

independent prognostic factors for higher local failure incidence, even with multivariate analysis. While studies like this remain the best that we have for extrapolating treatment decisions and outcomes, it is clear that we should be a little cautious in interpreting results when they are such a biased sample. There are a few very useful take-home messages here; clearly, surgery is the preferred option if at all possible. However, the outcomes are not unreasonable for all options.

### Preoperative evaluation prior to soft-tissue sarcoma excision: why can't we get it right?

■ There has been much attention on soft-tissue sarcomas (STS) recently, with some massive changes in the focus on early diagnosis and work-up, partly due to increasing evidence that many sarcomas are 'missed', leading to poor outcomes. In this retrospective review of 397 consecutive patient records (2000 to 2008) from **Nashville, Tennessee (USA)**, the authors set out to review the quality of the preoperative evaluation for patients undergoing STS excision.<sup>7</sup> They identified the diagnostic work-up in terms of primary site advanced imaging

(MRI or CT) and diagnostic biopsy procedures completed prior to the initial attempt at definitive surgical excision. Essentially, the aim of this paper was to define whether there was an association between the presence or absence of an appropriate preoperative work-up (preoperative advanced imaging studies, diagnostic biopsy) and the eventual outcome of an incomplete STS excision. Within this series, around a third of patients (n=149/397) underwent an incomplete primary excision prior to referral to this tumour centre. There was a significant difference in the quality of work-up, with complete excision associated with use of advanced imaging (91% vs 42%) and diagnostic biopsy (85% vs 16%). Those patients who had had a preoperative biopsy, a larger tumour size (> 5 cm), and a referral from an orthopaedic surgeon had a reduced risk of incomplete excision in multivariate analysis. This study concludes that only a minority of patients referred following incomplete excision of a STS had undergone an appropriate preoperative work-up prior to referral, leading to increased long-term morbidity following definitive re-excision. Educational efforts to heighten awareness of suspicious soft-tissue lesions remain vital.

### EURO-BOSS

■ The European Bone Over 40 Sarcoma Study (EURO-BOSS) is a landmark study in the sarcoma literature.<sup>8</sup> It represents a step away from the traditional retrospective cancer registry-type research in orthopaedic oncology and moves us into the brave new world of prospective international study of musculoskeletal tumours. This prospective study enrolled patients aged between 41 and 65 years, all presenting with high-grade bone sarcoma, who were treated with an intensive chemotherapy regimen derived from protocols for younger patients with high-grade skeletal osteosarcoma. The authors report the outcomes of over 200 patients, all treated for primary high-grade osteosarcoma and followed up to a mean of just under four years, giving a five-year overall survival of two-thirds in localized disease and one-fifth in metastatic disease. The take-home message is that, in patients aged over 40 years, an aggressive approach with chemotherapy does potentially offer survival rates comparable with those achieved in younger patients.

### REFERENCES

1. **Brown TS, Salib CG, Rose PS, et al.** Reconstruction of the hip after resection of

periarticular oncological lesions: a systematic review. *Bone Joint J* 2018;100-B(Suppl A): 22-30.

2. **Erstad DJ, Ready J, Abraham J, et al.** Amputation for extremity sarcoma: contemporary indications and outcomes. *Ann Surg Oncol* 2018;25:394-403.

3. **Barbier D, De Billy B, Gicquel P, Bourelle S, Journeau P.** Is the clavicular pro humero technique of value for reconstruction after resection of the proximal humerus in children? *Clin Orthop Relat Res* 2017;475:2550-2561.

4. **Slump J, Hofer SOP, Ferguson PC, et al.** Flap reconstruction does not increase complication rates following surgical resection of extremity soft tissue sarcoma. *Eur J Surg Oncol* 2018;44:251-259.

5. **Keung EZ, Chiang YJ, Voss RK, et al.** Defining the incidence and clinical significance of lymph node metastasis in soft tissue sarcoma. *Eur J Surg Oncol* 2018;44:170-177.

