Volume 92, the last quarter edition of the *British Medical Bulletin*, for 2009, once again has a wide variety of reviews on a series of important topics.

The first review is on **Global and regional causes of death** (page 7) by Mathers, Boerma and Ma Fat from the World Health Organization in Switzerland.

Their review is an overview of the data and methods used by WHO to develop global-, regional- and country-level estimates of mortality for a comprehensive set of causes, and provides an overview of global and regional levels and patterns of causes of death for the year 2004. Ischaemic heart and cerebrovascular diseases are the leading causes of death worldwide, followed by lower respiratory infections, chronic obstructive pulmonary disease and diarrhoeal diseases. AIDS and TB are the sixth and seventh most common causes of death, respectively, lower than in previous estimates. One-half of all child deaths are from four preventable and treatable communicable diseases. Six of the top 10 causes of death globally are from non-communicable diseases, 3 from communicable diseases and 1 from injuries. Injury mortality is highest in South-East Asia, Latin America and the Eastern Mediterranean regions. These results illustrate continuing huge disparities in risks and causes of death across the world.

Global mortality analyses of the type reported here have been criticized for making estimates of mortality for regions with limited, incomplete and uncertain data. Estimates presented here use a range of techniques depending on the type and quality of evidence. Better evidence on levels of adult mortality is needed for African countries. Acknowledging the controversies around use of incomplete and uncertain data, systematic assessments and synthesis of the available evidence will continue to provide important inputs for global health planning. Innovative methods involving sample registration, and the use of verbal autopsy questionnaires in surveys, are needed to address these gaps. Research on strategies to improve comparability of cause-of-death certification and coding practices across countries is also a high priority.

The next review is on **Mathematical modelling of infectious diseases** (page 33) by Keeling and Danon at the University of Warwick, UK.

They suggest that mathematical models allow us to extrapolate from current information about the state and progress of an outbreak, to predict the future and most importantly quantify the uncertainty in these predictions. They illustrate these principles in relation to the current H1N1 epidemic. Many sources of data are used in mathematical...
modelling, with some forms of model requiring vastly more data than others. Good estimation of the numbers of cases is vitally important.

Mathematical models, and the statistical tools that underpin them, are now a fundamental element in planning control and mitigation measures against any future epidemic of an infectious disease. Well-parameterized mathematical models allow us to test a variety of possible control strategies in computer simulations before applying them in reality. The interaction between modellers and public-health practitioners, and the level of detail needed for models to be of use is required. There is a need for stronger statistical links between models and data. Greater appreciation by the medical community of the uses and limitations of models and by modellers of the constraints on public-health resources is needed.

The third review is on Radionuclide imaging in ischaemic heart failure (page 43) by Stirrup, Maenhout, Wechalekar and Anagnostopoulos from the Royal Brompton Hospital and Harefield NHS Trust, London, and Barts and The London School of Medicine and Dentistry.

They make the point that many tests are available for the investigation of patients with heart failure. The identification of the underlying aetiology of ventricular dysfunction is crucial as early treatment may limit or even reverse myocardial abnormalities. This review describes cardiac radionuclide imaging techniques and their applications in ischaemic ventricular dysfunction. Evidence for the role of these techniques is summarized with particular reference to current guidelines. Both positron emission tomography (PET) and single photon emission computed tomography (SPECT) techniques are widely validated for the detection of myocardial viability and their use is recommended in both national and international guidelines.

Although assessments of ventricular phase and myocardial innervation hold promise for the stratification of patients to cardiac resynchronization therapy, the poor performance of echocardiographic predictors of response in the recently published PROSPECT trial suggest that these techniques face a tough challenge. The use of integrated multimodality imaging techniques such as PET/CT to assess for ischaemic causes of left ventricular dysfunction is an area that is currently under investigation, as is the role of nuclear techniques in the assessment of stem cell retention, distribution and function when used in patients with heart failure. On-going developments in radionuclide molecular imaging for assessment of angiogenesis, apoptosis and interstitial alterations during cardiac remodelling may have important implications for the prognosis and treatment of patients with heart failure.

The fourth review is on The implications of anti-tumour necrosis factor therapy for viral infection in patients with inflammatory bowel disease (page 61) by Shale at Imperial College, London.
He states that anti-tumour necrosis factor (TNF) therapy is increasingly used in the management of inflammatory bowel disease; however, concerns have been raised regarding the risk of infection with such drugs. Little is known about their effect upon viral infection. A search of PubMed was undertaken using the terms ‘infliximab’, ‘etanercept’, ‘adalimumab’ or ‘anti-TNF therapy’ combined with the names of specific viruses. A search of cited papers was used to identify further relevant reports. Numerous reports of the use of anti-TNF in patients with chronic or latent viral infection appear in the literature. Specific problems relating to hepatitis B virus and varicella zoster virus may exist. The safety profile of anti-TNF in chronic viral infection is generally reassuring.

Numerous consensus statements relating to pre-treatment serology or vaccination have recently appeared; however, significant variation exists in their recommendations. Increasing awareness of the implications of anti-TNF therapy on viral infection may allow safer use of such drugs. The clinical and cost-effectiveness of screening for viral infections prior to anti-TNF requires further study.

The next piece is on Recent advances in the understanding of bile acid malabsorption (page 79) by Pattni and Walter at Hammersmith Hospital, and Imperial College, London.

