTORS WHO CONSIDER TO ENGAGE ON A PHD-ROUTE SHOULD BE ENCOURAGED

This analysis also shows that establishing and supporting an endowed chair in Tropical Obstetrics and Gynaecology or Tropical Child Health, as has been done by the NVTG (Netherlands Society for Tropical Medicine) and The Netherlands Foundation for International Child Health has been successful.

Acknowledgements
I would like to thank Hans Wendte for his help and suggestions in preparing this analysis and the librarians of the VUmc, the AMC, the S.LucasAndreas and Spaarne hospitals for their assistance in tracing and recovering these dissertations.

DRIES VAN DER MEULEN, MD
OBSTETRICIAN/GYNAECOLOGIST N.P. TEACHING RESPONSIBILITIES, ERASMUS UNIVERSITEIT ROTTERDAM
VANDERMEULEN.A@TELFORT.NL

COLOPHON

MT Bulletin of the Netherlands Society for Tropical Medicine and International Health

ISSN 0166-9303

Chief editor
Hans Wendte

Editorial board
Joost Commandeur
Maarten Dekker
Esther Jurgens
Steven Smits
Silvia de Weerdt
Ed Zijlstra

Language editing
Elsa van Gelderen

Cover photo
Hanneke de Vries
Photo p 3 Wikipedia

design
Mevrouw VANMULKEN
Amsterdam

MY EXPERIENCE AS A PHD STUDENT

Interview with Linda Wammes, MD, PhD

CV

L.J. (LINDA) WAMMES
Born 1980, Woerden, the Netherlands

2005: MSc in Biomedical Sciences (Leiden University)

2007: MD (Leiden University)

2013: PhD: Immune Regulation during Parasitic Infections: from bench to field. (Collaborative project between the Leiden Parasite Immunology Group, Leiden University, the Netherlands and the Helminth Group, University of Indonesia, Jakarta, Indonesia)

2011 – present: Chair Uniting Streams (www.unitingstreams.com)

2013 – present: Resident in Clinical Microbiology, Erasmus Medical Center, Rotterdam

What is the subject of your PhD thesis?

Together with two other Indonesian PhD students, I was involved in a research project about immunoepidemiology of helminth and malaria infections. Among other studies, we performed a double blind, placebo-controlled, household-randomized trial in two villages on the island of Flores, Indonesia.

What are the main conclusions of your study?

We have shown that regulatory T cells (Tregs) were involved in immune suppression during helminth and malaria infections in humans. These Tregs are able to suppress immunologic reactions to other infections and vaccinations, like the BCG vaccine. With our trial we showed that eradication of helminths led to an increase of immune reactions in human hosts, together with increased prevalence of allergy (measured by skin prick tests). This could mean that deworming could lead to more inflammatory diseases in these populations.

How did you become interested in doing research in the field of tropical medicine?

My first experience with research in the tropics was during my study Biomedical Sciences, when I participated in a study on

perinatal mortality in Kigoma, Tanzania. I have always had a fascination for the clinical and biological aspects of infectious diseases and the power to answer relevant questions out of daily practice through science. This PhD project was the perfect opportunity for me to combine all these interests.

What were your first experiences in the field?

I knew from my experiences in Tanzania that the first weeks would be very intense and difficult. Though I did a short language course, I could not communicate fully with the local people. After one month of preparation in Jakarta, we moved to a small village on the Island of Flores. I was happy that my two Indonesian PhD colleagues accompanied me, because the locals did not speak any English and there were hardly any resources, nor internet. We built up our lab from scratch, but also had to collect the faeces samples in the two villages by motorbike.

In the beginning it took a lot of effort to explain our work to the locals. But after a while we got used to the situation and with some more support from the research team in Jakarta, we got over our frustrations and could look back on a great experience.

What were your biggest challenges?

Language and culture barriers were the biggest initial complicating factors. Later I also experienced ethical dilemmas, like when we gave half of these very friendly and co-operative people placebo pills. I am very grateful to the local people. Without them we would not have been able to investigate this very important and relevant subject.

What are the positive aspects of doing research in tropical settings?

First and foremost to work with an international team in a totally different environment and culture. I really enjoyed it, but also learned a lot personally and professionally. After the initial frustrations I really learned to be more patient, flexible and inventive. I could never have gained these experiences in another setting.