6. **Ahmed SK, Randall RL, DuBois SG, et al.** Identification of patients with localized Ewing Sarcoma at higher risk for local failure: a report from the children's oncology group. *Int J Radiat Oncol Biol Phys* 2017;99:1286-1294.

7. **Mesko NW, Wilson RJ, Lawrenz JM, et al.** Pre-operative evaluation prior to soft tissue sarcoma excision - Why can't we get it right? *Eur J Surg Oncol* 2018;44:243-250.

8. **Ferrari S, Bielack SS, Smeland S, et al.** EURO-B.O.S.S.: A European study on chemotherapy in bone-sarcoma patients aged over 40: outcome in primary high-grade osteosarcoma. *Tumori* 2017 (Epub ahead of print) PMID: 29218692.

## Children's orthopaedics

### Toxic shock and musculoskeletal infection: rare but not unheard of

■ Septic arthritis and osteomyelitis are fortunately rare in the paediatric general population but, when they do occur, they can be devastating. In the developed world, between 80% and 90% of these infections are caused by *Staphylococcus aureus* (of different varieties), and around 10% by group A beta-haemolytic *Streptococcus* (GABHS). Both organisms are capable of exotoxin production.

When released into the systemic circulation, the endotoxin can act as a superantigen that is the pathway for toxic shock syndrome. This study from multiple centres in the **USA** aimed to examine the incidence of intensive care unit admissions for severe systemic, multi-organ involvement and toxic shock syndrome in patients with *S. aureus* (both methicillin-sensitive (MSSA) and methicillin-resistant (MRSA)) and GABHS.<sup>1</sup> The authors describe their own retrospective series, which reports on the

local population of patients treated for septic arthritis or osteomyelitis over a nine-year period. The primary outcome was the reported rates of admission to an intensive care unit (ICU), although the authors also reported on differences in the course of the disease between organisms, as well as lengths of stay, number of surgeries, operative procedures, and cases of overwhelming sepsis. The authors collected a series of 208 patients (n=16) with osteomyelitis or septic arthritis, of whom 8% were

admitted to the ICU; patients with GABHS were ten times more likely to require this than those with *S. aureus*. Patients with MRSA were equally as likely as those with GABHS to require ICU care. Vigilance and early treatment is obviously advantageous in these patients; those who deteriorated to the point of requiring ICU had an average of three surgical procedures each and an inpatient stay of a month. Besides recommending the prompt assessment and treatment of systemic symptoms,

the authors suggest a low threshold for investigating for septic arthritis and osteomyelitis in patients who have a rapidly positive blood culture, give a positive Gram stain test result for Gram-positive cocci, and have a presenting C-reactive protein (CRP) > 15 mg/dl. Clearly, although rare, there are some definite take-home messages from this paper. Patients with MRSA or GABHS infections should be closely monitored and promptly treated to try to avoid ICU admission.

### **Bier's block for paediatric forearm fractures X-ref**

■ Obtaining adequate and safe analgesia for the manipulation of fractures in paediatric patients can be challenging. In many units there is an increasing tendency to use general anaesthesia, with all its attendant risks, to achieve what could just as easily have been achieved with sedation or regional blockade. In adult patients, Bier's block is an extremely effective way of delivering excellent analgesia for distal upper limb fractures and is commonly used in both emergency departments and fracture clinics. Although there is some concern about the potential for cardiac toxicity if incorrectly performed, there are very few recorded cases of problems, and many units routinely undertake the procedure. This is not so in paediatric emergency departments (EDs) in the United Kingdom, where concerns about the risk of systemic toxicity of local anaesthetic agents and adversity to the idea of double venous cannulation in the paediatric patient mean it is virtually never used. Instead, nitrous oxide and parenteral agents are generally used, and manipulations taking more than a few seconds frequently cause significant pain and suffering. These patients are often admitted to hospital, which is distressing in itself in this population; full procedural sedation in the ED is not easily available. This study from **Singapore City (Singapore)** retrospectively examined over 1700 Bier's block ED

