

# ROUNDUP<sup>360</sup>

## Research

**x-ref** For other roundups in this issue that cross-reference with *Research see: Hip roundup 6; Wrist & Hand roundups 2 and 8; Shoulder & Elbow roundup 1; Spine roundup 8; Trauma roundups 4 and 7; Oncology roundups 1 and 6.*

### Antibiotic loaded ceramic of use in osteomyelitis

■ Biodegradable ceramics provide a potentially uniquely useful combination in chronic osteomyelitis of dead-space management, osteoconductive properties and local elution of antibiotics to provide further osteomyelitis control. Researchers in **Oxford (UK)** have reported some of the first clinical evidence of use of tobramycin with a calcium sulphate carrier.<sup>1</sup> Impressively, the study team were able to report on the surgical management of 193 patients, all treated with this unique and novel approach. The cohort had a mean age of 46 years and the majority were Cierny–Mader type III and IV (144 and 38, respectively) with only 12 type I and a single type II case. The overall cure rate was 90.8% at a mean follow-up of 3.7 years, rising to 97.9% with an additional procedure. Patients often experienced a persistent wound ooze (thought to be associated with the Osteoset) up to two weeks following surgery. The authors concluded that Osteoset T was helpful in the management of chronic osteomyelitis, with partial or complete filling of the bone void seen in around 65% of patients. There were no patients in whom prolonged wound ooze was associated with recurrent infection.

### Fibronectin implicated in cartilage degeneration

■ The mystery of injury and training-related degenerative change is slowly unravelling. An increase in understanding of cartilage and matrix biology has allowed the process of post-traumatic degeneration to gradually be understood. However, the cascade of biological mediators occurring after a cartilage injury is a complex one and is far from understood. Researchers in **Iowa City (USA)**, reasoning that progressive cartilage loss occurs in post-traumatic degeneration, set out to establish if fibronectin-fragments which activate the matrix metalloproteinase family (MMPS) were implicated in this cascade and specifically in promotion of chondrolysis following injury.<sup>2</sup> They devised a drop tower system to create partial thickness chondral defects in a bovine model. Culture of injured and control explants was undertaken for two weeks and the levels of fibronectin-fragments and MMPs (1,3 and 13) and ADAMTS-5 was determined daily along with a measure of proteoglycan depletion of the cartilage matrix. Throughout the course of the experiment the damaged cartilage released higher levels of fibronectin, fibronectin fragments and proteoglycans. These were seen to correlate with MMP-3 upregulation, all pointing to an association and a potential causation. There is certainly food for thought in this thorough and well conducted research project. MMP-3 is intimately implicated in

post-traumatic cartilage breakdown and it appears from these results to be potentially causally related to fibronectin fragmentation.

### Zinc Chloride accelerates fracture healing in rats **x-ref**

■ One of the unsolved problems in orthopaedic trauma surgery is that of accelerating fracture healing. Although nonunion is relatively rare and it's treatment a matter of often contentious opinion, biological acceleration of fracture healing has many more routine applications than some of the biological therapies aimed fair and square at the tibial nonunion market. Accelerating fracture healing in a rat is no mean feat; rats heal so quickly that it can be difficult to accelerate that process meaningfully. Researchers in **Newark (USA)** have undertaken a pre-clinical study in an attempt to do just this. Hypothesising that ZnCl<sub>2</sub> has an insulin mimetic property, they designed an animal model with the intention of establishing the local effect of ZnCl<sub>2</sub> on the early and late parameters of fracture healing in a standardised rat femoral fracture model.<sup>3</sup> Outcomes were assessed using a combination of mechanical testing, radiological scoring and histomorphometry measurements. This has been interpreted in combination with immunohistochemistry and analysis of localised growth factors. Rats treated with ZnCl<sub>2</sub> outperformed those in the control group at four weeks post fracture. All outcomes were significantly better in the ZnCl<sub>2</sub> group,

with radiological scoring and histomorphometry showing increases in bridging callus and an increase in stiffness of 133% respectively. These mechanical changes were supported by increases in mineralised tissue and markers of cell proliferation and growth factors (including VEGF and IGF-I). All of the accumulated evidence supports the supposition that the insulin mimetic effects of ZnCl<sub>2</sub> result in improved fracture callus formation.