What is the added value of doing research in the tropics?

It is a unique possibility to set up and perform basic and relevant research in resource-poor settings. It will widen your vision on the world and will teach you to put things in perspective. Doing research could also be an interesting option for doctors who are more interested in working abroad in a non-clinical setting.

Research will contribute to capacity building among local health workers and the results can be used worldwide. For example, the results of our study led to recent trials in which is investigated if people with asthma or allergies could benefit from helminth infections.

Is there a future for PhD students in tropical medicine and international health?

At this moment most research is still performed in places where the global burden of disease is the lowest. There is, however, a great need for capacity building in low-resource settings. Both foreign and local research will benefit from doing research in low-income countries.

To promote this message I became chairman of Uniting Streams, a workgroup and platform for field research in International Medicine of the Netherlands Society for Tropical Medicine and International Health. Through providing information and sharing experiences from the field we try to make people more enthusiastic about research abroad.

MAARTEN DEKKER, MD
RESIDENT TROPICAL MEDICINE
M.DEKKER.VU@GMAIL.COM

SCIENTIFIC PUBLISHING: DOES THE DUTCH RESEARCH COMMUNITY REACH THOSE MOST IN NEED?

INTRODUCTION

In this contribution on scientific publishing some issues of particular relevance to international health are highlighted, from the perspective of an editor of *Tropical Medicine and International Health*, the official journal of the *Federation of European Societies for Tropical Medicine and International Health* (FESTMIH).
It is of course very important that research findings are shared with the scientific community, fellow researchers, programme managers, policy makers, but also with workers in the medical field, particularly in low-resource countries in the domain of tropical medicine and international health. While an evidence-base for tropical medicine is of importance to workers in this field, the evidence for public health interventions can usually not be immediately translated into practice by individual public health practitioners, but require the action of policy makers and programme managers.

ACCESSIBILITY OF SCIENTIFIC PUBLICATIONS

As scientific journals must be financially viable, the cost of publication (in print or on-line) must either be borne by readers (subscription fee) or by the authors (page fee). The latter is called "open access", although in this case access is not free of charge for authors. It is clear that this can be an obstacle for authors from low-income countries to publish. Some journals are entirely sponsored by societies or otherwise (e.g. *Memórias do Instituto Oswaldo Cruz*), others have a mixed model (e.g. *Tropical Medicine & International Health*). An increasing number of agencies funding research from public funds, demand "open access", and will include page charges for researchers in their grants.

Journals can be accessed through Medline or Pubmed for a fee, or through on-line access paid for by scientific institutions. SciELO (Scientific Electronic Library Online) is a Spanish-Portuguese language equivalent serving Latin America.

The HINARI (http://www.who.int/hinari/en/) Access to Research in Health Programme was launched in January 2002 by WHO together with major publishers to enable local, not-for-profit institutions in low- and middle-income countries to gain access to one of the world's largest collections of biomedical and social science literature, and in turn, contribute to improve world health.

Among the top 10 journals in the area of tropical medicine and international health all but one (Memórias do Instituto Oswaldo Cruz, Brasil) originate from Europe or the USA. Some initiatives attempt to counterbalance this: African Journals Online (http://www.ajol.info/) thrives to make African-origin research output available to Africans and to the rest of the world. Asia Journals Online (http://www.asiajol.info/) is a similar portal to scholarly journals published in South and S.E. Asia.

