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

Paediatrics Review

Meningococcal meningitis – a step further in control

Over the last 70 years Europe has been subject to epidemics of serogroup A and C Neisseria meningitidis and in the 1980s-90s serogroup C.1 Group W135 appeared in 1970 and again in 2000. More recently, group Y has been detected in both Sweden and the Czech Republic.

The main cause of bacterial meningitis in children in the UK is now capsular group B N.meningitidis. Infection by group C is presently controlled by immunisation with meningococcal group C conjugate vaccine at 3m and 4m of age. Although this already produces good herd immunity a booster dose of the vaccine for adolescents will be introduced in 2014.

Because of the antigenically diverse strains of group B N.meningitidis there have been difficulties in development of an effective vaccine.[2] In 2013, the European Medicines Agency licensed a four-component meningococcal serogroup B vaccine, 4CMenB, which covers 88% of strains of group B and some strains of group C meningococcus in the UK.[2] However, in 2011 the UK Joint Committee on Vaccination and Immunisation (JCVI) began a review of the value of 4CMenB vaccine and in 2013 decided that from available evidence it was not cost effective at any price but advised that additional information was necessary before making a decision. In 2014, following review of further information, the JCVI has recommended 4CMenB vaccine at 2, 4 and 12m subject to availability at a cost-effective price. JCVI advised omitting the recommended 3m dose and removing the 3m dose of group C vaccine subject to its effective implementation in adolescence.[2]

Over the last century there have been periodic and unpredictable epidemics of meningococcal meningitis in the Sahel and sub-Sahel region of Africa referred to as the African meningitis belt.[3] Incident rates of meningitis can reach over 300 cases per 100 000 population.[4] Control measures have comprised reactive vaccination with a polysaccharide vaccine after an outbreak reaches a definite threshold as well as routine vaccination of children in some countries. However, this has not been effective in preventing epidemics of group A or occassional group C meningococcal meningitis.[3] A recently developed serogroup A meningococcal polysaccharide-tetanus toxoid conjugate vaccine (PsA-TT, MenAfriVac) which can also prevent meningococcal carriage has demonstrated striking efficacy; it is also immunogenic in young children. The vaccine was developed by the Serum Institute, Pune, India with the support of the Meningitis Vaccine Project, established in 2001, and the Bill and Melinda Gates Foundation. The vaccine was licensed for use in sub-Saharan Africa in 2009, and in 2010 Burkino Faso became the first country to implement a national programme when 11.4 million people aged 1-29 years were vaccinated with PsA-TT. During the 14-year period before PsA-TT was introduced there were 148 603 cases of suspected meningitis and 17 965 deaths and 174 district-level epidemics.[5] After the vaccination campaign there was a 71% decline in risk of meningitis and 64% decline in risk of fatal meningitis. There was a statistically significant decline in risk of probable meningitis in the target age groups as well as those under one year and over 30 years who were ineligible for vaccination. There were no cases of group A N.meningitidis meningitis (NmenA) in vaccinated subjects.

In 2010, a cross-sectional meningococcal carriage study was undertaken in a representative group of the 1-29 year-old population in three districts in Burkino Faso before vaccination and then up to 13m after vaccination.[6] One district was vaccinated in September 2010 and the other two in December 2010. NmenA carriage in the unvaccinated districts was comparable to the baseline in 2009, but was absent in the vaccinated districts. Serogroup X N.meningitidis was the dominant meningococcus in both the vaccinated and unvaccinated districts. In 2011, further sampling was undertaken in the three districts (which were all vaccinated) and no NmenA was identified. NmenA was eliminated in both vaccinated and unvaccinated population from three weeks to 13 months after mass vaccination which supports strong herd immunity.

A recent report from Chad provides further evidence for the value of PsA-TT in controlling NmenA outbreaks. Between 2009 and 2012 nationwide meningitis epidemics occurred in Chad which were mainly NmenA with some NmenW.[7] In 2010-12 there were 12 813 cases. In December 2011, up to 1.8 million individuals aged 1-29 year received PsA-TT during a vaccination campaign in three regions around N'Djamena over a 10-day period. Vaccination coverage was approximately 100%. In March to June 2012 (before the onset of the 2012 epidemic), enhanced surveillance was undertaken in the three regions where PsA-TT was administered, and in one district where reactive vaccination with a polysaccharide vaccine was undertaken in a response to an outbreak of meningitis. Meningococcal carriage was also investigated in residents of a rural area 65km south of N'Djamena, Moissala, (a non-vaccinated area) 13-15m and 2-4m before and 4-6m after vaccination (in the N'Djamena region).

