The British Medical Bulletin, for its first print edition of the new year 2013, has another set of reviews on a wide range of topics and specialties, at the cutting edge of medical practice. These reviews are intended to be accessible to non-specialists, to bring the subjects to a wide audience.

The first review is entitled Policy reform to realize the commitments of the Political Declaration on noncommunicable diseases (page 7) by Mendis and Chestnov from the World Health Organization, Geneva, Switzerland.

They say that noncommunicable diseases (NCDs) caused an estimated 36 million deaths in 2008. Eighty per cent of the deaths occurred in low- and middle-income countries. Governments adopted the Political Declaration on NCDs at the United Nations General Assembly in September 2011, recognizing that NCDs are a global health and development priority. The cost of action and inaction are known as there are high impact interventions for prevention and disease management. Some of them are very cost-effective and applicable even for resource-constrained settings. Low- and-middle-income countries, at a minimum, should scale-up the very cost-effective, high impact NCD interventions to improve health outcomes and health equity with universal coverage, as a long-term public health goal.

The second review is on Colorectal cancer screening in Asia (page 29) by Ng and Wong from the Chinese University of Hong Kong.

They state that the incidence and mortality of colorectal cancer are rapidly rising in several countries in Asia. The incidence, anatomical distribution and mortality of colorectal cancer among Asian populations are comparable to those in Western countries. Flat and depressed colonic lesions are not uncommon. Male gender, smoking, obesity, metabolic syndrome and family history are risk factors. The optimal screening method in Asia remains unclear. Faecal occult blood test has been suggested as the first choice of screening test in countries with limited resources. The role of nurse endoscopists performing endoscopic procedures for colorectal cancer screening in Asia has not been defined. Screening for colorectal cancer should be a national health priority in most Asian countries.

The third review is on the Placenta as a reservoir of stem cells: an under-utilised resource? (page 43) by Pipino, Shangaris, Resca, Deprest, Sebire, David, Guillot and De Copp from University College London, London, UK, University Hospital Gasthuisberg, Leuven, Belgium, Great Ormond Street Hospital for Children and Imperial College London, London, UK.
They say that embryonic and adult tissues are sources of stem cells with therapeutic potential, but ethical considerations, difficulty in obtaining them and tumourigenicity can be a problem. As an alternative, the placenta is a foetal tissue that can be obtained during gestation and at term and represents a reservoir of stem cells with varying potential. Some studies describe a subpopulation of placenta stem cells expressing pluripotency markers, but for other studies, it is not clear whether pluripotent stem cells are present during gestation beyond the first few weeks. The expression of some pluripotency markers has been reported by the authors, but not by others. Understanding the role of placenta stem cells during pregnancy and their paracrine actions could help in the study of some diseases that affect the placenta during pregnancy.

The fourth review is on **New strategies for the restoration of hearing loss: challenges and opportunities** (page 69) by Rivolta from the University of Sheffield.

He states that for most types of hearing impairments, a definitive therapy would rest on the ability to restore hair cells and the spiral ganglion neurons. The only established technique to treat deafness is based on the functional replacement of hair cells with a cochlear implant, but this still has important limitations. New curative strategies, ranging from stem cells to gene and molecular therapy, are under development. Although still experimental, they have delivered some initial results that allow us to look at them with cautious optimism. The isolation of human auditory cells, the generation of protocols to control their differentiation into sensory lineages, their promising application *in vivo* and the identification of key genes to target molecularly offer an exciting landscape.

The fifth review is on the **Development of a cell-based medicinal product: regulatory structures in the European Union** (page 85) by Gálvez, Clares, Hmadcha, Ruiz and Soria, from Cartuja-93 Scientific and Technological Park, Seville and the University of Granada, Spain.

They state that new therapies with genes, tissues and cells are emerging for the treatment of many diseases. Advances on stem cell therapy research have led international regulatory agencies to harmonize and regulate the development of new medicines with stem cells. Cell therapy-based medicinal products should be subjected to the same regulatory principles as any other medicine. Their technical requirements for quality, safety and efficacy must be more specific and stringent than other biological products and medicines. Cell therapy medicinal products are at the cutting edge of innovation and offer a major hope for various diseases for which there are, presently, limited or no therapeutic options.
The sixth review is on **Augmentation techniques for rotator cuff repair** (page 107) by Papalia, Franceschi, Zampogna, D'Adamio, Maffulli and Denaro from the University of Rome, Italy and the Barts and The London School of Medicine and Dentistry, UK.

They say that there is a high rate of recurrence of tear and failed healing after rotator cuff repair. Several strategies have been proposed to augment rotator cuff repairs to improve postoperative outcome and shoulder performance. They systematically reviewed the literature on clinical outcome following rotator cuff augmentation. Heterogeneity of the outcomes scores makes it difficult to compare different studies. There is no dramatic increase in clinical and functional assessment after augmented procedures, if compared with control groups. More and better scientific evidence is necessary to use augmentation of rotator cuff repairs in routine clinical practice.

The seventh review is on the **Humoral theory of transplantation: some hot topics** (page 139) by Cai Qing, Tan and Terasaki from the Terasaki Foundation Laboratory, Los Angeles, USA.