### Advertisements and false claims

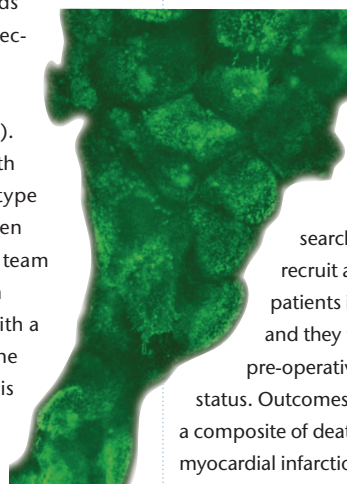
■ Advertisements are an essential part of the orthopaedic market economy. Promoting new products and through advertising revenues (essentially levied on the product sales) supporting academic publishing and meetings, advertisements are seen as essential by all parties. It is commonplace in this world of evidence based medicine for these advertisements to contain claims of efficacy or scientific study for the device or product being promoted. What is not clear following recent changes in legislation and the creation of a more transparent market place is what the basis for the claims supporting these products actually is. Researchers from **London (UK)** designed a simple study to evaluate the scientific basis for these claims.<sup>4</sup> The study team randomly selected 50 claims from 50 sample advertisements from six peer reviewed orthopaedic print journals published over a six month period in 2011. These were evaluated for the scientific

accuracy of the claims made. Three blinded orthopaedic surgeons were asked to rate the evidence supporting the claim from both a quality of evidence perspective and their view on if this was a sufficient evidence base to change practice. Of the 50 claims, only 28 were citations from published literature with a further four from public presentations. The remaining claims were supported by “data held on file” in 11 cases and 7 supplied no supporting evidence. Less than a quarter of the claims were rated as relying on high-quality evidence and only 22% of claims were rated as being well supported by the evidence they cited. The spearman’s R for intra-class correlation coefficient was 0.85 between raters, suggesting that there was validity and internal consistency in the study methodology. It is extremely concerning to read that this problem of misleading scientific claims (sometimes verging on the fraudulent) is still a widespread problem within the scientific literature. This is not just a problem for the industry, but also for the publications that print the advertisements. An advertisement in a well-respected journal gains some credence from the publication in which it is published – it is high time that the industry worked to correct this problem, until they do it seems likely that the widespread skepticism surrounding manufacturers’ claims will remain.

#### Net Promoter Score: substance or rhetoric?

■ Assessing outcomes in healthcare can be a challenge. Recent political impetus has focused around the assessment of outcomes in healthcare and particularly the patient experience side. In the UK there is a new and slightly unique take on the problem, the so called “family and friends test” where patients are asked if they would recommend the service/treatment/surgeon to their family and friends. Multiple responses results in a ‘net promoter score’ i.e. the chances of any individual

recommending their healthcare experience to anyone else. This is a concept that has moved across from the service industries and unlike many other scores has been widely adopted due to the political impetus, despite the complete lack of validation behind the test for use in a healthcare setting. Given the widespread adoption in the UK and the general view that this may be a discriminator of healthcare performance, researchers in **Edinburgh (UK)** set out to provide some evidence to inform its use.<sup>5</sup> The study team assessed over 6000 individuals undergoing lower limb arthroplasty and also undertook some subscale analysis to establish what components contributed to the binary score of ‘yes/no’. The chances of a ‘positive’ promoter score were contributed to by pain relief (odds ratio (OR) 2.13), expectation meeting (OR 2.57), and hospital experience (OR 2.33). When combined with information on the type of surgery undertaken (OR 2.31), the study team were able to explain 95% of responses with a predictive model. The general conception is that a net promoter score provides a ‘recommendation’ for services and individuals, however despite shared surgeons, institutions and probably experiences there was a difference in satisfaction responses and given differences in net promoter score between THR (NPS 71) and TKR (NPS 49) it does appear that further work is definitely required and adjustment for case mix is essential. The net promoter score adds an important dimension to existing metrics, but shouldn’t be used as a ‘definitive’ outcome measure without further work. This paper really is essential reading for any surgeon providing



healthcare in the UK and we cannot recommend it enough to anyone with more than a passing interest in healthcare outcomes.