The incidence of meningitis in the three vaccinated regions undertaken the previous year was 2.48 per 100 000 compared to 43.8 in regions without mass PsA-TT vaccination (94% difference in crude incidence). In Moissala, there were 32 group A carriers 2-4m before the vaccination and only one isolate after vaccination which approximates to 98% decrease in carriage rate.

This study confirms the value of PsA-TT in controlling

the meningococcal epidemic in the three vaccinated regions and markedly reducing the carriage rate of NmenA and enhancing the herd effect. Other districts subsequently required a reactive vaccination campaign.

Continued high quality surveillance is required over the next few years to ascertain the ability of PsA-TT to control carriage rates of NmenA and prevent further epidemics of meningococcal meningitis.

A mathematical model, estimates that following mass vaccination of persons aged 1-29 year with conjugate MenA further vaccination regimens would be required as follows: (a) the most effective, mass campaigns every 5 years for children 1-5 year; (b) somewhat less effective, less frequent campaigns covering broader age groups; (c) introduction of the vaccine into the EPI schedule at 9m of age. This predicts higher incidence of meningitis than mass campaigns.[8]

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Medicine Review

New drug for vivax malaria

In Africa, Plasmodium falciparum is the commonest malarial parasite, but P.vivax is nevertheless frequently encountered, and in many parts of the world it is main cause of malaria. Because P.vivax is less common and less serious an infection in Africa, it receives relatively little attention. However, P.vivax differs from P.falciparum in that it forms hypnozoite stages in the liver, which can lie dormant for months or years, but then cause a relapse of clinical malarial infection. A 'radical' cure of vivax malaria therefore requires drugs which will kill both the erythrocytic and hepatic stages of the life cycle. For many decades, the only available drug active against the P.vivax hypnozoites has been primaquine. A major drawback of this drug is that it can lead to severe haemolysis in patients with the inherited disorder glucose-6-phosphate dehydrogenase (G6PD) deficiency – a condition which is very common in many parts of the world, including in Africa. A recent report, however, has shown very promising results with the drug tafenoquine for the radical cure of vivax malaria.[1]

The trial took place in 4 countries where vivax malaria is particularly common – Peru, Brazil, Thailand and India. A total of 329 patients with parasitologically proven P.vivax infection were recruited, and all were given a 3 day course of chloroquine to cure the acute infection (erythrocytic stage), and were then divided into 4 groups receiving either tafenoquine 50 mg (single dose), 100 mg, 300 mg, or 600 mg; as well as 2 further groups receiving either chloroquine alone, or primaquine 15 mg daily for 15 days. The groups were randomly chosen, and G6PD deficiency was excluded in all participants. Patients were followed for 6 months to assess the proportion in each group who suffered a malarial relapse.

Relapse rates were 42% for tafenoquine 50 mg, 46% with 100 mg, 11% with 300 mg and 8% with 600 mg. For primaquine, the relapse rate was 22%, and for chloroquine alone it was 62%. No major adverse events occurred, apart from electrocardiographic (ECG) Q-T prolongation in 11 (3%) of patients, though they were evenly distributed across the groups.

These results are encouraging. The authors conclude that 300 mg is the optimal dose for tafenoquine, and that when combined with a standard course of chloroquine, results in a reduction in relapse rate superior to chloroquine plus primaquine. The single dose regimen for tafenoquine is also much simpler than the awkward 15 day course of primaquine (indeed the authors commented that poor compliance with primaquine may have been a factor in its relatively high relapse rate of 22%).

There are, unfortunately, some drawbacks to this promising new drug. It is not yet available for use and further longer-term trials will be needed, as vivax malaria relapses can occur well beyond six months after primary infection. Also, as with primaquine, it can cause haemolysis in G6PD deficient patients, so the same precautions in use as with primaquine will be needed. An accompanying editorial comment on the paper[2] points out that what is urgently needed is a reliable and rapid point-of-care test for G6PD deficiency, so that this problem can be immediately excluded when malaria treatment is planned.

