

ROUNDUP³⁶⁰

Research

Not everyone is an arthroscopist

■ ³⁶⁰ found it difficult to decide where best to place this summary but, after much deliberation, the Research section seemed best. You see, can everyone handle an arthroscope? The way some folk talk you would have thought so. However, a team from **Oxford (UK)** has looked at this in detail by investigating the effect of training on the arthroscopic performance of a group of medical students in order to determine whether all students can be trained to a level of competence. They took 33 medical students with no previous experience of arthroscopy and randomised them to a 'Trained' or 'Untrained' cohort. Each medical student was required to perform 30 episodes of two simulated arthroscopic tasks (one shoulder and one knee). The primary outcome variable was task success at each episode. Individuals achieved competence when their learning curve stabilised. The secondary outcome was technical dexterity, assessed objectively using a validated movement analysis system. By the end of the study, there were six students in the 'Untrained' cohort who had failed to achieve competence in the shoulder task, compared with one in the 'Trained' cohort. During the knee task, two students in each cohort failed to achieve competence. Based on the objective motion analysis parameters, the 'Trained' cohort performed better on the shoulder task but there was no significant difference for the knee.¹ ³⁶⁰ thus notes that although specific

training can improve the arthroscopic performance of novices, there are some who may never achieve competence despite focused training. So can everyone handle an arthroscope? Clearly not.

Bupivacaine, triamcinolone and chondrotoxicity

■ Some laboratory research is only distantly related to clinical practice but some is directly relevant. No more so, perhaps, than work from **Loma Linda (USA)** into the effects of bupivacaine and triamcinolone on human chondrocytes. Countless joints are injected with these materials globally on a daily basis for the management of chronic pain symptoms associated with degenerative disease, and after arthroscopic procedures. The authors asked themselves three questions: 1) were bupivacaine and triamcinolone, alone and combined, chondrotoxic to chondrocytes in culture? 2) could buffering of the reagents used reduce any toxicity of the bupivacaine and triamcinolone? and 3) could the superficial layer of articular cartilage protect against toxicity? To do this they obtained articular cartilage from three patients undergoing joint replacement and set up monolayer chondrocyte cultures. They harvested 21 articular plugs from each patient. A Live/Dead assay was used to determine chondrocyte survival. The results were impressive. Bupivacaine, triamcinolone, and their combination were toxic to human chondrocytes in the monolayer comparisons and the addition of buffering did not mitigate

chondrocyte death. With the intact superficial layer, bupivacaine was not toxic but all the other reagents (triamcinolone, combination bupivacaine/triamcinolone, buffered bupivacaine, buffered triamcinolone, and buffered combination) produced chondrotoxicity.² ³⁶⁰ feels these results are worrying. As the authors report, although this work does not necessarily reflect *in vivo* conditions, it does suggest we should be aware of the potential *in vitro* chondrotoxicity of bupivacaine and triamcinolone when contemplating intra-articular administration. Watch that space. More to follow, we are sure.

Reducing scarring in injured skeletal muscle

■ Muscle injuries are common musculoskeletal problems encountered in sports medicine clinics and the development of scarring within skeletal muscle can lead to a lifetime of trouble as well as a significant decline in sporting performance. Consequently, work from **Shanghai (China)** is interesting. Researchers looked at the effect of lentivirus-mediated small interfering RNA (siRNA) targeting Smad4 on the suppression of the fibrosis in injured skeletal muscles. Smad4 is a 552-amino acid protein involved in cell signalling. They found that Smad4-siRNA could efficiently knock down the expression of Smad4 in the mouse myoblast cell line known as C2C12 and in damaged mouse gastrocnemius muscle. The expression of mRNA level of Smad4 compared with the control group decreased to

11% and 49%, respectively, and the expression of protein level decreased to 13% and 57%, respectively. Furthermore, the muscle function of the mice injected with lentivirus-mediated Smad4-siRNA improved in terms of both fast-twitch and tetanic strength. These results suggest that the gene therapy of inhibiting Smad4 by lentivirus-mediated siRNA could be a useful approach to prevent scar tissue formation and improve the function of injured skeletal muscle.³

Horny Goat Weed and the repair of osseous defects

■ The treatment of serious osseous defects remains a great challenge in orthopaedic surgery, as a team from **X'ian (China)**, the home of the terracotta army, reminds us. For the enhancement of bone regeneration and repair of bone defects, the implantation of biomaterials that can carry and efficiently release osteoinductive agents at the required location is what many seek. Icarin, a plant-derived flavonol glycoside, has been shown to be an osteoinductive agent for bone regeneration. It is a compound derived from several species of plants, which are commonly known as Horny Goat Weed or Yin Yang Huo and used in many aspects of Chinese herbal medicine, including as an aphrodisiac. The team developed an icariin-loaded chitosan/nano-sized hydroxyapatite system that could control the release of icariin to enhance bone repairing in an *in vitro* study. First, the researchers found that icariin was stable within their system and did not undergo any chemical changes.

Their results suggested that the icariin was released steadily over time and the release kinetics could be governed by degradation of both chitosan and hydroxyapatite matrix. Additionally, the team's *in vitro* bioactivity assay revealed that the icariin was biologically active. This was evidenced by stimulation of bone-marrow-derived stroma cell alkaline phosphatase activity and the formation of mineralised nodules.⁴ 360 feels this new delivery method of osteoinductive agents may well be promising and a useful scaffold design for bone regeneration. We look forward to the team's future research once it moves from *in vitro* to *in vivo*.