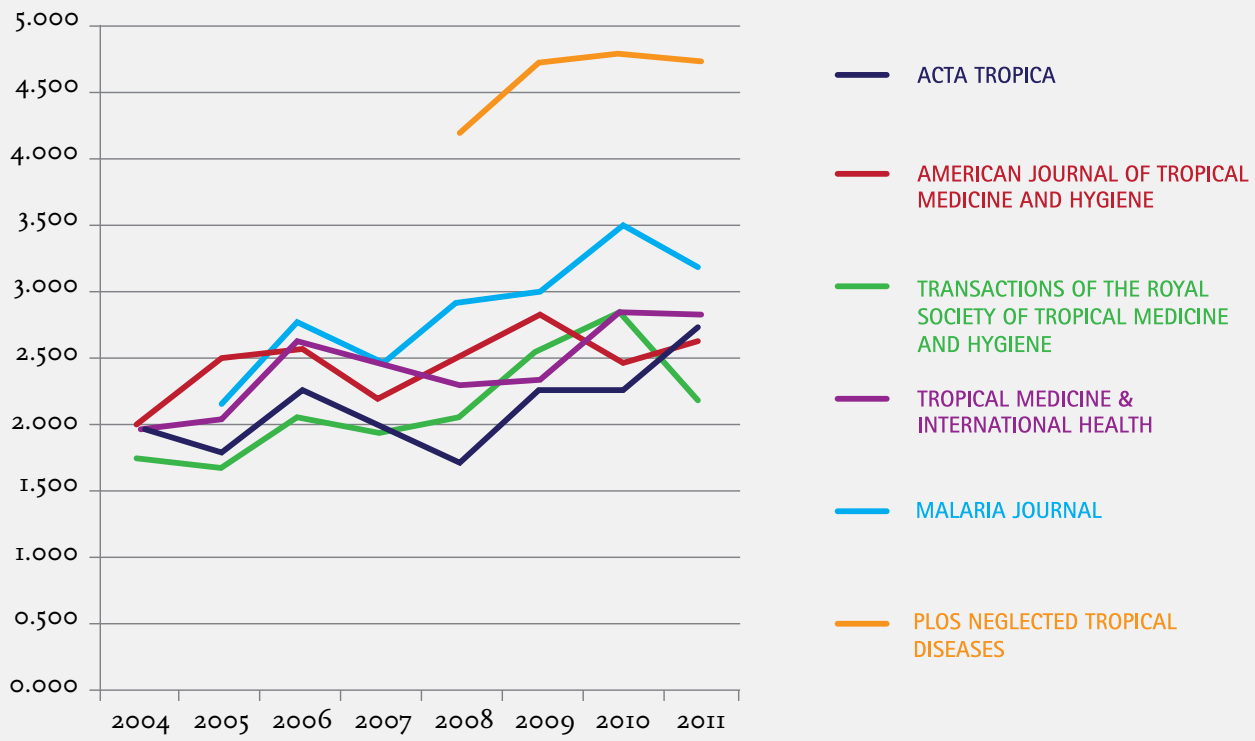
QUALITY OF SCIENTIFIC PUBLICATIONS

The quality of scientific research is assured in various ways. Peer review is the cornerstone of quality assurance. In addition various journal ranking systems are operational: the Impact Factor of the ISI Web of Knowledge, the SJC Factor of SCOPUS and Google Scholar Metrics.

The impact factor (IF) is determined by the average number of citations per original research article over the first two calendar years. It can also be summarized by scientific institution and by researcher; some academic institutions use the IF for the continuous assessment of staff, departments and research groups.

While easy to calculate, the IF does not reflect societal relevance or public utility of a scientific publication. An alternative is hard to find; to some extent the number of downloads of an article reflects public utility. As far as "relevance" or "impact" goes, the most relevant journal is the one that gets an article in the hands of the most people who will use the findings as evidence-base in their work as policy makers, programme managers and health practitioners.

Figure 1 Impact factor of TMIH compared with other journals in the same field (editors report TMIH 2011)



CHALLENGES TO USE RESEARCH EVIDENCE

There is widespread evidence of failure to implement health interventions that have been demonstrated to be cost-effective by high-quality research. Low-income countries face additional challenges to using research evidence including: the weakness of their health systems and a lack of access to evidence; operational research requires much more attention, as it can reveal hindrances, and remedies, for implementation of health interventions.

Scientific publishers and editorial boards can to some extent improve societal relevance of published research, for instance by providing a forum for operational research.

Publishers can play a more substantive role by providing "open access", joining HINARI, and/or waiving fees for downloading published material (some journals allow free access twelve months after publication or of selected key materials, e.g. Tropical Medicine and International Health).

Funding agencies and programme managers (e.g. through research priority setting workshops), however, remain more directly influential in steering the research agenda.

CONCLUSION

In comparison with the Belgian and German societies, a considerable number (142 of 988) NVTG members have a personal TMIH subscription (36 hardcopy, 106 on-line). In addition, students and staff members of academic institutions have on-line access through their institutions. As co-authors of original research and surely as authors of editorials and reviews, however, the Dutch are lagging behind, while the Dutch are leaders in various areas of tropical medicine, safe motherhood and sexual and reproductive health. May this serve as a call to Dutch experts in tropical medicine and international health to fill this gap!

