The British Medical Bulletin, Volume 104, for its fourth print edition of 2012, contains 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 in order to bring these subjects to a wide audience.

The first review is entitled ‘Neural stem cells: therapeutic potential for neurodegenerative diseases’ (page 7) by Gincberg, Arien-Zakay, Lazarovici and Lelkes from the Hebrew University of Jerusalem, Israel and the Temple University, Philadelphia, PA, USA.

They state that neural stem cells (NSCs) from specific brain areas or developed from progenitors of different sources are of therapeutic potential for neurodegenerative diseases (NDs). The ability of NSCs to home into areas of CNS injury allows their delivery by intravenous injection. There is also general agreement about the neuroprotective mechanisms of NSCs involving a ‘bystander effect’. However, individual laboratories may be using phenotypically diverse NSCs, since these cells have been differentiated by a variety of neurotrophins and/or cultured on different ECM proteins, therefore differing in the expression of neuronal markers. Optimization of the dose, delivery route, timing of administration of NSCs, their interactions with the immune system and combination therapies in conjunction with tissue engineered neural prostheses are under being developed. These areas are central for further use in cell therapy. We need to be careful in translating NSC therapy from animal models to patients.

The second review is on ‘Peripheral arterial disease’ (page 21) by Abdulhannan, Russell and Homer-Vanniasinkam from Leeds General Infirmary, UK.

They state that peripheral arterial disease (PAD) is a common vascular condition that affects both the quality of life and life expectancy with an increased risk of cardiovascular events. Aggressive risk factor modification is needed to reduce cardiovascular-related mortality in PAD patients. The choice of endovascular or surgical intervention remains controversial. There is a rapid expansion of endovascular technologies aiming to improve effectiveness. Gene therapy and therapeutic angiogenesis are potential future treatments. Tissue engineering is a developing area and aims to produce grafts with similar patency and infection profiles to those of autologous material. Further elucidation
of the pathophysiology of atherosclerosis is required to provide new targets for pharmacotherapy.

The third review is on the ‘Therapeutic application of monoclonal antibodies in cancer’ (page 41) by Modjtahed, Ali and Essapen from Kingston University London, UK and the Royal Surrey County Hospital, Guildford, UK.

They say that monoclonal antibody-based products are highly specific for a particular antigen. This characteristic feature of the molecules makes them an ideal tool for many applications including cancer diagnosis and therapy. Treatment of cancer patients with antibodies when used alone or in combination with chemotherapy and radiotherapy, or conjugated to drugs or radioisotopes, prolong overall survival. However, therapeutic antibodies are expensive and may have side effects. There are no reliable predictive biomarkers for sensitivity or resistance to certain therapeutic antibodies. There should be additional studies to discover novel therapeutic targets, to develop more effective antibody-based drugs with fewer side effects, to identify more reliable predictive biomarker(s) for response to therapy with antibody-based drugs and to develop alternative strategies (e.g. transgenic plants, transgenic farm animals) for production of large quantities and more affordable batches of therapeutic antibodies.

The fourth review is on ‘Laparoscopic surgery for colorectal cancer’ (page 61) by Lai and Law from the University of Hong Kong, China.

They state that laparoscopic surgery for colorectal cancer has undergone tremendous advances in the last two decades, with maturation of techniques and integration into current practice. A large body of evidence has attested to the improved short-term outcomes and long-term oncological safety of laparoscopic surgery for colon cancer. Laparoscopic colectomy can be recommended to suitable patients where expertise is available. Laparoscopic resection for rectal cancer is feasible, with good evidence of faster post-operative recovery and adequate surgical quality, but requires more data on long-term oncological outcomes. It is still controversial as to whether laparoscopic surgery confers a survival advantage for colorectal cancer patients. The role of single-incision laparoscopic surgery and robotic surgery in colorectal cancer and barriers to the adoption of the laparoscopic technique need more research.

The fifth review is on ‘Sparing the anterior cruciate ligament remnant’ (page 91) by Papalia, Franceschi, Vasta, Di Martino, Maffulli and Denaro from Campus Biomedico University of Rome, Italy and the Barts and The London School of Medicine, UK.
Anterior cruciate ligament (ACL) rupture is the most common surgically treated ligament injury. The role of the ACL remnant is debated, because, although it may increase the risk of impingement and the formation of cyclops lesion, its preservation can improve proprioception, biomechanical functions and vascularity. However, the current assessment methods to assess proprioception, vascularisation and the ligamentization do not lead to hard evidence that preservation of the remnant confers clinically relevant advantages over its excision. The ACL remnant has been demonstrated in experimental studies to have a role in improving revascularization, ligamentization and reinnervation of the graft, but these findings are still not supported by clinical findings. A more direct way to assess proprioceptive function after ACL reconstruction, and appropriately conducted powered and rigorously prospective randomized double-blind studies comparing the clinical outcomes of excising the remnant to leaving it in situ are necessary.

