The British Medical Bulletin has another edition for the last quarter of 2015. This set of reviews is, as usual, about developing ideas in medicine for trainee specialists and people who are wishing to get up-to-date in a specialty with which they are not familiar. Reviews that we believe to be of particular and general interest will appear on the Oxford University Press blog.

The first review for the present edition is entitled ‘Potential compounds for the treatment of mitochondrial disease’ (page 5) by Rai, Russell, Lightowlers and Turnbull from Newcastle University, UK.

They say that mitochondrial diseases are a group of heterogeneous disorders for which no curative therapy is currently available. Several drugs are currently being pursued as candidates to correct the underlying biochemistry that causes mitochondrial dysfunction. Several compounds under investigation display poor pharmacokinetic profiles or numerous off-target effects. Drug development teams should continue to screen existing and novel compound libraries for therapeutics that can enhance mitochondrial function. Therapies for mitochondrial disorders could hold potential cures for a myriad of other ailments associated with mitochondrial dysfunction such as neurodegenerative diseases.

The second review is entitled ‘Human embryonic and induced pluripotent stem cells in clinical trials’ (page 19) by Dusko, Devito, Miere and Codognotto from King’s College School of Medicine, London, UK.

They state that human embryonic and induced pluripotent stem cells (hESC and hiPSC) have tremendous potential for clinical implementation. In spite of all hurdles and controversy, clinical trials in treatment of spinal cord injury, macular degeneration of retina, type 1 diabetes and heart failure are already ongoing. The initial results from multiple clinical trials demonstrate that hESC-based therapies are safe and promising. Development of hESC- and/or iPSC-based cellular therapy for other diseases look like useful areas for future research.


In 2013, responsibility for public health returned to local government from the NHS in England. This review describes, as a case study, a fresh approach to tackling health inequalities, which built on a desire by local councils in the north of England to re-think approaches and collaborate on new ideas to improving health and reducing health inequalities. Four areas for action were recommended: linking poverty with economic prosperity, devolution and public sector reform, investment in early years and renewed impetus for the health sector. The so-called North–South divide appears to be widening, and renewed efforts are needed locally and nationally to tackle these wider determinants of health. The examples of local action indicate the need for research on ‘asset-based approaches’ to improving community health, presented so to empower local lay decision-makers such as councillors rather than for technical experts.

The fourth review is entitled ‘Clinical trial transparency: many gains but access to evidence for new medicines remains imperfect’ (page 43) by Mintzes, Lexchin and Quintano from the University of Sydney, Australia, the University of Toronto, Canada and Health Action International in The Netherlands.

They state that although selective and incomplete publication is widely acknowledged to be a problem,
full access to clinical trial data remains elusive. Existing sources of information provide an incomplete overview of scientific research. Persistent arguments about commercial confidentiality and the potential difficulties in de-identifying raw data block important progress. Requirements for trial registration are increasing. Important regulatory changes in particular in Europe have the potential to result in the release of more information. Documenting the effects of prospective trial registration and requirements for proactive clinical trial publication on healthcare decisions, public health and rational resource allocation is needed.

The fifth review is entitled ‘Small joints replacement for hand osteoarthritis’ (page 55) by Papalia, Tecame, D’Adamio, Maffulli and Denaro from the University of Rome, Italy, Barts and The London School of Medicine and Dentistry, UK and the University of Salerno, Italy.

Small joints replacement is a valid treatment for moderate to severe osteoarthritis of the hand. Several designs and materials are now available for prosthetic procedures with very different clinical and functional outcomes. Good functional and clinical outcomes can be achieved with silicone and pyrolic carbon implants, either for trapeziometacarpal and metacarpophalangeal joints. Major complications, such as persistent pain and implant loosening, have a variable rate of occurrence. Larger cohorts treated with the same implant should be investigated in better designed trials, to draw more clinically relevant conclusions from the evidence presented.

The sixth review is entitled ‘Eradication of tetanus’ (page 69) by Thwaites and Loan from the Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam and University of Oxford, UK.

The causative agent of tetanus, Clostridium tetani, is widespread in the environment throughout the world and cannot be eradicated. To reduce the number of cases of tetanus, efforts are focused on prevention using vaccination and post-exposure wound care. The maternal and neonatal tetanus elimination initiative has resulted in significant reductions in mortality from neonatal tetanus throughout the world. Although there are few data available, it is likely that large numbers of children and adults, particularly men, remain unprotected due to lack of booster immunization. It remains unclear how HIV and malaria affect both responses to vaccination and transplacental transfer of antibodies or how this might affect timing of vaccination doses.

The seventh review is entitled ‘New paradigms in hepatitis B management: only diamonds are forever’ (page 79) by Coffin and Lee from University of Calgary, Canada.