HENRI A.G.H. VAN ASTEN, MD, MPH
EXPERT INTERNATIONAL PUBLIC HEALTH RADBOUD UNIVERSITY MEDICAL CENTRE
EDITOR TROPICAL MEDICINE & INTERNATIONAL HEALTH
HENRI.VANASTEN@RADBOUDUMC.NL

REFERENCES

1. Mgone C, Volmink J, Coles D, Makanga M, Jaffar S, Sewankambo N. Linking research and development to strengthen health systems in Africa. Trop Med Int Health 2010; 15: 1404–06.
2. Haines A, Kuruvilla S & Borchert M (2004) Bridging the implementation gap between knowledge and action for health. Bulletin of the World Health Organization 82, 724-731. Discussion 732.

A young girl presenting bowing of the lower legs

The X-ray of the left lower leg showed anterior bending of the diaphysis of the tibia with signs of microfractures and an old fracture. The fracture could have caused the more pronounced bending of the left leg. Besides the old fracture and the anterior bending, no other abnormalities were observed.

SETTING

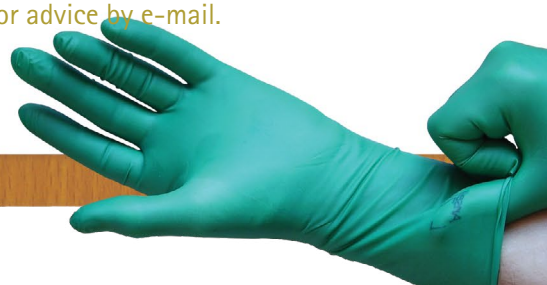
The **Haydom Lutheran Hospital** is located in the North of Tanzania, around 300 km southwest of Arusha. It is the largest hospital in the Mbulu area, with more than 400 beds, serving around 300,000 people directly and 2 million as referral hospital. There are 700 staff members including 10-15 doctors. The nearest referral hospitals are in Arusha, six hours away by car. The hospital provides a limited number of laboratory tests, X-rays and a CT-scan (which is often not functioning). There are four major operating theatres with basic facilities. Trauma surgery is performed almost on a daily basis by an orthopaedic clinical officer or by visiting doctors from abroad. Screws, plates and nails are available.

CASE REPORT

A seven-year-old girl was seen in the outpatient department. She presented with malformations of both lower legs, which had been present since birth. There was no recent trauma. A fracture of the left tibia, due to a minor trauma one year ago, had negatively influenced her mobility and currently she was only able to walk a few metres. Further development was normal, besides a relatively short stature.

On physical examination a healthy-looking girl was observed. There were no signs of mental retardation. In both legs, anterior bending of the lower leg was observed. The left lower leg was bent about 90 degrees. The right lower leg was bent about 20 degrees. Neurological examination of both legs was normal. No other abnormalities were observed in other bones or joints.

In conclusion, a young girl presented with disabling (probably congenital) malformations of both lower legs and a short stature. The initial differential diagnosis included osteitis deformans, rickets and osteogenesis imperfecta. Because of the limited diagnostic and treatment options in Haydom Lutheran Hospital, the specialists of Consult Online were asked for advice by e-mail.



ADVICE FROM THE SPECIALISTS

Differential diagnosis

Four specialists replied within two days. The e-mail was also sent to a travelling orthopaedic specialist who would visit Tanzania shortly. One of the specialists had treated a patient with similar malformations and suggested it might derive from congenital syphilis. Others thought that fluorosis or rickets may cause these malformations. Concluding, congenital syphilis and fluorosis were added to the differential diagnosis. The probability of these diagnoses will be discussed shortly.

Congenital syphilis is syphilis which is present in utero or at birth. One of the many possible clinical features is bone malformation. The stages of bone involvement vary considerably [1]. It may involve isolated syphilitic periostitis; however, metaphysitis and osteitis often occur concomitantly. Late effects are most commonly observed on the tibia. Rarely, the "sabre" tibia, also known as "sabre" shin, may be seen as the result of thickening of the anterior aspect of the tibia. Radiographically this appears as cortical sclerosis [1].

