2B.8

Delayed presentations of crush injury and the controversies surrounding the missed compartment or wipe out syndrome

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The crush and reperfusion injury phenomenon are well described. The experiences in Israel and the associated literature warned of the consequences of performing fasciotomies in 'missed compartment syndrome' also known as 'wipe out' syndrome.

The high incidence of infection and increased morbidity/mortality suggested a conservative, non-surgical approach to be the preferred treatment in these cases.

However, we present two cases of crush injury which presented late and were initially thought to have wipe out syndrome, yet displayed very unusual disease progression and thus had significant delay to fasciotomy. These patients experienced 'staged' compartment syndrome during their inpatient stay and had phased fasciotomies over a 48-h period. Both of these patients had viable muscle at operation, suggesting that crush injury patients have a unique disease process. Whilst the term 'compartment syndrome' may actually be a misnomer in this type of injury, the consequence of the underlying pathology is ultimately identical, even if their presentation and pathophysiology are different.

We review the literature surrounding this subject and warn against the presumption that prolonged crush injury represents a missed opportunity.

Keywords: Crush; Compartment; Delayed; Wipe-out

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2B.9

Exposure and experience: A survey of UK Orthopaedic Trainees exposure to limb threatening trauma

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Aim: To establish the levels of confidence, exposure to caseload and perceived adequacy of training of UK (UK) Orthopaedic Specialist Trainees in the assessment of limb viability and amputation surgery following high energy trauma.

Methods: A web-based survey was sent to a sample of orthopaedic trainees. Scenarios included the assessment of limb viability and amputation surgery following high energy trauma.

Statistical analysis required 214 responses from 713 trainees to achieve a <0.05 error rate with 90% confidence. 225 responses were received and analysed by means of descriptive statistics.

Results: Limb viability:

27.8% of trainees were fully confident. A positive correlation exists between training year and fully confident reports. 68.6% encounter such injury either every 6 months or less frequently. 18.6% regard their training in these cases inadequate. No correlation is seen between experience and perceived adequacy of training.

Amputation:

10.3% of trainees were fully confident. A positive correlation exists between time in training and perceived fully confident reports.

57.3% encounter such injury either every 6 months or less frequently. 36.3% regard their training in these cases inadequate. No correlation is seen between experience and exposure to cases or perceived adequacy of training.

Conclusion: Current training provides limited opportunities for decision making in limb viability and amputation. Confidence in dealing with such cases is seen to increase with training. Perceived adequacy of training and exposure to cases did not change over time. In the light of established concerns in deficiencies in training it can be seen that focussed attention should be given to complex extremity injury as part of an educational strategy for ensuring that future generations of orthopaedic surgeons are able to manage complex injuries.

Keywords: Training; Limb viability; Amputation; Survey

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2B.10

Pattern of tendon and nerve injuries: How accurate is pre-operative diagnoses?

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Hand injuries rank as the second most common category in A&E medicolegal claims. Accurate diagnosis and treatment is essential, with a high index of suspicion and low threshold for exploration. The first clinical examination for tendon and nerve injuries is crucial for prioritisation in a busy unit and surgical/anaesthetic planning.

St Andrew's centre is a tertiary level referral unit for hand injuries and has a significant throughput of trauma (head to feet) with 10–15 cases daily. Most patients are reviewed in the daily consultant/senior trainee-lead trauma clinic, with entries recorded on a computerised trauma database.

We analysed the pattern of tendon and nerve injuries and accuracy of pre-operative assessment compared to operative findings. The database for a 12-month period was reviewed. After exclusions, 1670 sequential cases of adults with below elbow, soft tissue injuries and complete clinical/operative notes were included. There were 1573 structures potentially injured in 823 digits, including 994 named tendons and 568 nerves. Knife and glass injuries predominated and 89% were operated on within 24 h of assessment.

Anatomical accuracy was greater than 98% for both tendons and nerves. Border nerves (index radial and little finger ulnar) were particularly at risk. Assessment of severity (nil, partial or total) was accurate in 68% overall.

This findings support our practice of low threshold for exploration. Distribution and accuracy by structure and zone are discussed, with recommendations for diagnostically difficult regions.

Knowledge of potential pitfalls may prevent inappropriate choices of anaesthetic and aids prioritisation.