They say that the hepatitis B virus (HBV) causes chronic hepatitis B (CHB) in ~350 million people worldwide who have an increased risk of end-stage liver disease and/or hepatocellular carcinoma (HCC). There has been great progress in CHB therapy with the development of standard and pegylated interferon (i.e. PEG-IFN) as well as nucleos/tide analogues (NA). NA inhibit viral reverse transcriptase, have few side effects and prevent liver disease progression, but cannot offer a cure as they have little effect on the resilient HBV covalently closed circular DNA (cccDNA) intermediate. Potential new therapies include viral entry inhibitors, RNA-interference technologies (i.e. RNAi) and small molecules that modulate cccDNA transcription, as well as novel immunomodulatory therapies to boost HBV-specific T-cell responses. The ultimate goal of new tests and anti-HBV therapies to reduce the burden and expense of life-long CHB treatment, as ‘only diamonds are forever’.

The eighth review is entitled ‘Microfracture produces inferior outcomes to other cartilage repair techniques in chondral injuries in the paediatric knee’ (page 93) by Chawla, Twycross-Lewis and Maffulli from Imperial College London, Barts and the London School of Medicine and Dentistry, UK and University of Salerno School of Medicine and Dentistry, Italy.

Chondral injuries are becoming increasingly common in the paediatric knee. First-line surgical
therapy is usually microfracture (MF), but the emergence of alternative techniques raises the question of what is the optimal treatment in paediatric patients. Each technique demonstrated a significant post-surgical improvement in clinical outcome scores. However, MF demonstrated poorer outcomes in larger lesions (>3 cm²) and shorter durability. The quality of the available literature is poor, and there is a lack of comparative trials. The impact of defect characteristics, mechanism of injury and concomitant surgeries should be investigated. Appropriately powered randomized controlled trials with suitably long follow-up and condition-specific outcome measures should compare different techniques against each other and placebo.

The ninth review is entitled ‘Antibiotic resistance: what, why, where, when and how?’ (page 105) by Sabtu, Enoch and Brown from Cambridge University Hospitals NHS Foundation Trust, UK.

Antibiotic resistance is a threat to the effective prevention and treatment of an ever-increasing range of infections caused by bacteria, parasites, viruses and fungi. There is consensus about the development and spread of antibiotic resistance, the reasons for the development of antibiotic resistance and the clinical impact. There is more debate about the most appropriate way of tackling this increasing problem. This review discusses a number of initiatives (local and global) that are being undertaken to protect the antibiotics we currently have available for use and to encourage the development of newer agents.

The tenth review is entitled ‘Efficacy and safety of extracorporeal shock wave therapy for orthopaedic conditions’ (page 115) by Schmitz, Csaszar, Milz, Scheiker, Maffulli, Rompe and Furia from Ludwig-Maximilians-University of Munich, Germany, the University of Salerno School of Medicine, Italy, Queen Mary University of London, UK, the Ortho Trauma Evaluation Institute, Mainz, Germany and Evangelical Community Hospital, Lewisburg, PA, USA.

They state that extracorporeal shock wave therapy (ESWT) is an effective and safe non-invasive treatment option for tendon and other pathologies of the musculoskeletal system. An optimum treatment protocol for ESWT appears to be three treatment sessions at 1-week intervals, with 2000 impulses per session and the highest energy flux density the patient can tolerate. The distinction between radial ESWT as ‘low-energy ESWT’ and focused ESWT as ‘high-energy ESWT’ should be abandoned. There is no scientific evidence in favour of either radial ESWT or focused ESWT with respect to treatment outcome. Future RCTs should primarily address systematic tests of the aforementioned optimum treatment protocol and direct comparisons between radial and focused ESWT.

The eleventh review is entitled ‘The development of urban community health centres for strengthening primary care in China’ (page 139) by Wang, Wang, Wong, Wong, Mercer and Griffiths from Sun Yat-Sen University, Guangzhou, P.R. China, The Chinese University of Hong Kong, University of Glasgow and Guangzhou Medical University, P.R. China.

This review outlines the development of China’s primary care system, with implications for improving equitable health care. Community health centres (CHCs) are being developed as the major primary care provider in urban China, with some achievements. The road towards a strong primary care-led system is promising but challenging. Healthcare disparities exist in the health system wherein universal health coverage and gatekeepers have not yet been established. Future prospective studies should aim to provide solutions for strengthening the leading role of CHC In providing equitable care in response to population ageing and multimorbidity challenges.

The twelfth review is entitled ‘Endoscopic cubital tunnel release: a systematic review’ (page 155) by Smeraglia, Del Buono and Maffulli from University of Naples, Italy, Ospedale Vaio Fidenza (PR), Italy, University of Salerno, Italy, Barts and The London School of Medicine and Dentistry, London, UK.

Theoretical advantages of endoscopic cubital tunnel release are the short incision, lower risk of
nerve damage, reduced manipulation of the nerve and possible faster recovery. Endoscopic release is effective for cubital tunnel entrapment and allows adequate visualization of the site of entrapment. There is a negative association between the severity of the compression and reported outcomes. Injury to the medial branch of the antebrachial cutaneous nerve is less frequent, thanks to the limited dissection. The shorter time to return to work and the cosmetic appearance of the scar can be considered advantages of the endoscopic technique. The literature pertinent to endoscopic cubital tunnel release is lacking in the evaluation of the learning curve. Further investigations are necessary to assess the role of ulnar nerve instability.

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