Fluorosis is an acquired disorder caused by high-level exposure to fluoride, resulting in dental malformations, skeletal symptoms and gastrointestinal complaints. Normally the dental manifestations precede the skeletal symptoms. Skeletal fluorosis most often manifests as stiffness, pain in the joints and bone changes including osteomalacia, osteoporosis, exostoses and osteoarthritis [2]. Since the presented patient had bone malformations which were present at birth without the described dental deviations and/or stiffness and pain in the joints, fluorosis seems to be unlikely.

Osteogenesis imperfecta is a group of autosomal dominant inherited collagen disorders which mainly affects the bones, but shows a wide spectrum of clinical manifestations. The most severe form of osteogenesis imperfecta is characterized by bone deformations resulting from multiple fractures. One of the possible malformations is bowing of the tibia. Bowing without preceding fractures is unlikely [3].

Osteitis deformans, also known as Paget's disease, is a chronic condition of the bone characterized by a disorder of the normal bone remodelling process. It normally starts after the 5th decade of life. Symptoms are local pain, easy fractures and asymmetrical bone deformations. Patches of bone thickening are sometimes observed radiographically [4]. As our patient was only seven years old and her condition started with symmetrical isolated tibia bowing, Paget's disease seems unlikely.

Rickets is a condition of the bone caused by vitamin D and calcium deficiency. The primary defect is inadequate mineralization of the osteoid. Rickets is often seen in young children including neonates. The first symptoms are craniotabes, ankle and wrist swelling, and leg deformities. The most typical leg deformity is acquired and manifests as leg bowing (genu varum). However, genu valgum, windswept deformities and bowing of the long bones occur as well. Sometimes isolated tibia bowing is observed [5]. The absence of other manifestations makes neonatal rickets unlikely.

Our literature research revealed Weismann-Netter syndrome as another cause of isolated "sabre" tibia. Since it was described in 1954, more that 100 case reports have been published. The Weismann-Netter syndrome is characterized by short stature, anterior bowing of the tibia and fibula, increased mass of the fibula, and posterior cortical thickening of both bones in the lower leg [7]. In several case reports the Weismann-Netter syndrome was accompanied by mental retardation. The aetiology of the syndrome is unknown, but the incidence of familial cases suggests a genetic component [7].

In summary, it is not easy to determine which underlying cause is responsible for the bone malformation in the presented patient; especially since not all diagnostic tools were present. In our opinion the Weismann-Netter syndrome is probably the most likely diagnosis because of the presence since birth and the short stature.

SUGGESTIONS FOR MANAGEMENT

As the malformations seemed to be isolated and not progressive, the need for an exact diagnosis was not considered as the first priority. All specialists shared the opinion that an operation would be difficult but inevitable. On the X-ray no contraindications for orthopaedic surgery were seen.

Because of the disabling curvature all specialists agreed that the left lower leg should be operated (first). Concerning the right leg, they agreed on an expectative management at that moment. One specialist suggested that the curvature of the right leg might even decrease during growth. Depending on the available materials and the surgical skills of the local doctors different treatment options were suggested.

To correct the curvature of the left leg, the only option would be a wedge osteotomy of both the tibia and the fibula. Two big challenges must be faced: the condition of the soft tissue and the stabilization of the bone structures after surgery.

Concerning the soft tissue, two options were discussed: performing the wedge osteotomy with or without shortening of the lower leg. If one does not shorten the lower leg the traction on the soft tissue on the dorsal side of the lower leg may lead to high tension and necrosis. Incisions could reduce the tissue tension, but it was highly doubted this tension reduction would be sufficient. The safer option would be the combination of the wedge osteotomy with a shortening procedure. The biggest disadvantage of this technique would be the possible function loss of the extension muscles of the foot, as the soft tissue on the ventral side would be too long. If function loss would appear, one could try to treat this with a plaster cast or splint.

The second problem is the stabilization after surgery. One could choose to use a plaster cast which does not inflict any soft tissue damage, but often results in insufficient stability. The second option is external fixation. This leaves the wound in sight and can be used in combination with a leg splint to increase

stability. Moreover, it offers the opportunity to adjust the bone position postoperatively. The third option would be internal fixation using osteosynthesis material (e.g. a plate, large bore K-wire, Rush pin or Steinmann pin). This would result in good osseal stability but could cause more soft tissue damage.

