Clinical Review

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

Paediatrics Review

Buruli ulcer

Buruli ulcer (BU) derives its name from work in the 1960s–1970s in Buruli County near Lake Kyoga, formed by the Nile delta in Northern Uganda. More recent studies have found many foci of infection in West Africa. However, *Mycobacterium ulcerans* was first cultured from a patient in Bairnsdale, Victoria, Australia in 1948. BU occurs in localised places in a number of tropical rainforest areas around swamps and river banks. It is transmitted through minor skin injuries after contact with water, soil, or vegetation.[1] Polymerase chain reaction (PCR) studies have detected *M ulcerans* in the salivary glands of water bugs and small fish.[1]

BU starts as a subcutaneous nodule, plaque or area of oedema on exposed areas, often a leg or arm or, less commonly, the face, eyes, or genitalia, and gradually progresses to a large, painless ulcer with deep, undermined edges. Perhaps a third of small lesions heal spontaneously.[1] Healing may result in contractures if the lesion is adjacent to a joint. Peak age is 5–15 years but any age group may be affected.

Typical histopathology shows areas of subcutaneous fat necrosis and acute or chronic inflammation.[1] It is considered that *M ulcerans* proliferates freely in subcutaneous fatty tissue where the temperature is optimum for growth. *M ulcerans* secretes a potent toxin, mycolactone, which causes fat necrosis.

Sensitivity for laboratory detection is as follows: Ziehl–Neelsen stain (40–43%), culture (60%, it grows slowly), histology (82%), and PCR (98–100%).[1] In poor rural areas, confirmation of the disease is seldom possible.[1]

Until recently, standard treatment was widespread surgical resection with skin grafting, making sure that all affected tissue is removed. Recurrence rate after surgery ranges between 6 and 17%.[1] This depends on the extent of the lesion and the quality of surgery.

In 2004, following animal and human pilot studies, the World Health Organization (WHO) Advisory Group on Buruli Ulcer issued guidelines that early lesions should be treated with streptomycin and rifampicin for 8 weeks. Surgery should be reserved for debridement or skin grafting to enhance healing.

An uncontrolled study in Benin used the above regimen in 224 patients and 96% were considered to be treatment successes.[2] Some 47% were treated with antibiotics exclusively and 53% received antibiotics and surgical excision with skin grafting; 73% of patients with lesions >15 cm diameter required surgery compared with 17% of those with lesions <15 cm.

A recent randomised trial involving two regimens in Ghana confirmed the results of the Benin trial.[3] Eligibility requirements included patients 5 years or older, early disease (<6 months), lesion diameter <10 cm and *M ulcerans* confirmed by PCR. Group 1 received streptomycin (15 mg/kg IM daily) and oral rifampicin (10 mg/kg once daily) for 8 weeks. Group 2 received streptomycin and rifampicin for 4 weeks, followed by rifampicin and clarithromycin (7.5 mg/kg once daily) for 4 weeks. End point was lesion healing 1 year after commencing treatment without lesion recurrence or requirement for extensive surgical debridement. Lesions were photographed and traced on to acetate sheets to record the rate of healing.

Ninety-six per cent (96%) in the 8-week streptomycin group and 91% in the 4-week streptomycin group had healed lesions at 1 year. Three patients had vestibulotoxic events (one in the 8-week streptomycin group and two in the 4-week group).

This study confirms that early, limited BU can be treated with antibiotics.[4] For large or complicated lesions skilled surgery will also be required.

New WHO growth standards

WHO have recently published new growth standards for children over 5 years[5] and growth references for children aged 5–9 years.[6] These will replace the NCHS/WHO reference charts presently used in developing countries.[7] The term *growth standard* is used when the growth of young children studied has taken place under optimal conditions.[8] *Growth reference* refers to a method of comparing growth measurements of children where no judgement has been made regarding reasons for growth difference between study participants.

The *NCHS/WHO growth reference* comprised American children based on references developed in the 1970s and included longitudinal and cross-sectional data on child growth.[7] The cohort of children aged 0–2 years were white, middle class, and largely artificially fed (thus likely to be heavier than breastfed infants). Children over 2 years varied in ethnicity and socioeconomic status. The growth charts were introduced in USA in 1978 and published as an international reference in 1983.