Keywords: Hand; Lacerations; Tendon injuries; Nerve injuries

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K1

Keynote Lecture

New technologies for the enhancement of skeletal repair

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Introduction: The ability to stimulate fracture repair, enhance spinal fusions, heal nonunions or restore lost segments of bone is a common goal among orthopaedists, traumatologists, and scientists who investigate wound healing responses. Whilst in most clinical set-
tings these processes are already biologically optimised, many patients still experience delayed or impaired healing. Methods to ensure or accelerate these healing responses are greatly needed and the ability to restore skeletal integrity without the morbidity associated with bone graft harvesting would be a major advance in orthopaedic surgery.

This syllabus reviews emerging pharmacological and biotechnological methods to stimulate skeletal repair and restore lost bone. It presents technologies available today to meet some of these challenges and describes current investigations into new technologies that carry the promise of improving bone repair and regeneration in the future.

Biological enhancement—local

A. Peptide signalling molecules

These peptide growth factors stimulate the activity of chondroprogenitor and osteoprogenitor cells. They may also stimulate fully differentiated chondrocytes and osteoblasts and enhance angiogenesis. They do not induce cartilage or bone formation from undifferentiated cells.

Current investigations to test the effects of these molecules on skeletal healing responses are based on the observations that these molecules are expressed during the normal healing process and thus can be assumed to participate in it.

1. Fibroblast growth factor (FGF)

Fibroblast growth factor (FGF) has been shown to be expressed during fracture healing. Investigators have shown that an injection of α-FGF or β-FGF into fractures leads to an enhancement of fracture healing. A recent study reported that fibroblast growth factor-2 in a hyaluronan gel accelerates fracture healing in non-human primates. Basic FGF (4 mg/ml) and hyaluronan (20 mg/ml) were combined into a viscous gel formulation and injected percutaneously into fresh fractures. A bilateral 1 mm gap osteotomy was created in the fibulae of baboons. Radiographic analysis showed that callus area was significantly larger at the treated sites than in untreated sites. Load at failure and energy to failure were significantly increased when compared to controls. By histological analysis, the callus size, periosteal reaction, vascularity and cellularity were consistently more pronounced in the treated osteotomies than in untreated controls. Phase III multi-centre clinical trials on FGF-2 injections into fresh fractures are currently underway.

2. Vascular endothelial growth factor (VEGF)

Because of its ability to induce angiogenesis, vascular endothelial growth factor (VEGF) has been investigated for its potential role in the enhancement of fracture repair. In an investigation in which mice were treated with a soluble, neutralising VEGF receptor decreased angiogenesis, decreased bone formation and decreased callus mineralisation in femoral fractures was observed. Inhibition of VEGF also dramatically inhibited the healing of a tibial cortical defect. In separate experiments, exogenous VEGF enhanced blood vessel formation, ossification and callus maturation in mouse femur fractures which promoting bridging of rabbit radial segmental defects.

3. Platelet derived growth factor (PDGF)

PDGF is involved in the inflammatory process and is known to induce chemotaxis and mitosis in osteoblasts. A recombinant form, rhPDGF (Regranex gel 0.01%, Ethicon, Inc., Somerville, NJ), has been used with success as a topical solution in the treatment of diabetic foot ulcers. Its efficacy was shown in a study of 382 patients with type 1 or type 2 diabetes with chronic foot ulcers in which those patients treated with rhPDGF the wounds healed 32% sooner than controls. Adverse events were rare and similar between the two groups.

A similar study showed that rhPDGF was effective in healing foot ulcers and preventing amputation. This was a large study including 24,898 patients with diabetic foot ulcers, of which 2394 patients received rhPDGF. The relative risk for healing an ulcer whilst using rhPDGF was 1.32 and whilst the risk of amputation was 0.65.

A recent study has demonstrated accelerated fracture healing in aged osteoporotic rats with PDGF. It has also been shown that pulsed delivery of PDGF is able to simulate bone growth, whilst constant release was inhibitory. These results indicate that there is both an optimal concentration and time during bone regeneration to deliver rhPDGF, and elucidating this combination with an effective means of delivery, will likely result in improved clinical results.