The osteotomy with or without shortening of the leg is a difficult procedure and the postoperative complications can be severe. If there is no doctor with sufficient surgical skills, no adequate postoperative care and/or no possibility to refer the patient, an amputation of the left lower leg under the knee joint is a worst-case option. This is only acceptable if it is believed to improve the patient's condition, there are no better alternatives, and adequate prostheses are available. The operation itself is less complicated and the postoperative recovery and revalidation are less difficult compared to the options mentioned above.

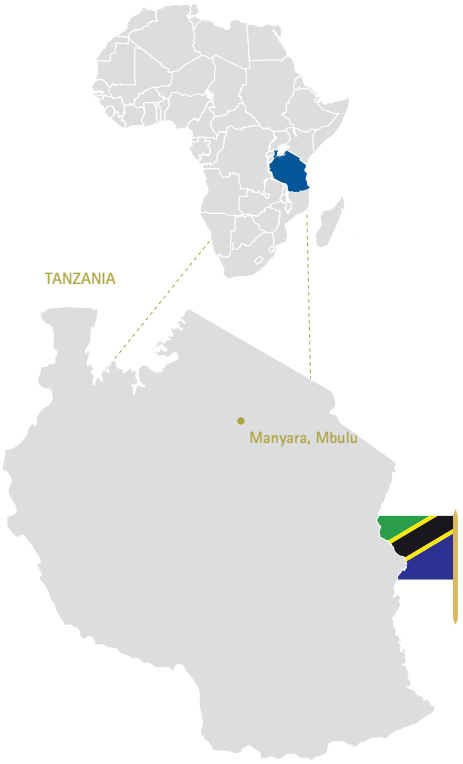
CASE REPORT – FOLLOW UP

A visiting tropical doctor from the Netherlands discussed the treatment options with the father of the young girl. He concluded that in order to improve the patient's condition and to prevent new fractures, the patient should be operated on by a surgeon with experience in this kind of malformations.

The preferred method would be multiple osteotomies and intramedullary fixation (the "shish kebab technique"). A Dutch orthopaedic surgeon which was contacted by the specialists of Consult Online would be able to do such an operation in Arusha a couple of weeks later. The costs would be taken care of.

After the treatment options had been discussed, the father explained that they did not come for an operation. They only required a written letter from a doctor that explained the condition of the child. Without this letter the girl was not allowed to go to school. According to the father it would not be a big problem if his daughter was not able to walk in the future: 'We are happy with her the way she is and she is happy too.'

Both the requested letter for the school and a referral letter containing all the clinical information were written and given to the father. If the family ever changed their mind, they would possess the information on the treatment options. After the final consultation father and daughter returned to the small village where they lived.



REFERENCES

1. Palmer and Reeder, The Imaging of Tropical Diseases, with Epidemiological, Pathological and Clinical Correlation, 2nd edition, ISBN 3540662197, Springer 2001.
2. Gilber, A Small Dose of Toxicology, 2nd Edition, ebook 2011Castriota-Scanderbeg, Abnormal Skeletal Phenotypes: From Simple Signs to Complex Diagnoses, 1st edition, ISBN 3540679979, Springer 2005.
3. Van der Meer, Interne geneeskunde, 13th edition, ISBN 9031341789, Springer 2008.
4. Van der Brand, Kindergeneeskunde, 3de druk, ISBN 9035227115, Elsevier/Bunge 1998.
5. Weismann-Netter and Stuhl. Congenital osteopathy eventually familial defined especially by antero-posterior incurvation and thickening of both bones of the leg; diaphyseal tibio-peroneal toxopachyostosis. Presse Med. 1954;62:1618–1622.
6. Peippo et al., Weismann-Netter syndrome and mental retardation: a new patient and review of the literature. Am J Med Genet A. 2009;149A(11):2593-601

