

Clinical Review

Clinical Review identifies issues in the medical literature of interest to clinicians in Africa. Essential references are given at the end of each section

Medicine

Neonatal sepsis

There is continuing interest in methods of identifying those acutely admitted medical patients who may be at increased risk of in-patient mortality. If this can be done accurately at an early stage, vigorous treatment may possibly improve outcome. Several scoring systems have been developed in western medical practice, but a recent report from Uganda suggests that a very simple measurement of nutritional status may be an accurate marker of hospital mortality risk.¹

In a group of 899 acutely ill adult medical patients, mid-upper arm circumference (MUAC) was measured. This is a simple marker of nutritional status recommended by the World Health Organisation (WHO). The MUAC ranged from 1.5 to 42.0 cm, and of the 50 patients with a circumference less than 20.0 cm, 12 (24%) died, with an Odds Ratio (OR) of 4.84. Of 237 patients with an MUA of over 28.0 cm only 6 (2.5%) died – OR 0.27. Thus, those with a MUAC below 20 cm were almost five times more likely to die in hospital than those with a MUAC over 28 cm.

This is a very interesting and practical study – in acutely ill patients other nutritional markers (for example body mass index) may be logistically difficult to measure, whereas mid-arm circumference is simple. Physicians in Africa should consider adopting this very appropriate risk measurement.

Zika virus and Africa

Zika virus has very much ‘hit the headlines’ in recent years, particularly related to South American epidemics, and its apparent association with microcephaly in the infants of mothers infected with the virus during pregnancy. Zika has also been identified in Africa, and recently cases have been identified in Luanda in Angola. A multi-national group of researchers have examined the potential for spread of Zika from Angola to other parts of Africa via air travel routes.²

Passenger routes and volumes from Luanda to other Africa cities were analysed, and other factors were included in the risk model such as seasonality of transmission and local occurrence of the *Aedes aegypti* mosquito necessary for Zika virus transmission.

The highest risk destinations for Zika transmission were Windhoek (Namibia), Maputo (Mozambique), Durban (South Africa), Kinshasa (DRC), and Nairobi (Kenya). Hopefully the Zika virus will not spread

widely throughout Africa, but this interesting study shows that air travel may contribute to this unwelcome possibility.

References

1. Fitzgerald E, Mlotha-Mitole R, Ciccone EJ, et al. A pediatric death audit in a large referral hospital in Malawi. *BMC Pediatr* 2018; 18:75.

HIV and hypertension

Anti-retroviral drug (ARVs) have revolutionised the outcome of HIV infection in Africa, but these drugs come with significant side-effects. From a metabolic viewpoint a number of ARVs can lead to central adiposity with associated glucose intolerance, dyslipidaemia and insulin resistance. Hypertension is also a potential outcome of these metabolic disturbances but has not been accurately quantified as a potential ARV adverse effect.

A study by workers from Nigeria and the United Kingdom³ has examined the prevalence of hypertension (BP >140/90) in a group of 1,524 ARV-naive HIV-infected adults, and also in the same group 12 months after initiation of ARV treatment. Before starting treatment 19.3% of patients were hypertensive, but after 12 months of ARV treatment this had risen to 50.2%. The rise in hypertension rate was associated with increased age and body mass index (BMI), but not the type of ARV treatment or markers of severity of HIV infection (CD4+ counts and viral load).

This study shows a striking rise in hypertension apparently associated with ARV treatment. There are obvious significant implications for future health resources in Africa.

Cholera burden in Africa

The continuing problem of cholera in Africa has recently been re-examined by a multi-national group of researchers using novel methodology.⁴ They examined cholera occurrence in 2,283 locations in 37 countries. Incidence was mapped and correlated with sanitation and fresh water supply. Over 140,000 cases of cholera were identified, and though these were widely distributed geographically, particularly high incidence areas were identified (defined as more than one case per 1,000 people). If these high incidence areas could be specifically targeted, a potential 38% reduction in overall cholera occurrence could be achieved.

What is particularly interesting about this research is that it mirrors the original work of John Snow in London in 1854. Snow related cholera cases with water supply, demonstrating for the first time the water-borne transmission of the disease. Over 160 years later, mapping technology is again being used to fight this continuing problematic disease.