forearm manipulations in children as young as five years old.<sup>2</sup> All of the patients underwent a Bier's block and manipulation of a forearm fracture. Reassuringly, there were no deaths or major complications, and 96% of these patients were discharged from the ED with a fracture clinic appointment. As this is a retrospective study, we do not know how many children during this time underwent other analgesic techniques, nor how the treating doctor determined the suitability for the technique. However, 83% of the patients were male, suggesting a significant selection bias. That said, the approach was likely pragmatic, and the length of stay in the ED for the Bier's block patients was significantly shorter than for the patients undergoing procedural sedation. Paediatric analgesia in the ED can be an emotive subject and, here at 360, we are impressed with the outcomes of this large group of patients.

### **Total hip arthroplasties in patients under 16 years old X-ref**

■ The management of unsalvageable end-stage joint disease in paediatric patients is a complex challenge with no single solution. It is also perhaps commoner than one might think, with end-stage juvenile arthritis, developmental dysplasia of the hip (DDH), cerebral palsy (CP), Perthes' disease, and slipped upper femoral epiphysis (SUFE) all potentially leading to a very poor result. Arthroplasty is fraught with difficulty, including acute technical issues such as limited bone stock and complex anatomy following previous procedures, as well as leg-length discrepancies and longevity of the implants. The longevity and abnormal geometry pose perhaps the biggest challenge in these patients. The patient is often left with fewer fixation options, greater and imbalanced muscle forces around the hip, and a longer lifetime over which treatment will be required, which is perhaps not a recipe for

success in hip arthroplasty. Much of the historical literature concerns the outcomes of cemented implants in rheumatoid patients, so newer series reporting contemporary implants are welcome here at 360. This study from **Melbourne (Australia)** reports good outcomes, albeit at a relatively short current follow-up of 3.8 years.<sup>3</sup> The authors report their series of 18 children (with 24 hip arthroplasties), all under the age of 16 years (with a mean age of 14 years and some as young as 11 years old). For obvious reasons, arthroplasty usually tends to be performed in those closer to skeletal maturity. All patients had cementless total hip arthroplasty (THA) for a variety of underlying conditions leading to unsalvageable hip arthritis. A total of 24 hips in 18 patients were included and all patients improved from a severely impaired gait, including four wheelchair users, to a completely unrestricted gait with reduced pain and increased range of motion. One patient required further surgery to correct an adductor contracture. At final follow-up, all hips were in good alignment, with no wear, radiological lucencies, or revisions. A longer follow-up of this cohort would obviously be ideal to allow firm conclusions to be drawn, especially with regard to the longevity of the implants, but the initial results are to be commended.

### **Which malpositioned pedicle screws should be revised? X-ref**

■ The literature would suggest that up to 15% of free-hand pedicle screws are malpositioned, and that around one in 300 patients will have to undergo a revision surgery due to a malpositioned screw. Given the numbers of screws used in a typical fixation, that would suggest a rate of revision for malposition of, at the most, 1:1200 screws, but more likely 1:2400. In this study from multiple centres in the **USA**, the authors looked to determine which types of malpositioned pedicle screws were considered to be unacceptable and

to require revision surgery.<sup>4</sup> A group of 12 experienced high-volume spine surgeons were presented with 32 cases of malpositioned pedicle screws with variable location and degree of breaches, and were asked whether they would revise the screw dependent on the time of presentation. In what is really an expert opinion piece, this study achieved good levels of concordance between experts in some areas. Essentially, the results showed good agreement among surgeons as to which screws were malpositioned, but greater variability as to which screws ought to be revised. Of those surgeons sampled, 83% recommended revision for asymptomatic screws that approached the dura, whereas there was greater variability for screws that approached the aorta at 58%, or if the entire screw diameter was in the canal. Revision surgery was not recommended for asymptomatic patients with screws partially violating the canal (less than half the screw diameter), malpositioned laterally in the rib head, or with small anterior cortical violations remote from a vascular structure. The surgeons were more likely to recommend revision for the intraoperative scenarios before rod placement (65%), compared with after rod placement (45%), or for asymptomatic patients in clinic (22%). Decisions in these high-stakes situations are clearly difficult, as demonstrated by the relatively low levels of concordance between surgeons in some of the scenarios. Further studies are clearly mandated, especially as to what the longer-term clinical consequences are for the various scenarios. Given the rarity of the problem, we may be waiting some time for a better study than this one!