LOIC DE JONGH
RESIDENT TROPICAL MEDICINE, CONSULT ONLINE

KIRSTEN KORTEKAAS
MEDICAL RESIDENT, HAYDOM LUTHERAN HOSPITAL, TANZANIA

ISAACK MALLEYECK
ORTHOPAEDIC ASSISTENT, MEDICAL OFFICER, HAYDOM LUTHERAN HOSPITAL, TANZANIA

MATTHIJS BOTMAN
RESIDENT IN PLASTIC, RECONSTRUCTIVE AND HANDSURGERY VUMC

CONSULTONLINE@TROPENOPLEIDING.NL

The importance of the first step: Neurology Training in Tanzania

Up to 2013, Tanzania was a country without a national neurology training programme with arguably the lowest number of neurologists per 100,000 population (0.009/100,000; a total of 4 neurologists). All current Tanzanian neurologists were trained abroad, but the only viable solution in the future will be training within the country.
To develop a post-graduate neurology training programme within Tanzania would be a long-lasting investment in improving 'brain health' in one of the world's lowest-income countries.

BACKGROUND

Neurological disorders are an important source of morbidity and mortality [1]. They account for 7% of the burden of disease worldwide, which is only slightly less than the combination of HIV/AIDS, Malaria and Tuberculosis [1,2]. Likewise, neurological disease makes up a significant proportion of in-patient hospitalizations. Among neurological conditions, stroke, migraine and epilepsy are responsible for the largest burden of disease. Despite this substantial disease burden, the necessary human resources to solve this major health problem are still almost entirely lacking.

THE WHO RECOMMENDS A RATIO OF BETWEEN 1 AND 5 NEUROLOGISTS PER 100,000 POPULATION

Also, as in various other low-resource countries, the overall lack of diagnostic and therapeutic resources in Tanzania severely limits quality of health. For example, epilepsy is a prevalent disorder in Eastern Africa, but in a large survey the majority of individuals with epilepsy in the East African Community (EAC) was not on any anti-epileptic drug [1,3,4]. However, it is reasonable to assume that as soon as adequate human resources are available, epilepsy treatment rates will improve substantially [5].

NEUROLOGY CAPACITY IN EAST AFRICA: PRESENT AND FUTURE

To date, prospects for improving the number of neurologists in the EAC have been poor: presently there are no nationwide neurology training programmes in all of East Africa, which is directly reflected by the number of neurologists. The geographically nearest adult and child neurology post-graduate training programmes are in South Africa. Neurologists who are currently in practice in the EAC have all been trained in South Africa, Europe and the United States. The World Health Organization (WHO) recommends a ratio of between 1 and 5 neurologists per 100,000 population [6,7,8]. Whereas for instance the United States and many European countries have >5 neurologists per 100,000 population, Kenya has 0.025 neurologists per 100,000 population (a total of 10 neurologists in active clinical practice). Similarly, Uganda has 0.018 neurologists per 100,000 population (a total of 5 in clinical practice) [6,7,8] and Tanzania only 0.009 per 100,000 population (a total of 4 in clinical practice).

In Tanzania, all neurologists work in the two academic centres of the country, being Muhimbili University School of Health and Associated Sciences (MUHAS) in Dar-es-Salaam, and Kilimanjaro Christian Medical Centre (KCMC) in Moshi, Northern Tanzania. Two neurologists have passed retirement age but continue to work, partly because there is simply no one to take over. Three more internal medicine specialists are in various stages of neurology training, which is an ad hoc programme driven by the availability of temporary funds. Paediatric neurology remains out of the focus of this description, but is even worse off in terms of capacity.

As mentioned before the WHO recommends a ratio of between 1 and 5 neurologists per 100,000 population [6,7,8]. Thus in Kenya, between 400 and 2,000 neurologists would be needed and in Uganda, between 330 and 1,650. According to this calculation, Tanzania with even fewer neurologists and the largest population of the EAC, will require anywhere between 500 and 2,500 neurologists. These goals are high, yet every new neurologist would mean a significant gain to Tanzanian health care.

PROGRAMME PLANNING OF POSTGRADUATE NEUROLOGY TRAINING

We propose to set up the Tanzanian Postgraduate Neurology Training, which will consist of an additional two years of neurology training for General Medicine specialists (these individuals have already received 3-4 years of specialist training). The first year of training will take place internally in Tanzania, consisting of specific clinical neurological patient care and becoming familiar with neurophysiological and neuroradiological diagnostic procedures. The second year of training will be spent in an academic hospital equipped with neurophysiological (EEG, EMG), neuroradiological (CT, MRI) and neurosurgery facilities, which will have to take place in a higher-resource country. Other regional training sites in East Africa such as relatively affluent Nairobi or even Addis Abeba are attractive in this respect and are 'African Neurology-proof' venues. Muhimbili University in Dar-es-Salaam, the country's largest city, has already entered a pilot MSc Clinical Neurology programme in collaboration

with Vellore, India. In order to optimalize training capacity, we intend to make this a nationwide programme.