Platelet-derived growth factor and fracture healing

■ Anything that might accelerate the healing of fractures is to be welcomed, so work on platelet-derived growth factor (PDGF) undertaken by a researcher from **Constanta (Romania)** may prove to be helpful. PDGF is known to stimulate osteoblast or osteoprogenitor cell activity. Using a rat model, the effect of locally applied PDGF from poly-D L-lactide (PDLA)-coated implants on fracture healing was assessed. A closed fracture of the right tibia of 40 four-month-old rats was stabilised with implants coated with a biodegradable PDLA *versus* implants coated with PDLA and PDGF. Radiographs were taken throughout the study, and a marker of DNA activity, bromodeoxyuridine (BrdU), was injected before the rats were killed at three, seven and ten days. The radiographs showed consolidation of the callus in the PDGF-treated group compared with the control group at all three time points. In the PDGF-treated group, immunohistochemical staining of BrdU showed that the distribution of proliferating cells was higher after ten days compared with that at three and seven days. These results indicate that local application of PDGF from biodegradable PDLA-coated implants significantly accelerates fracture healing in experimental animals.⁵ Again, 360 feels, this is tremendous work but

in vivo studies are essential.

Importance of the reserve zone in a child's growth plate

■ Little is known about the growth potential of the different zones of a child's growth plate. Researchers from **Vienna (Austria)** have looked at this in a laboratory study of 20 New Zealand white rabbits. The right and left ulnae of each animal were used, giving a total of 40 bones. Animals were assigned to one of five groups. In groups I and II resection of the metaphyseal or epiphyseal segment of the growth plate was performed. In group III resection of the growth plate and reimplantation was performed. In group IV the growth plate was resected and reimplanted after a 180° rotation. Animals in group V served as controls. Histological and radiological examinations were then performed to assess the growth process at one, two, four and 12 weeks after surgery. In groups I, III, and IV a temporary growth disturbance was seen, although this was compensated for within a short time. Resection of the epiphyseal part (group II) resulted in growth arrest of the distal ulna in combination with normal growth of the radius. This then led to a valgus deformity of the limb.⁶ 360 previously felt that the reserve zone of a growth plate, the part on the epiphyseal side, was relatively inactive. However, this work goes against that, stressing the importance of the reserve zone for the proper functioning of a growth plate.

Coping with advanced arthritis

■ How do patients really cope with advanced arthritis, particularly in the developing world? Some interesting work on this has come out of the Dominican Republic, published from **Boston (USA)**. The authors conducted semi-structured, one-to-one interviews with economi-

cally disadvantaged Dominican patients with advanced knee and/or hip arthritis in the Dominican Republic. The interviews, conducted in Spanish, followed a moderator's guide that included topics such as the patients' understanding of the aetiology of their disease, any support networks, and the patients' coping mechanisms. The interviews were audiotaped, transcribed verbatim in Spanish, and then systematically analysed using content analysis. The team interviewed 18 patients (mean age 60 years, 72% women). Patients invoked religious and environmental theories of disease aetiology, stating that their illness had been caused by God's will or through contact with water. While all patients experienced pain and functional limitation, the social effects of arthritis were gender-specific. Women noted interference with homemaking and churchgoing activities, while men experienced disruption with occupational roles. The coping strategies used by patients appeared to reflect their beliefs about disease causation and included prayer and avoidance of water.⁷ 360 finds this work to be simple but humbling. For those of us who have the good fortune to live in reasonably wealthy parts of the world we find it hard enough to cope with arthritis. The fact that these Dominican patients cope as well as they do is truly remarkable.

Hydroxyapatite and platelet-rich plasma for bone defects

■ Hydroxyapatite is known to be an excellent osteoconductive material. Human platelet-rich plasma (hPRP) is also thought to be osteoinductive. What about combining the two? A team from **Shiraz (Iran)** has now done this. The researchers examined the effect of a combination of hydroxyapatite and hPRP on osteogenesis *in vivo*, using

a rabbit model of bone healing. A 10-mm defect was created in the radial diaphysis of 36 rabbits and either supplied with hydroxyapatite-hPRP or hydroxyapatite, or was left empty (control group). Radiographs of each forelimb were taken post-operatively on the first day and then at weeks two, four, six and eight after injury to assess bone formation, union and remodelling of the defect. The operated radiuses of half of the animals in each group were removed on day 56 post-operatively and were examined grossly and histologically. In addition, biomechanical tests were also performed on the operated and normal forearms of the other half of the animals in each group. This study demonstrates that hydroxyapatite-hPRP can promote bone regeneration.⁸ Perhaps this could be an attractive alternative for the reconstruction of major diaphyseal defects suggests the authors, and thinks 360, too.

Calcium phosphate and bone regeneration

■ Osteoinduction has also been the focus of a team from **London and Stanmore (UK)**. Here, they investigated the osteoinductivity of silicate-substituted calcium phosphate and stoichiometric calcium phosphate by using ectopic implantation in the paraspinal muscles of six female sheep. They found silicate substitution to have a significant effect on the formation of bone, both within the implant and on the implant surface during a 12-week period. The area of bone within the implant was greater in the sheep that had received silicate-substituted calcium phosphate than for those that had received stoichiometric calcium phosphate. The amount of bone formed at the surface of the implant was also greater in the former group. In essence, however, the formation of bone within muscle during this 12-week period showed both silicate-substituted calcium phosphate and stoichiometric calcium phosphate to be osteoinductive in an ovine model. The use of a silicate-substituted calcium phosphate material instead



of stoichiometric calcium phosphate ceramic during orthopaedic surgery may substantially augment repair and regeneration of bone.⁹ 360 notes these various publications in the field of osteoinduction, a much-needed area of research, and trusts these studies will lead to helpful clinical advances soon.

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