### **The Dunn procedure under the spotlight**

■ In this issue of 360, we include two papers examining the modified Dunn procedure, i.e. open sub-capital realignment of slipped upper femoral epiphysis (SUFE). Slipped



upper femoral epiphysis is the commonest condition affecting the adolescent hip, and Dunn's procedure is an open reduction aided by a closing osteotomy to maintain the retinacular blood supply. Dunn's procedure is designed to allow for reduction without worsening the risk of avascular necrosis (AVN). Of paramount importance when taking the decision to realign an unstable SUFE is the need to avoid damage or compression of the retinacular vessels and subsequent AVN. Although described in the last century, there has been a resurgence of interest in the procedure that, when combined with a blood supply-sparing approach to the hip, makes the tantalizing promise of restoring mechanical alignment without compromising blood supply. The first study that caught our eye, from multiple centres in the **USA**, directly examined pre- and postoperative blood flow to the femoral head with pre- and postoperative selective angiography of the medial femoral circumflex artery, with the aim of establishing whether the Dunn osteotomy is indeed a blood supply-preserving approach.<sup>5</sup> The authors undertook angiography and also measured the intraoperative blood flow using an intracranial pressure (ICP) monitor in nine patients undergoing the Dunn procedure. Preoperatively, six of the nine patients with unstable SUFE did not have arterial flow to the femoral head visible on the preoperative angiography, and flow

was restored postoperatively in four of these. Interestingly, in one patient there was no ICP waveform after initial reduction but this returned after removal of additional callus, suggesting that the hypothesis of 'tenting' of the retinacular vessels by callus formation may be true. At 22 months' follow-up, two patients had gone on to develop AVN; one of these did have an ICP waveform after reduction and, as such, this intraoperative test, even in this small sample, was not entirely predictive of avoiding this complication. The second study that is worth a mention is a large consecutive series of unstable SUFEs treated with the modified Dunn procedure in **Columbus, Ohio (USA)**.<sup>6</sup> The authors report a clinical outcome series of 31 patients, all of whom were operated on within 24 hours of presentation and were felt to have a clinically unstable slip. In terms of operative results, the authors had restored the pre-slip anatomy. In terms of success, just two patients (6%) went on to develop AVN at an average of 19 weeks following surgery. In terms of other complications, there were three patients (10%) who developed mild heterotopic ossification and two who eventually required removal of symptomatic metalwork. The cohort were followed and results reported up to 30 months postoperatively. With only two patients going on to develop AVN by this stage, this paper does support the use of the Dunn procedure in an acute unstable slip. Open reduction is certainly not a 'Dunn deal' in SUFE. There are plenty of series demonstrating a steep learning curve and high rates of AVN, even in expert hands, in chronic slips. However, these two papers add weight to the rationale that the Dunn procedure is a reasonable way to treat these patients.