References

1. Opio MO, Namujwiga T, Nakitende I, Kellett J, Brabrand M. The prediction of in-hospital mortality by mid-upper arm circumference: a prospective observational study of the association between mid-upper arm circumference and the outcome of acutely ill medical patients admitted to a resource-poor hospital in sub-Saharan Africa *Clinical Medicine* 2018; 18: 123-127
2. Kraemer MUG, Brady OJ, Watts A et al. Zika virus transmission in Angola and the potential for further spread to other Africa settings. *Trans Roy Soc Trop Med & Hyg* 2017; 111: 527-529
3. Isa SE, Kangombe AR, Simji GS et al. Hypertension in treated and untreated patients with HIV; a study from 2011 to 2013 at the Jos

University Teaching Hospital, Nigeria. *Trans Roy Soc Trop Med & Hyg* 2017; 111: 172-177

- 4 Lessler J, Moore SM, Luquero FJ et al. Mapping the burden of cholera in sub-Saharan Africa and implications for control : an analysis of data across geographical scales. *Lancet* 2018; 391:1908-1915

Public health

Which Neglected Tropical Diseases Can Be Eliminated by 2020?

Two things we need to note about the list of 20 diseases that the World Health Organization and partners classify as Neglected Tropical Diseases (NTDs).¹ First, diseases like Rabies, Snakebite/envenoming, and Leprosy, while certainly more common in the tropics now, have in the past been global in distribution. Secondly some of the diseases have not been neglected. Onchocerciasis or river blindness has been the focus of a global partnership since 1975,² and transmission in the Americas and much of the Sahel in Africa has been halted. Elimination of Dracunculiasis or Guinea Worm has also been the subject of many World Health Assembly Resolutions, and concerted effort has brought the number of cases down from 3.5 million in 1986 to 30 in 2017.³ What is more to the point about these diseases is that they affect neglected people,⁴ the poor and vulnerable in remote rural areas or urban slums.

Still, when we can compare NTD control programmes with the rise of major disease control efforts like the Global Fund to fight AIDS, Tuberculosis and Malaria, the President's Emergency Program For AIDS Relief, the President's Malaria Initiative, World Bank Malaria Booster Programme, Global A Vaccine Initiative among others, we can see that the global community has been able to focus major financial resources on a few diseases. Now with the Sustainable Development Goals, that focus expanded from infectious to Non-Communicable Diseases. It is natural therefore to fear that tropical health problems that are responsible for major loss of life and economic capacity will not be adequately addressed.

Based on the World Health Organization's 2020 Roadmap on NTDs,⁵ the London Declaration on NTDs recognised a 'tremendous opportunity to control or eliminate at least 10 of these devastating diseases by the end of the decade' (i.e. by 2020).⁶ These include eradication of Guinea worm disease, and elimination by 2020 of lymphatic filariasis (LF), leprosy, sleeping sickness (human African trypanosomiasis) and blinding trachoma. In addition drug access programmes should help control by 2020 schistosomiasis, soil-transmitted helminths (STH), Chagas disease, visceral leishmaniasis and river blindness (onchocerciasis).

Five of the diseases are notable in that they can either be controlled or eliminated through Mass Drug Administration (MDA) using Preventive Chemotherapy (PCT). This effort is aided by drug donation programmes at the global level and community based MDA at the local level. Ten companies were signatories to the London Declaration and contributed to drug donation programmes to achieve MDA.⁷ According to WHO,⁸

Preventive chemotherapy is aimed at optimising the largescale use of safe, single-dose medicines and offers the best means of reducing the extensive morbidity associated with four helminthiasis (lymphatic filariasis, onchocerciasis, schistosomiasis and soil-transmitted helminthiasis) (6). Additionally, the large-scale administration of azithromycin – a key component of the SAFE strategy for trachoma (that is, lid surgery (S), antibiotics to treat the community pool of infection (A), facial cleanliness (C) and environmental improvement (E)) – is amenable to close coordination and, in future, possibly co-administration with interventions targeted at helminthiasis.