#### Aspirin for Venous thromboembolism prophylaxis x-ref

■ The contention surrounding venous thromboembolism prophylaxis continues to cause a stir in both the scientific and clinical communities. Despite this intense interest there are few independent high quality studies other than those funded as part of drug company trials. This paper published in the New England Journal of Medicine aimed to evaluate the efficacy of aspirin as a thromboprophylactic agent in non-cardiac surgery (not just orthopaedics). The researchers from **Hamilton (Canada)** designed a 2-by-2 factorial study with

the aim of evaluating a range of aspirin protocols including placebo, placebo and clonidine, and aspirin.<sup>6</sup> The researchers were able to recruit an amazing 10,010 patients into the study and they were stratified by pre-operative aspirin therapy status. Outcomes were assessed as a composite of death and non-fatal myocardial infarction at 30 days follow-up. There was an overall incidence rate of 7.0% (n = 351/4998) in the aspirin group compared with 7.1% (n = 355/5012) in the placebo group. Major bleeding was seen much more commonly in the aspirin group than the placebo group. (4.6% vs 3.8%, hazard ratio 1.23). Primary and secondary outcome measures were however similar between the two stratification groups. In what is the largest randomised controlled trial evaluating the outcomes of death and myocardial infarction, this study does not provide any evidence to support the use of aspirin as a thromboprophylaxis regime in these patients.

#### Dissection, stress and the soul

■ Generating a stress-free learning environment is essential when maximising learning. With the advent of newer simulated experiences, the use of the traditional dissection room experience has fallen a little from the fore of medical student and surgical teaching. However, as dissection becomes a rarer experience, it also becomes more valuable. Researchers in **Otago (New Zealand)** took a slightly different look at the determinants of the learning experience during dissection. They conducted a series of structured electronic questionnaires to establish the stress associated with dissection room experience (both anticipatory and experienced).<sup>7</sup> They asked a number of demographic and religious questions, most interestingly what the students’ belief about the existence or otherwise of a soul was. Overall, 51.6% of students believed in the concept of a soul and those who did were more likely to have religious beliefs. There were many students who believed in the soul who did not have a religious belief, suggesting that this belief extends beyond formalised religious belief structures. Those students who reported they believed in a soul underwent significantly higher levels of stress, both anticipatory and during dissection. This unusual but interesting research paper suggests that students who believe in the soul do not have an ideal learning environment in the dissection room. This stress could potentially be ameliorated by including some philosophical or other teaching prior to starting the dissection.

#### REFERENCES

1. Ferguson JY, Dudareva M, Riley ND, et al. The use of a biodegradable antibiotic-loaded calcium sulphate carrier containing tobramycin for the treatment of chronic osteomyelitis: a series of 195 cases. *Bone Joint J* 2014;96-B:829-836.
2. Ding L, Guo D, Homandberg GA, Buckwalter JA, Martin JA. A single blunt impact on cartilage promotes fibronectin fragmentation

and upregulates cartilage degrading stromelysin-1/matrix metalloproteinase-3 in a bovine ex vivo model. *J Orthop Res* 2014;32:811-818.

3. **Wey A, Cunningham C, Hreha J, et al.** Local ZnCl<sub>2</sub> accelerates fracture healing. *J Orthop Res*

2014;32:834-841.

4. **Davidson DJ, Rankin KS, Jensen CD, et al.** Are the claims made in orthopaedic print advertisements valid? *Int Orthop* 2014;38:1067-1072.

5. **Hamilton DF, Lane JV, Gaston P, et al.** Assessing treatment outcomes using a single question: the net promoter score. *Bone Joint J* 2014;96-B:622-628.

6. **Devereaux PJ, Mrkobrada M, Sessler DI,**

**et al.** Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014;370:1494-1503.

7. **Martyn H, Barrett A, Nicholson HD.** A belief in the soul may contribute to the stress experienced in the dissecting room. *J Anat* 2014;224:345-351.