4. Prostaglandin agonists

It has been well known for many years that prostaglandin E2 (PGE2) increases bone mass and strength when administered systemically or locally to the skeleton. However, due to side effects, PGE2 is considered an unacceptable therapeutic option. Recent investigations have shown that PGE2 mitigates its tissue-specific pharmacological activity via four different receptors, EP1, EP2, EP3 and EP4. However, it is now known that EP1 and EP3 mitigate the objectionable side effects whilst EP2 and possibly 4 are associated with bone formation. A recently identified EP2 selective agonist has been shown to enhance the healing of canine long bone segmental defects and fractures without the side effects associated with administration of PGE2. Moreover, the potent anabolic activity of this synthetic agonist may offer a therapeutic alternative for the treatment of fractures and bone defects in patients. Further investigation, including a clinical trial, concerning the use of EP2 selective agonists is currently in progress.

B. Osteoinductive molecules

Definition: Osteoinduction is a phenomenon in which there is a mitogenesis of undifferentiated perivascular mesenchymal cells leading to the formation of osteoprogenitor cells with the capacity to form new bone.

Over the past 20 years, investigators have applied the principles of bone induction to the treatment of musculoskeletal conditions in a variety of uncontrolled case reports or case series. Whilst these reports have suggested the potential clinical efficacy of various preparations of demineralised bone matrix or purified human bone morphogenetic proteins, only three randomised clinical trials have supported the use of recombinant bone morphogenetic proteins.

1. A prospective, randomised clinical trial involving 122 patients with 124 tibial nonunions was conducted with the use of rhBMP-7 (osteogenic protein-1; OP-1). All nonunions were at least 9 months old and had shown no progress towards healing for the 3 months prior to the enrollment of the patient in the study. The patients were randomised to receive either standard treatment with reduction and fixation with an intramedullary nail and autologous bone-grafting or resection and fixation with an intramedullary nail and implantation of rhOP-1 in a type-1 collagen carrier. The results showed that, at 9 months of follow up, 81% of 63 patients treated with rhOP-1 and 85% of 61 patients treated with autologous bone-grafting were judged to be healed according to clinical criteria (p = 0.524). Radiographic assessments suggested healing in 75% and 84% of these patients, respectively (p = 0.218).

Although it is possible that reaming and intramedullary nailing of tibial nonunions could have led to a similar rate of healing in both groups, it was noted that prior reaming and nailing had been performed in 54% of the OP-1 treated group and in 44% of the autograft group. In addition, prior bone-grafting had been performed in 43% of the patients in the
1. **Growth hormone (GH)**

   Growth hormone, in combination with other growth factors such as insulin like growth factors, is involved in the daily physiologic remodelling of the skeleton as well as having significant anabolic effects. Its actions are thought to be through stimulation of osteoblastic cells and induction of angiogenesis. Individuals with increased production of GH, such as in acromegaly, have increased bone mass and decreased fracture risk. The opposite effect is seen in growth hormone deficient states.

   Fracture repair in animal studies supplemented with recombinant growth factor have shown promising results. Yucatan mini pigs subjected to 1 cm tibial bone defects were treated with daily subcutaneous injections of either 100 μg/kg of rhGH or saline control for 6 weeks. The treatment group had a significant increase in bone mineral content whilst no difference was seen in bone mineral density. The physical strength of the fractured bone was also significantly greater in the treated animals. Both torsional failure load and torsional stiffness were increased by 70% and 83%, respectively.

   The effects of upregulation of GH are seen with an increase in the anabolic state and result in stimulation of wound healing and preservation of lean body mass. Clinical trials have been conducted in both trauma and post-surgical patients using GH to attempt to modulate the catabolic state that occurs in these situations. These studies have shown conflicting results, but have demonstrated that GH treatment has a low incidence of adverse events. Recently, a large, randomised, double-blind trial was conducted using varying concentrations of growth hormone (15, 30, or 60 μg/kg) or placebo alone in the treatment of open and closed tibial fractures treated with intramedullary nail. Treatments were started within 3 days of operative fixation and continued until radiographic healing was obtained or until 16 weeks post-operatively, whichever came first. Results at 12 months did not show a positive correlation between GH treatment and time to fracture healing. A post hoc analysis of closed tibial fractures, however, found a significant decrease in the time to radiographic healing in the 6-μg/kg treated individuals, with fractures healing on average at 95 days compared to 129 days in the control group. Another important finding was that there were no differences in major adverse events noted in this study, with oedema and transient arthralgias being the only significant complaints. The positive results in close fractures will need to be further studied, and it is likely that these and other results will encourage further research in this area.