Targets for the 5 PCT diseases vary. The aim is to eliminate LF and Trachoma by 2020. Although the efforts against onchocerciasis have been running the longest, the refocus from control to elimination meant increasing the geographical scope of intervention, and now elimination may not be feasible until 2025. With a focus mainly on the school aged and based populations, programmes against schistosomiasis and STH talk of control, not elimination, although some endemic countries hope that elimination may be possible if the focus of these programmes expands. So far, Togo is the only Sub-Saharan African country to have eliminated LF,⁹ and Ghana to have eliminated Trachoma.¹⁰

WHO lists the milestones towards validation of elimination beginning with stopping the spread of infection through mass drug administration, implementing MDA in all endemic areas (100% geographical coverage), reducing infection below a threshold at which transmission is not sustainable in all endemic areas and stop MDA, and finally demonstrating sustained reduction of infection below the threshold no earlier than four years after stopping MDA.¹¹ WHO also encourages countries to alleviate suffering by managing morbidity such as lymphedema and prevent disability.

By 2015 the partners providing PCT achieved a milestone. As WHO reports, 'Preventive chemotherapy is achievable, as proven by the increasing numbers of people being reached each year. In 2015, over 1.5 billion treatments were administered to almost 1 billion individuals for at least one of the targeted infections: lymphatic filariasis, onchocerciasis, schistosomiasis soil-transmitted helminthiasis and trachoma.¹² At a low cost – between US\$ 0.30 and US\$ 0.50 per person treated in most settings – preventive chemotherapy remains the most affordable, cost-effective strategy for controlling and eliminating these diseases.' WHO also explains that to be fully sustainable and to maximise impact, PCT should be combined and delivered with other interventions, including improving access to safe drinking-water, hygiene, disease management and vector control.

USAID as one of the major NTD partners has spent nearly \$700 million since 2006 to build the capacity of 33 endemic countries to plan and implement the MDA strategy for the five PCT diseases. By 2016, 'USAID-assisted NTD programmes had provided a total of more than 2 billion treatments in the respective countries, representing 935 million persons treated.'¹³ Over these

MDA not started	MDA started but not at scale	MDA scaled to all endemic IUs	Post-MDA surveillance	Eliminated as a public health problem
Eritrea Equatorial Guinea Gabon São Tomé and Príncipe South Sudan New Caledonia	Angola, Cameroon, Central African Republic, Chad, Comoros, Congo-Brazzaville, Congo-Kinshasa, Ethiopia, Guinea, Guinea-Bissau, Madagascar, Nigeria, Sudan Guyana Indonesia Papua New Guinea	Benin, Burkina Faso, Côte d'Ivoire, Ghana, Kenya, Liberia, Mali, Mozambique, Niger, Senegal, Sierra Leone, Zambia, Zimbabwe Dominican Republic, Haiti, India, Myanmar, Nepal, Timor Leste French Polynesia, Fiji, FSM, Lao PDR, Malaysia, Samoa, Brunei Darussalam, Philippines, Tuvalu	Malawi Brazil Yemen Bangladesh American Samoa, Kiribati, Palau, Vietnam, Wallis and Futuna	Togo Egypt Maldives, Sri Lanka Cambodia, Cook Islands, Marshall Islands, Niue, Thailand, Tonga, Vanuatu
(6)	(16)	(30)	(9)	(11)

MDA status of countries as of April 2018

years the number of persons living in implementation units (e.g. districts) that no longer require MDA has steadily increased. Of the 25 countries USAID has supported for LF MDA, 'Three had already stopped MDA treatment in 2015 (Togo, Cambodia, and Vietnam), Four were expected to stop MDA in 2017, and 10 more countries by 2020. There were eight countries where the date for stopping treatment was anticipated beyond 2020.' Likewise, 'Most countries are on track to reach WHO 2020 elimination goals for trachoma,' and nearly all countries shown anticipate reaching post-MDA surveillance by 2021.