They state that bile acid malabsorption (BAM) is a syndrome of chronic watery diarrhoea with excess faecal bile acids. Disruption of the enterohepatic circulation of bile acids following surgical resection is a common cause of BAM. The condition is easily diagnosed by the selenium homocholic acid taurine (SeHCAT) test and responds to bile acid sequestrants. Idiopathic BAM (IBAM, primary bile acid diarrhoea) is the condition where no definitive cause for low SeHCAT retention can be identified. Evidence is accumulating that BAM is more prevalent than first thought. Management of chronic diarrhoea involves excluding secondary causes. Treatment of the condition is with bile acid binders.

SeHCAT testing is not widely performed, limiting our awareness of how common this condition can be. The underlying mechanism for IBAM has been unclear. Increasing awareness of the condition is important. Alternative mechanisms of IBAM have been suggested, which involve an increased bile acid pool size and reduced negative feedback regulation of bile acid synthesis by FGF19. New sequestrants are available. Further research into the precise mechanism of IBAM is needed. Improvements in the recognition of the condition and optimization of treatment are required.

The sixth review is on Injuries, risk factors and prevention initiatives in youth sport (page 95) by Frisch, Croisier, Urhausen, Seil, and
Theisen at the Public Research Centre for Health, Luxembourg and the Université de Liège, Belgium.

They show that sports injuries in young athletes are a public health issue that deserve special attention. Effective prevention can be achieved with training programmes originating from the field of physical therapy and medicine. They did a systematic literature search on injury prevention in youth sport on the MEDLINE database. For prevention programmes to reduce sports injuries, critical factors must be considered, such as training content, duration and frequency, as well as athlete compliance.

Home-based programmes could be inferior to supervised training, but are efficient if compliance is high. So far prevention programmes have focused on team sports and their efficiency in individual sports remains to be proven. Active prevention programmes focusing specifically on the upper extremity are scarce. Initiatives enhancing the awareness of trainers, athletes and therapists about risk factors and systematic prevention measures should be encouraged.

The seventh review is Bone health in HIV infection (page 123) by Pollock, Klotsas, Compston and Gkrania-Klotsas at the University of Cambridge and Luton and Dunstable Hospital, UK.

Osteoporosis is among the chronic problems emerging as the human immunodeficiency virus (HIV) positive population ages. They reviewed the English language bibliography using Pubmed 2.0, Web of Science and Embase for relevant abstracts and articles. The prevalence of low bone mineral density and fracture is increased in the HIV-positive population.

The pathogenesis is multifactorial; there is some evidence that HIV infection is an independent risk factor and that highly active antiretroviral therapy has adverse skeletal effects. Physicians should routinely review the bone health of all HIV patients. More studies of the mechanisms of bone loss, the skeletal effects of antiretroviral therapy and the therapeutic outcome of bone protective therapy in HIV-positive individuals are needed.

The eighth review is on Age-associated cognitive decline (page 135) by Deary, Corley, Gow, Harris, Houlihan, Marioni, Penke, Rafnsson and Starr from University of Edinburgh, Edinburgh, UK.

They state that age-associated cognitive decline is an important human experience that differs in extent between individuals. The determinants of the differences in age-related cognitive decline are not fully understood. From early adulthood there are declines in mental domains such as processing speed, reasoning, memory and executive functions, some of which are underpinned by a decline in a general cognitive factor. There are contributions to understanding individual differences in normal cognitive ageing from genetics, general health and medical
disorders such as atherosclerotic disease, biological processes such as inflammation, neurobiological changes, diet and lifestyle. Many of these effect sizes are small, some are poorly replicated and in some cases there is the possibility of reverse causation, with prior cognitive ability causing the supposed ‘cause’ of cognitive ability in old age.

Genome-wide scans are likely to establish genetic contributions. The role of vascular factors in cognitive ageing is increasingly studied and understood. The same applies to diet, biomarkers such as inflammation, and lifestyle factors such as exercise. There are marked advances in brain imaging, affording better in vivo studies of brain correlates of cognitive changes. There is also a growing appreciation that factors affecting general bodily ageing also influence cognitive functions in old age.

The ninth review is on Management of calcaneal fractures. Systematic review of randomized trials (page 153) by Gougoulias, Khanna, McBride, and Maffulli, from University Hospital of North Staffordshire and Barts and The London Scholl of Medicine and Dentistry, London.

They say that the optimal management of calcaneal fractures is controversial, as correlation between anatomical restoration and outcome has not been proven, and complications after surgery are frequent. They searched MEDLINE, EMBASE, CINAHL, Google scholar, the Cochrane Controlled Trials Register and the Cochrane Musculoskeletal Injuries Group Trials Register using the keywords ‘calcaneal’ and ‘fractures’, without time limits or restriction to language. Results showed no difference in residual pain, but favoured surgical management on ability to return to the same work and to wear the same shoes as before the fracture. Surgery reduced the need for subsequent subtalar fusion. Workers’ compensation affected the outcome.

It is unclear whether general health outcome measures, injury-specific scores and radiographical parameters improve after operative management, and whether the benefits of surgery outweigh the risks. The existing trials are of relatively poor quality. There is still a need for a carefully designed large-scale trial comparing surgery and non-operative management. Other forms of fixation (external fixation or minimally invasive internal fixation) should be compared with ‘conventional’ surgery. Trials investigating joint reconstruction versus primary subtalar fusion for highly comminuted fractures, and impulse compression versus placebo could be of value.

Norman Vetter
October 2009