The sixth review is on ‘Renal complications of diabetes’ (page 113) by Min, Stephens, Kumar, and Chudleigh from Singleton Hospital, Swansea, UK.

They make the point that diabetic nephropathy is a leading cause of chronic kidney disease (CKD) in the UK. These patients are at significantly increased risk of cardiovascular disease and of progression to end-stage renal disease. Early multifactorial intervention including strict blood pressure control, the use of ACE inhibitors or angiotensin 2 receptor blockers (A2RBs) and good metabolic control attenuates cardiovascular risk and slows the rate of progression of renal disease. Current areas of uncertainty include the relative benefits of ACE inhibitors and A2RBs in combination, whether direct renin inhibitors are harmful in patients with diabetes and the positioning of hypoglycaemic agents as renal function declines. The appropriate metabolic and blood pressure targets for patients with diabetes are uncertain. Therapeutic strategies as kidney function declines need to be developed.

The seventh review is on ‘A review of resting left ventricular function elite weightlifters’ (page 129) by Dhamu, Malliaras, Twycross-Lewis and Maffulli from the William Harvey Research Institute, Queen Mary University of London, London, UK.

This review aims to establish what effect weightlifting has on the systolic and diastolic function of the left ventricle (LV). Stroke volume, posterior wall thickness and ventricular filling time and rate were seen to increase. A decrease in the resting heart rate was seen. Blood pressure and LV morphological changes were equivocal. Weightlifting causes recognizable functional change to the LV. Some of these changes may confer benefits such as improvements in systolic function.
Discrepancies exist with regard to the regional LV morphological change, as the evidence suggests the LV does not adapt in a homogenous manner. Attempts should be made to separate performance-enhancing drug users from those who compete drug free.

The eighth review is on ‘Occupation and chronic obstructive pulmonary disease (COPD)’ (page 143) by Cullinan from Imperial College, London, UK.

There is growing interest in preventable, non-smoking causes of chronic obstructive pulmonary disease (COPD), among which are chronic exposure to respiratory irritants in the workplace. There is good evidence for an increased risk of COPD from certain specific exposures (coal mine dust, silica, welding fume, textile dust, agricultural dust, cadmium fume). Less clear is the causal role of non-specific dusts or fumes/gases in general populations where the available literature is notably uncritical. Other specific exposures, such as diesel fumes, interactions between specific exposures and cigarette smoking need to be explored as does the development of safe working limits. Occupations with large numbers of exposed employees, particularly in low-income countries, need to be studied.

The ninth review is on ‘Shoulder stiffness and rotator cuff repair’ (page 163) by Papalia, Franceschi, Vasta, Gallo, Maffulli and Denaro from the University of Rome, Italy and the Barts and The London School of Medicine, UK.

Shoulder stiffness is a frequent complication of surgical repair of rotator cuff tears (RCT). Post-operative stiffness negatively affects surgical outcome leading to substantial comorbidity and to the failure of surgical treatment. The management of shoulder stiffness is still controversial. The role of rehabilitation programmes (standard versus early passive mobilization) after RCT repair on the development of stiffness is not clear. The role of arthroscopic capsular release for post-operative stiffness is better defined, although a threshold of decreased range of movement for which capsular release is advised has not been identified. The post-operative rehabilitation protocol remains controversial. We are still far from definitive guidelines for the management of pre- and post-operative stiffness, and prospective double-blinded randomized clinical trials are needed to obtain evidence allowing establishing a reliable and effective management plan.

The tenth review is on the ‘Management of trypanosomiasis and leishmaniasis’ (page 175) by Barrett and Croft from the College of Medical, Veterinary and Life Sciences, University of Glasgow and the School of Hygiene & Tropical Medicine, London.
The current treatments for human African trypanosomiasis (HAT), Chagas disease and leishmaniasis (collectively referred to as the Kinetoplastid diseases) are far from ideal but, there has been some recent progress. For HAT the only advances in treatment over the past two decades have been the introduction of an eflorenithine/nifurtimox co-administration and a shorter regime of the old standard, melarsoprol. For cutaneous leishmaniasis, treatments are lagging behind. There are three compounds in development for the treatment of the central nervous system stage of HAT: fexinidazole, currently due to enter Phase II clinical studies, a benzoxaborole in phase I trials and a diamidine derivative, in advanced pre-clinical development. For Chagas disease, two anti-fungal triazoles are now in clinical trial. In addition, clinical studies with benznidazole, a drug previously recommended only for acute stage treatment, are close to completion to determine the effectiveness in the treatment of early chronic and indeterminate Chagas disease. For visceral leishmaniasis new formulations, therapeutic switching, in particular AmBisome, and the potential for combinations of established drugs, have significantly improved the opportunities for the treatment in the Indian subcontinent, but not in East Africa. Improved diagnostic tools are needed to support treatment, for test of cure in clinical trials and for monitoring and surveillance of populations in control programmes.

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