CONCLUSION

As yet, there are no financial resources for the programme. Efforts are made in Tanzania but also EAC wide to reinforce this initiative, which has become an important focus in world neurology. The World Federation of Neurology is now involved and further discussion about the current situation has taken place during the World Conference on Neurology (Vienna, Austria Sept 21-26). After all, Tanzania is still the world's last large country without national neurology training facilities. If there is no first structural step towards future home-trained neurologists in a country like Tanzania, there will never be viable neurological patient care.

MARIEKE CJ DEKKER, MD, PHD
CONSULTANT NEUROLOGIST, KILIMANJARO CHRISTIAN MEDICAL CENTRE, MOSHI, TANZANIA / RADBOUD UNIVERSITY MEDICAL CENTRE, NIJMEGEN, THE NETHERLANDS
M.DEKKER@AIG.UMCN.NL

REFERENCES

1. Howlett W. Neurology in Africa. University of Bergen/Kilimanjaro Christian Medical centre, Moshi, 2012. Free download available. http://www.uib.no/cih/en/resources/neurology-in-africa
2. Murray C, Vos T, Lozano R, et al. Disability-adjusted life years (DALYs) for 291 diseases and injuries in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 2012;380:2197-2223.
3. Meyer A-C, Dua T, Ma J, Saxena S, Birbeck G. Global disparities in the epilepsy treatment gap: a systematic review. Bulletin of the World Health Organization 2010;80:260-266.
4. Mbuba C, Ngugi A, Newton C, Carter J. The epilepsy treatment gap in developing countries: A systematic review of the magnitude, causes and intervention strategies. Epilepsia 2008:vol; 1-13.
5. Feksi A. Epilepsy: A community approach. Tropical and Geographical Medicine 1993;45:221-222.
6. World Health Organization, World Federation of Neurology. Atlas: Country Resources for Neurological Disorders. Geneva, 2004.
7. Jowi J. Provision of Care to People with Epilepsy in Kenya. East African Medical Journal 2007;84:97-99.
8. Hooker J. Nurturing Neurology and Neuroscience in Kenya and East Africa - Some Reflections. Paper presented at: Kenya Association of Physicians Annual Scientific Conference 2013; Nairobi, Kenya.

NVTG

Membership of the **Netherlands Society for Tropical Medicine and International Health** (NVTG) runs from January 1st to December 31st and may commence at any time. Membership will be renewed automatically unless cancelled in writing before December 31st. Membership includes MT and International Health Alerts. An optional subscription to TM&IH carries an additional cost.

Non NVTG members can subscribe to MT through a student membership of the Society for € 22 per year by sending the registration form through our website **www.nvtg.org/lidworden** or by sending name and postal address by e-mail to **nvtg@xs4all.nl** or **MTredactie@xs4all.nl**.

Contributions and announcements should be submitted to the editorial office by e-mail: nvtg@xs4all.nl or MTredactie@xs4all.nl. Closing date for N° 01 / March 2014: 14-02-2014.

Disclaimer: all views expressed in this journal are of the authors only and are not necessarily shared by the editors of MT. Letters and articles may be edited for purposes of (clarity and) space.

Netherlands Society for Tropical Medicine and International Health
President: A.A.L.J. (Ankie) van den Broek
Secretary: M. Lagro
Secretariat: J.C. Hoppenbrouwer
P.O. Box 82
3738 ZM Maartensdijk
The Netherlands
+31(0)6-53515773
nvtg@xs4all.nl
www.nvtg.org

COTG (Concilium Opleiding Tropische Gezondheidszorg)
Sluiskade Noordzijde 96
7602 HW Almelo
+31(0)546-451765
concil@xs4all.nl

International Health Alerts

THE LATEST EDITION OF IHA CAN BE FOUND ON THE NVTG WEBSITE
www.nvtg.org