The *WHO 2006 growth standards* for children in the birth to 2-year group is compiled from a multicentre growth reference study of 8500 children from six centres (Brazil, Ghana, India, Norway, Oman, and USA) undertaken between 1997 and 2003.[8] The study was longitudinal and comprised children reared under optimal infant-care practices (non-smoking mothers, exclusively breast-feeding). Data for the 18–71 month group were based on single measurements. The *WHO 2007 growth reference* for children aged 5–19 years was compiled from three (multi-ethnic) USA databases. Care was taken not to over represent obese children. Body mass index (BMI) for age is included which caters for obesity better than it does for malnutrition.[8]

Comparison between the 2006 and NCHS standards for under-5s demonstrates that using the 2006 standard, the exclusively breastfed boy whose growth follows the reference median is heavier and taller in the first 6 months of life but lighter thereafter.[9] Also, a child will

be considered moderately or severely underweight for height at a greater weight for height than when using the NCHS reference data.

A recent analysis of growth using data from vitamin A supplementation studies in Ghana, India, and Peru found that the prevalence of stunting, wasting, and underweight in infants over 6 months of age was higher with the 2006 WHO than the NCHS standards, but the prevalence of underweight in infants aged 6–12 months was lower with WHO standards.[10] The WHO Standards were better then the NCHS references at predicting mortality.

A recent questionnaire on use of growth charts in developing countries found that the *Road-to Health* charts are widely used, also weight-for-height charts and the Wellcome classification (in sub-Saharan Africa).[8] It will take some time before the *WHO 2006 Standards* are in regular use in developing countries and translated into user-friendly charts, particularly for detection of growth failure and malnutrition. It is a long distance from Geneva to a small health centre in a rural area where nutritionists and mothers with limited education are trying to understand growth charts. Even in hospitals growth charts are rarely available for routine ward work.

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Medicine Review

More on 'tryps'

Over the last 2 years, we have twice reviewed literature on treatment advances in human African trypanosomiasis ('sleeping sickness'), in particular with regard to the recently introduced drug eflornithine. Much of the fieldwork comparing eflornithine with the more traditional melarsoprol was carried out by Médicins sans Frontières (MSF), the well-known humanitarian crisis aid agency. A comprehensive review of sleeping sickness has recently appeared in the *Lancet*, appropriately written by workers from MSF and the Tropical Institute at Basel, Switzerland.[1]

Most African trypanosomiasis is due to *Trypanosoma brucei gambiense*, with the more serious *Trypanosoma brucei rhodesiense* now restricted mainly to Zimbabwe, Zambia, Botswana, Malawi, Tanzania, Rwanda, and Kenya. Uganda has an overlap with both parasites.

The disease is both endemic and occasionally epidemic. Disease control is mainly by tsetse fly control as well as case-finding and prompt treatment. Identification of domestic cattle reservoirs and prevention of their movement can sometimes help. Control is not easy, but rates of *T b gambiense* infections are certainly falling, and the World Health Organization (WHO) regards the disease as potentially amenable to eradication.

Rhodesian sleeping sickness is well-known to present as a fulminant and often fatal meningoencephalitis. A trypanosomal chancre and lymphadenopathy may also be present. Interestingly, a more chronic form of Rhodesian trypanosomiasis has been recognised recently in some parts of southern sub-Saharan Africa, notably Malawi. Gambian sleeping sickness has much more chronic and diverse clinical features. A chancre is rarely seen at presentation, and the disease has two phases. The first is a non-specific febrile phase, but when neurological invasion occurs (the second phase), a variety of neuropsychiatric symptoms appear. These include sleeping disturbance, confusion, psychosis, tremor, and Parkinsonian features. Interestingly, both forms of African trypanosomiasis can involve the heart, but unlike South-American trypanosomiasis (Chagas disease) – where heart block and heart failure are common – the effects of African trypanosomiasis are normally sub-clinical, though electrocardiographic (ECG) QT prolongation is commonly observed.

Pentamidine or suramin (usually the former) can be used for first-stage Gambian disease. Melarsoprol is used for second-stage Gambian disease, and generally all cases of Rhodesian infections (which almost always present with central nervous system (CNS) involvement). The drug is highly toxic, and also complex to use, and the recent introduction of eflornithine is very welcome. A number of trials have now shown its superiority over melarsoprol in patients with second-stage *T b gambiense* infection, and it is now the drug of choice for this condition (if available). Its effectiveness in *T b rhodesiense* infections has not, however, been adequately assessed, and there is also some evidence that *T b rhodesiense* may be less sensitive to eflornithine than *T b gambiense*. Melarsoprol remains the treatment of choice for Rhodesian sleeping sickness.