They say that antibodies are a major cause of allograft injury. Donor-specific antibody (DSA) monitoring not only helps to identify patients for risk of antibody-mediated rejection (AMR), but also serves as a biomarker to personalize patient’s maintenance of immunosuppression. Some autoantibodies are directly involved in allograft injury, whereas others only serve as biomarkers of tissue injury. It remains controversial whether DSA-positive patients without symptoms need to be treated. In addition, given the variation in study designs and patient’s characteristics, there is discrepancy regarding which treatment regimens provide optimal clinical outcome in preventing or treating AMR. Research in B-cell targeted therapies to prevent and treat AMR is rapidly growing. It requires extensive clinical research to determine the best approach to inhibit or delete antibody and how to balance drug efficacy with safety.

The eighth review is on **PET a tool for assessing the in vivo tumour cell and its microenvironment?** (page 157) by Buscombe and Wong from Addenbrooke’s Hospital, Cambridge and the Royal Free Hospital, London, UK

They say that PET has started to develop beyond its roots in glucose imaging expanding to study other parameters of the tumour and its microenvironment. Therapeutic outcomes for patients can only be obtained by assessment and continued reassessment, not only of the tumour microenvironment, but also how this is changed by treatment. Although PET offers a tool by which the tumour and its microenvironment can be assessed in vivo without the need for multiple interventional procedures, the cost of multiple PET scans is high. As the quantity and quality of the
agents that can be used to perform PET imaging increase, we are able to assess tumour cell turnover, metabolism, hypoxia, angiogenesis and a variety of other factors that may affect tumour survival and response to treatment.

The ninth review is on Autologous conditioned serum in osteoarthritis and other possible applications in musculoskeletal disorders (page 169) by Frizziero, Giannotti, Oliva, Masiero and Maffulli from the University of Padova, Padova and University of Rome, Italy and the Barts and London School of Medicine and Dentistry, UK.

They say that the therapeutic use of IL-1 cytokine receptor antagonists (IL-1RA) has promoted the development of new biological therapies for osteoarthritis (OA). Autologous conditioned serum (ACS) is an alternative, safe and well-tolerated treatment in OA. ACS, containing endogenous anti-inflammatory cytokines including IL-1RA and several growth factors, could reduce pain and increase function and mobility in mild to moderate knee OA. Although previous clinical data are encouraging and confirm the safety of this modality, given the limitations of current studies, there should be additional, controlled trials to further confirm efficacy for the use of ACS in OA treatment. ACS can lead to an enhancement of tissue regeneration and reduce degenerative mechanisms.

The tenth review is on the Epidemiology and burden of osteoarthritis (page 185) by Litwic, Edwards, Dennison and Cooper, from the University of Southampton and Southampton General Hospital, UK.

They state that OA is a degenerative joint disease involving the cartilage and many of its surrounding tissues. Disease progression is usually slow, but can ultimately lead to joint failure with pain and disability. OA of the hips and knees tends to cause the greatest burden to the population as pain and stiffness in these large weight-bearing joints often lead to significant disability requiring surgical intervention. Symptoms and radiographic changes are poorly correlated in OA. Established risk factors include obesity, local trauma and occupation. Available data do not allow definite conclusion regarding the roles of nutrition, smoking and sarcopenia as risk factors for developing OA. Further research is required to fully understand how OA affects an individual physically and psychologically and to determine their healthcare needs.

The eleventh review is on What is new in the management of wet age-related macular degeneration? (page 201) by Sivaprasad and Hykin from the Moorfields Eye Hospital, London.

They state that the hallmark of wet age-related macular degeneration (AMD) is choroidal neovascularization (CNV). The key cytokine
involved in the pathogenesis of CNV is vascular endothelial growth factor (VEGF). Since 2005, anti-VEGF therapy has revolutionized the management of this condition. Anti-VEGF therapy has resulted in improvement in visual function and performance. Currently, practitioners are spoilt for choice of these agents. Bevacizumab is unlicensed for intraocular use, but has a better market share than ranibizumab in the treatment of wet AMD as it is approximately 40 times cheaper than ranibizumab, if used in smaller doses for intraocular use. Well-designed clinical trials have shown that both drugs are equally effective. Another dilemma for the physicians is the choice of treatment regimens with anti-VEGF agents that include fixed dosing, guided re-treatment, treatment and extent or a combination of proactive and reactive dosing. Real-life outcomes of re-treatment with these agents are inferior to outcomes reported in clinical trials.

The twelfth review is on Diabetic gastroparesis (page 213) by Vanormelingen, Tack and Andrews from the University of Calgary, Canada.

Diabetic gastroparesis (DGP) is a gastric complication of diabetes mellitus that causes nausea, vomiting, early satiety, bloating and abdominal pain, in addition to significant morbidity. Diagnosis of DGP requires endoscopy and the measurement of gastric emptying. Management requires prokinetic therapy, usually in addition to antinausea or other medications. The pathogenesis of DGP is poorly understood. Management strategies are highly variable. Prokinetic and neuromodulatory medications are presently being tested in human clinical trials for gastroparesis. Further understanding of the molecular pathology leading to DGP is required to arrest the development of this serious diabetic complication. Evaluation of novel agents for use in DGP is sorely needed.

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