Africa and polio eradication

We have previously discussed in these columns the progress towards a world free of poliomyelitis (polio). A major step forward took place on January 13th 2014 when India was declared polio-free. No cases had been recorded for three years, fulfilling the World Health Organization (WHO) criteria for polio eradication. This was a giant step in progress towards polio eradication; as with its massive, diverse and scattered population, India has been long considered a particularly difficult country to achieve a disease-free state.[3]

This leaves Nigeria, Afghanistan and Pakistan as the three remaining countries in which polio remains endemic. Political disruption, and intimidation of (and

even violence against) vaccination teams have hampered progress in Pakistan and Afghanistan. The next step forward may therefore be to achieve freedom from polio in the continent of Africa. Progress is certainly being made in Nigeria – over the last 12 months only 42 cases have been recorded, compared with 104 in the previous 12 months. Also, between September 2013 and January 2014, only 6 confirmed cases of polio were found.

However, there have also been some backward steps. In 2013 there were polio outbreaks in four African countries previously free of polio. These were Cameroon, Kenya, Somalia and Ethiopia; with a total of 240 cases. Of these 199 (83%) were in the horn of Africa (Ethiopia, Kenya and Somalia), and were caused by strains of virus imported from Kenya. These outbreaks are diminishing due to massive vaccination campaigns, but their occurrence shows that there is no room for complacency if we are to achieve freedom from polio in the African continent.

Polio vaccine manufacturers are helping by reducing vaccine costs. There are also ongoing moves to switch where possible from oral to parenteral vaccine. The traditional oral vaccine contains attenuated live virus, but this occasionally becomes 'wild' and spreads the viral pool. The injectable polio vaccine uses totally inactive virus that cannot spread in this way.

The eradication of polio in India will hopefully stimulate current efforts in Africa to free the continent of this ancient and devastating disease. However, even if eradication is achieved in the near future, the legacy of polio will continue for many years to come. This is seen in most African towns and cities in the form of severely disabled past polio-sufferers begging for food and money to sustain their lives; surely one of the saddest outcomes of any tropical disease.

Commotio cordis

I suspect that most readers will never heard of the condition 'commotion cordis'. I certainly had not until I came across a case whilst working as a medical officer in Zambia many years ago. I was reminded of the event when I came across a case report in a recent edition of the Lancet[4]. Commotio cordis is cardiac ventricular damage and arrhythmia caused by a severe blow to the chest, and is a potential cause of sudden death during sporting activities (eg cricket, football, tennis, squash, boxing). In the recently reported case a 25 year old man in Australia was struck on the praecordium by a cricket ball travelling at high speed during a practice session. He collapsed unconscious, and cardio-pulmonary resuscitation (CPR) was begun. When paramedics arrived he was found to be in ventricular fibrillation (VF) and was successfully defibrillated. He was transferred to hospital and went on to make a full recovery.

My case in Zambia was an 11 year old boy playing football in a local township league match. He was hit in the centre of the chest by a ball and collapsed. The team manager had some first aid training, and found him to be unconscious with no respirations or peripheral pulses. CPR was started and within a few chest compressions the boy regained consciousness. He was brought to hospital and I happened to be on duty at the casualty department. He was fully conscious, was in sinus rhythm and had a normal blood pressure. There was redness and early bruising over his praecordium, clearly caused by a high-velocity ball. A 12 lead electro cardiogram (ECG) showed marked anterior ST elevation. I discussed this with colleagues, and we assumed that the ECG changes represented a 'current of injury' due to myocardial contusion. We assumed that he had collapsed in a probable VF arrest, which responded to his team manager's prompt CPR. The boy was admitted and remained well. Over the next three days his ECG pattern slowly returned to normal and he was discharged.

Commotio cordis is an uncommon but serious and dramatic sport-related emergency. As these two cases demonstrate, it is worth keeping the diagnosis in mind. Fortunately, both patients (in Australia and Zambia) made a good recovery, which unfortunately is not always the case.

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Africa HEALTH CPD Challenge

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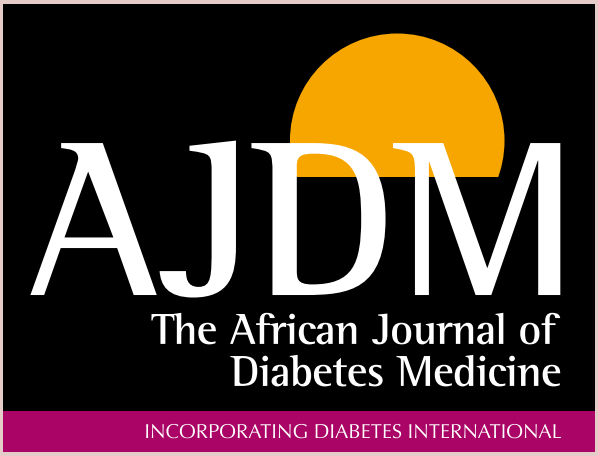

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