For future control of African sleeping sickness, control measures (particularly related to tsetse fly eradication) need to be extended and intensified, and the availability of eflornithine must be increased. Safer and better drugs than melarsoprol must also be sought for the treatment of *T b rhodesiense* infections.

Snakebite

In 2009, snakebite was accepted as a 'neglected tropical disease'. This is a welcome move, as the problem is common and leads to considerable morbidity and

communities in tropical developing countries.[2] Under-reporting makes reliable epidemiological statistics difficult to obtain for the problem, but it is estimated that in excess of 5 million episodes of human snakebite occur annually, resulting in about 400 000 amputations, and between 20 000 and 125 000 deaths.[2] This burden of mortality is in excess of that of several other well-known tropical diseases – for example cholera, schistosomiasis, leishmaniasis, and dengue. Inclusion of snakebite into the WHO neglected tropical diseases programme is thus highly justified.

At a meeting in Melbourne, Australia, recently a group of snakebite experts from around the world formed the 'Global Snakebite Initiative',[3] aimed at reducing the health toll of snakebite. The group are linking with academic institutions, tropical country governments, the pharmaceutical industry, and other relevant stakeholders, to promote practical approaches to the problem. These include the following actions:

- Community education on the prevention and first-aid treatment of snakebite.
- Promoting mandatory reporting of snakebite to improve assessment and monitoring of the problem.
- Encouragement of snakebite-related clinical and basic science research.
- Development of appropriate local guidelines for care of snakebite victims.
- Support for the prequalification of antivenoms, and research to improve their effectiveness.
- Promotion of the rehabilitation of disabled victims (e.g. amputees).
- Building of effective public health policies and financing programmes to support snakebite control and treatment.

These are sensible and potentially achievable aims, and the 'Global Snakebite Initiative' deserves congratulations and support.

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Family Medicine

Communication

Patient–provider communication is frequently cited as one of the most critical factors in patient outcomes. Three recent articles highlight different aspects of this. In arranging any investigations for patients, doctors usually make the decisions regarding what is best for their patients, even when there are not clear clinical reasons for those choices, perhaps assuming that patients will be too swayed by non-clinical reasons. Shokar and colleagues examined patient preferences for screening tests for colorectal cancer in Texas.[1] They estimated patient preferences for faecal occult blood testing (FOBT), flexible sigmoidoscopy, colonoscopy, and double-contrast barium enema after the test attributes (such as accuracy and scientific evidence) were explained to them, and were asked to rank the test attributes in terms of importance. The attributes considered most important by patients were test accuracy, scientific evidence for efficacy, amount of colon examined, and need for sedation. In terms of colorectal cancer screening, participants tended to prefer colonoscopy and FOBT, because they wanted an accurate test with a maximum amount of colon examined, a minimum amount of discomfort, strong evidence for reducing deaths due to colon cancer, and few complications. The authors argue that, on the basis of their findings, clinicians should discuss with their patients all the available screening tests for colorectal cancer, focusing on the accuracy of the tests. This can be applied to any screening tests, or even diagnostic interventions; patients will make rational choices of the approach to follow if they are given the appropriate information. Ultimately they want to be reassured about their state of health, or otherwise, and to be sure they can rely on the outcome of the tests going forward. A full explanation of the tests is very important in providing this reassurance.

The Ask Me 3 (AM3) health communication programme is a campaign of the US National Patient Safety Foundation to enhance health literacy in that country. It encourages patients to ask three specific questions with the intention of improving understanding of their health conditions and adherence to treatment recommendations, viz. What is my main problem? What do I need to do (about the problem)? Why is it important for me to do this? (go to http://www.npsf.org/askme3/ for more information). The American Academy of Family Physicians National Research Network did a study to evaluate whether implementing AM3 improves patients' question-asking behaviour and increases adherence to prescription medications and lifestyle recommendations.[2] While they did not find evidence of this, their conclusion was that it was because their patient population already ask questions at a high rate and have fairly high levels of adherence. In Africa, patients tend not to ask questions of their healthcare providers, for many reasons. There is a long way to go in terms of developing higher levels of health literacy in African patients. A good start might be for doctors in primary care to begin by encouraging their patients to ask the three questions described, both when they are seeing their primary care providers but also – and perhaps more importantly – when they are referred to other levels of care, because of communication breakdowns and lack of replies to referral letters that are so frequently the norm.