2. **Parathyroid hormone (PTH)**

   Calcium homeostasis is maintained in large part due to the effects of parathyroid hormone (PTH). When serum calcium levels are low, PTH is secreted by the parathyroid gland that then stimulates the small intestine to increase calcium absorption, whilst suppressing calcium loss in the kidneys. It also acts on osteoclasts, through the direct activation of osteoclasts, to increase bone turnover and release of calcium from the bone.

   The physiological effects of continuous exposure to PTH result in increased bone turnover and a decrease in bone mass, and this would not seem productive in fracture healing. Intermittent dosing of PTH, however, may result in improved bone remodelling and in increase in bone formation. Andreasen et al. treated rats with tibial fractures with very high intermittent doses of either 60 or 200 μg/kg/day of PTH (1–34). They found that 20 days of treatment with the higher dose resulted in an increase in fracture callus volume and ultimate load strength of 75% and 99%, respectively. By 40 days, load strength was increased by 175% when compared to controls.

   Recombinant human parathyroid hormone [rhPTH (1–34)] has been approved in several countries for treating post-menopausal osteoporosis and is marketed under the trade name FORTEO®. Side effects have included mild increases in serum calcium levels, but the real concern is with the potential for enhancement of tumor formation. Recent studies in rats and mice with PTH (1–34) show the enhancement of fracture
healing at doses comparable to those tolerated in patients. A clinical trial on the use of PTH (1–34) to stimulate distal radial fracture healing is currently in progress.

3. Statins

Statins (HMG-CoA reductase inhibitors) are lipid-lowering drugs that inhibit cholesterol synthesis by blocking mevalonate acid production. Mevalonate acid is a precursor for both cholesterol and geranyl geranyl pyrophosphate (GGPP). Multiple intracellular pathways in osteoclast depend on the actions of GGPP, including those involved in maturation. By blocking these pathways, fracture repair may proceed through increased bone formation secondary to a decrease in bone turnover. In addition, statins have been shown to induce the BMP promoter in bone cells.

Oral simvastatin use has been shown to increase bone mineral density in several human studies and subsequent animal studies have supported these results. With regards to fracture healing, Skoglund et al. tested simvastatin in a mouse model of femur fractures. They produced internally stabilised femur fractures in 81 mature BALB/c mice. Half of these mice then received a daily oral dose of 120 mg/kg of simvastatin for up to 21 days. Their results showed that at day 14, the mechanical strength of the simvastatin group was 64% greater than in the control mice and the callus was 53% larger. Whilst their study did not find a continuation of these trends at 21 days, their study demonstrated that simvastatin could be effecting accelerating the healing process.

The statins currently in use target the liver, and much of the drug is metabolised (first pass effect) and not available for action in bone. For this reason, systemic use of statins to target bone will require further development. In a study to test the local application of a statin, Garrett et al. combined lovastatin with biodegradable polymer nanobeads of poly[(lactic-co-glycolic acid) and injected this mixture into femur fractures in rats. At 4 weeks, they noticed a decrease in the fracture gap as measured by microcomputed tomography. Clinical trials are necessary to determine if these studies will translate into clinically significant gains in fracture healing.

Further reading


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Foot and ankle trauma

3.1

3: BTS–DGU joint session

Osteosynthesis of pilon fractures: Tips and tricks

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Pilon fractures are some of the most demanding fractures of the skeleton especially C-type fractures with additional severe soft tissue injury. Our concept of operative treatment is related to both the fracture type and the soft tissue damage. If possible B-fractures are treated by arthroscopy and fluoroscopy with reduction and percutaneous screw fixation or anterior buttressing using small plates. If soft tissues allow C1- and C2-fractures are treated with the AO manual technique of tibial osteotomies in rabbits. Bone 1994;15(2):203–8.

If soft tissues allow C1- and C2-fractures are treated with the AO procedure with primary tibio-tarsal transfixation. If possible B-fractures are treated by AP approach with cross-fusion. In C3-fractures (31.C1–C3) with significant soft tissue damage, a 2-stage procedure with primary tibio-tarsal transfixation should always be performed. After 10–12 days, secondary fibula and tibia reconstruction should be performed and fixated with a pilon plate. In cases of type II/III fractures with severe closed soft tissue injuries, according to Tscherne, treatment should include minimally invasive open reduction through limited approaches or arthroscopy.