In conclusion, Robollo and Bockarie remind us that, 'Interventions against neglected tropical diseases (NTD), including lymphatic filariasis (LF), (were) scaled up dramatically after the signing of the London Declaration (LD) in 2012... but some countries are considered not on track to meet the 2020 target using the recommended preventive chemotherapy and morbidity management strategies.' They believe that LF can be eliminated by 2020 'using cross-sectoral and integrated approaches' that incorporate the synergistic effect of the Sustainable Development Goals related to poverty reduction and water and sanitation.¹⁴

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References

- World Health Organization. Neglected Tropical Diseases. http://www.who.int/neglected_diseases/diseases/en/. Accessed 22 May 2018
- Boatin B. The Onchocerciasis Control Programme in West Africa (OCP). *Ann Trop Med Parasitol*. 2008 Sep;102 Suppl 1:13-7. doi: 10.1179/136485908X337427.
- Hopkins DR, Ruiz-Tiben E, Eberhard ML, Weiss A, Withers PC, Roy SL, Sienko DG. Dracunculiasis Eradication: Are We There Yet? *Am J Trop Med Hyg*. 2018 Jun 4. doi: 10.4269/ajtmh.18-0204. [Epub ahead of print]

- Rey JL, Milleliri JM. Derrière les maladies tropicales négligées, il y a des malades... trop négligés (Behind neglected tropical diseases are... neglected people with diseases). *Med Sante Trop*. 2016 May 1;26(2):116-7. doi: 10.1684/mst.2016.0576.
- World Health Organization. Implementing the WHO Roadmap on neglected tropical diseases – partners celebrate five years of collaboration. 30 January 2017, http://www.who.int/neglected_diseases/news/WHO_Roadmap_five_years_of_collaboration/en/
- Uniting to Combat Neglected Tropical Diseases. London Declaration on Neglected Tropical Diseases. 2012. http://unitingtocombatntds.org/wp-content/uploads/2017/11/london_declaration_on_ntds.pdf
- Cohen JP, Silva L, Cohen A, Awatin J, Sturgeon R. Progress Report on Neglected Tropical Disease Drug Donation Programs. *Clin Ther*. 2016 May;38(5):1193-204. doi: 10.1016/j.clinthera.2016.02.031. Epub 2016 Mar 31.
- WHO Department of Control of Neglected Tropical Diseases. Accelerating work to overcome the global impact of neglected tropical diseases – A roadmap for implementation. World Health Organization, 2012, Geneva, http://www.who.int/neglected_diseases/NTD_Road-Map_2012_Fullversion.pdf
- World Health Organization. Togo: first country in sub-Saharan Africa to eliminate lymphatic filariasis. 8 April 2017 | Brazzaville | Geneva. http://www.who.int/neglected_diseases/news/Togo_saying_good-bye_lymphatic_filariasis/en/
- World Health Organization. Ghana eliminates trachoma, freeing millions from suffering and blindness. 13 June 2018 | Brazzaville | Accra | Geneva. <http://www.afro.who.int/news/ghana-eliminates-trachoma-freeing-millions-suffering-and-blindness>
- Global Alliance to Eliminate Lymphatic Filariasis (GAELF). Progress to elimination. <http://www.gaelf.org/progress-elimination> accessed 20180612
- WHO/Department of control of neglected tropical diseases. Crossing the Billion. Preventive chemotherapy for neglected tropical diseases: lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiasis and trachoma. Editor: Dr G. Biswas, April 2017. ISBN: 978-92-4-069647-1 http://www.who.int/neglected_diseases/resources/9789240696471/en/
- Burnham G and Brieger W. USAID NEGLECTED TROPICAL DISEASE PROGRAM 2016 EVALUATION. United States Agency for International Development. Washington, March 2018 USAID Contract No. AID-OAA-C-14-00067; Evaluation Assignment Number: 185. <https://www.neglecteddiseases.gov/resources/newsroom/usaids-neglected-tropical-disease-program-2016-evaluation>
- Rebollo MP and Bockarie MJ. Can Lymphatic Filariasis Be Eliminated by 2020? *Trends in parasitology*, Volume 33, Issue 2, p 83–92, February 2017. [https://www.cell.com/trends/parasitology/fulltext/S1471-4922\(16\)30165-9](https://www.cell.com/trends/parasitology/fulltext/S1471-4922(16)30165-9)