In the last Family Medicine Review, I discussed the issue of nutrition, in relation to obesity in children[3]. Whether one is dealing with poor nutrition due to inadequate intake, over-intake, or bad eating habits, it is essential that children, and even more so their parents, understand what they need to do. While failure on the part of mothers to implement dietary changes is usually assumed to be due to limited resources, poor food preparation skills, and lack of interest or conviction, it is important to be sure that dietary recommendations are properly communicated. A recent Welsh study[4] examined the understanding of dietary recommendations in mothers of children under 16 years of age in a socioeconomically deprived area. The researchers found that the main

messages of the importance of a healthy diet and what constitutes a healthy diet had reached the mothers, but were not well understood. These mothers struggled to make sense of how to eat healthily. For other lifestyle changes, such as smoking cessation, there is a clear message (stop smoking), whereas promotion of healthy eating is complex. Thus promotion of natural foods and a diet rich in fruit and vegetables, may lead to consumption of fruit juices that are high in sugar and acid, with detrimental health consequences. For many mothers the concept of a balanced diet relates to balancing the good with the bad. Thus it is important for clinicians to deliver very clear, simple, and unambiguous messages regarding diet, and to test the understanding of these.

Obstetric care in district hospitals

A retrospective audit by Moodley and colleagues in a rural district hospital in South Africa looked at the management of breech presentations.[5] They found a rate of 2.4% singleton term breech deliveries. Of the 297 women who had antenatal care and had been allocated to planned caesarean section, 271 subsequently had the operation. There were no neonatal deaths in this caesarean section group. There were higher maternal complication rates in the emergency caesarean section group and higher neonatal complication rates in the group that had unplanned vaginal deliveries. While the fact that the mode of delivery for breech presentations is usually a planned caesarean section is certainly positive, the authors raise a question about the fact that external cephalic version (ECV) was attempted in only two (0.5%) of the 365 booked singleton breech patients diagnosed at the antenatal clinic in this study. This is despite the fact that ECV at 36 weeks is recommended by the NICE clinical guidelines[6] and a Cochrane review showing that it is a safe and effective way to reduce planned caesarean sections,[7] which are associated with increased maternal morbidity. Thus, while planned caesarean sections are certainly the preferred management over unplanned procedures or vaginal delivery, the increased use of ECV would obviate many problems, and clinicians who are not familiar with the procedure should seek to develop the necessary skills to do this routinely.

This audit is a good example of how simple record reviews can provide a wealth of useful information to change practice Ideally, however, such reviews should be done as a regular part of clinical practice, at every level of care. An excellent example of this is the recently published account from a deeply rural district hospital in South Africa, Zithulele, of how 3 years of effort focused on regular auditing to identify problems and improve service was reflected in significantly increased deliveries in the hospital and a sharp drop in the perinatal mortality rate.[8] Gaunt describes how attention to accuracy and detail, regarding women who deliver, using the Perinatal Problem Identification Programme (PPIP) version 2.2.3 for data entry and analysis, and monthly perinatal mortality meetings led to a growing change in services. Implementation of standardised protocols, consistent use of the partogram, extended training activities, and outreach to feeder clinics were some of the changes that arose. The process provides an encouraging example to primary care physicians, midwives, and others working in rural hospitals of how getting the basics right, based on regular audit reviews and commitment to act on the findings, can have a significant impact on patient outcomes.

Domestic violence

Violence against women is recognised globally as both a serious public health concern and a human rights violation, with lifetime prevalence of physical or sexual partner violence, or both, varying between 15% and 71% in 10 countries in a WHO report.[9] Domestic violence during pregnancy is associated with a range of adverse pregnancy outcomes. A recent South African study sought to establish the prevalence of domestic violence amongst pregnant women in a rural district.[10] The authors found a prevalence rate for reported domestic violence of 31% (95% CI: 26%; 36%), with this being higher in a younger age group. Abuse was both psychological, including threats of physical violence, and physical; 10 pregnant women experienced violence on a regular basis. Pregnant women who knew their HIV status were twice as likely to be a victim of domestic violence. The main perpetrators were intimate partners (80%). While there may be reasons for higher prevalence of domestic violence in South Africa, it is likely to be similar in other African countries with a history of conflict or social instability, and certainly no society or culture is immune to it. The interventions required to address this problem are multi-factorial, and must include changing individual and community attitudes towards domestic violence. Every primary care clinician should maintain a high index of suspicion for this problem, and enquiry about domestic violence should be a routine part of antenatal care, with support for appropriate intervention.

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CPD Challenge

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