#### **Meniscal entrapment more common than thought in tibial spine avulsions X-ref**

■ Meniscal entrapment is a well-recognized phenomenon in

paediatric tibial spine avulsion (TSA) fractures, but other injuries can also be associated with this relatively common condition. The paediatric skeleton exhibits different viscoelastic properties to those of the adult, and, as such, avulsions are more common than ligament tears, with the tibial spine avulsion among the most common. The seminal papers on tibial spine avulsion handed down the wisdom that surgery could be avoided if the fracture reduced in extension (suggestive of no meniscal entrapment). However, now that there is a wealth of literature supporting the stretching of the anterior cruciate ligament (ACL) prior to the spine avulsion, these cases, for the most part, are treated operatively. This paper from **Boise, Idaho (USA)** set out to examine the relative incidence and the utility of MRI in identifying these knee injuries.<sup>7</sup> The authors report a 163-patient series collected and reviewed as part of a multicentre study. The vast majority (88%, n=144/163) underwent surgical stabilization of the tibial spine; in the perioperative period, 77 patients underwent MRI scans. The take-home message from this paper is that meniscal entrapment was found in nearly 40% of all patients at the time of operation, and that this was poorly diagnosed with MRI. However, meniscal pathology is not the only concomitant injury seen in these patients, and those MRI scans did have much greater utility in diagnosing osteochondral pathology, including bone bruising, which was invariably not identified at surgery. One-third of patients were also identified to have an injury to a ligament other than the ACL on MRI. The importance of the identification of bone bruising in these patients is limited, as management is not likely to change from this alone. However, the high incidence of undiagnosed meniscal injuries is concerning, and means that MRI is not reassuring when excluding these injuries; based on this series, all

patients presenting with a displaced tibial spine avulsion require expert arthroscopic evaluation.

#### **Femoral shaft fractures: a national perspective X-ref**

■ The advent of the Major Trauma Network in the United Kingdom has brought a number of changes to trauma patient care. Many of the changes are undeniably beneficial, such as the improved mortality rates in more severely injured patients. Others may have led to possibly unintended variations in practice. There is, as yet, little evidence as to the nature of the effect of the trauma networks on paediatric trauma care. This large study from **Manchester (UK)** of the epidemiology and management of paediatric femoral shaft fracture in England aims to examine the effects of the Major Trauma Centre (MTC) network on paediatric femoral fracture care.<sup>8</sup> Examining almost 2000 cases, in addition to establishing the general demographics of this injury, it was identified that children aged four to six years treated in MTCs were more likely to be managed with open reduction and internal fixation compared with those treated in trauma units (TUs). The mean length of stay was also shorter in MTCs, but the reasons for these variations and effects on outcome are not clear from this study. This study only included closed isolated fractures, so cases were unlikely to be transferred within the Major Trauma Network; the paper could be read as a comparison between a select group of large tertiary centres and all other hospitals. 'Big data' studies such as this are very important, and this variation in practice would not have been identified easily otherwise, but further work is obviously required to elicit the reasons for, and effects of, this.

#### **REFERENCES**

1. Kerr DL, Loraas EK, Links AC, Brogan TV, Schmale GA. Toxic shock in children with bone and joint infections: a review of seven years of patients admitted to one intensive care unit. *J Child Orthop* 2017;11:387-392.

2. **Chua ISY, Chong SL, Ong GYK.** Intravenous regional anaesthesia (Bier's block) for pediatric forearm fractures in a pediatric emergency department-Experience from 2003 to 2014. *Injury* 2017;48:2784-2787.

3. **Van de Velde SK, Loh B, Donnan L.** Total hip arthroplasty in patients 16 years of age or younger. *J Child Orthop* 2017;11:428-433.

4. **Flocarci LV, Larson AN, Crawford CH III, et al.** Which malpositioned pedicle screws should be revised? *J Pediatr Orthop* 2018;38:110-115.

5. **Jackson JB III, Frick SL, Brighton BK, et al.** Restoration of blood flow to the proximal femoral epiphysis in unstable slipped capital femoral epiphysis by modified Dunn procedure: a preliminary angiographic and intracranial

pressure monitoring study. *J Pediatr Orthop* 2018;38:94-99.

6. **Persinger F, Davis RL II, Samora WP, Klingele KE.** Treatment of unstable slipped capital epiphysis via the modified Dunn procedure. *J Pediatr Orthop* 2018;38:3-8.

7. **Rhodes JT, Cannamela PC, Cruz AI, et al.** Incidence of meniscal entrapment and associated

knee injuries in tibial spine avulsions. *J Pediatr Orthop* 2018;38:e38-e42.

8. **Talbot C, Davis N, Majid I, et al.** Fractures of the femoral shaft in children: national epidemiology and treatment trends in England following activation of major trauma networks. *Bone Joint J* 2018;100-B:109-118.

## Research

**X-ref** For other Roundups in this issue that cross-reference with *Research see: Hip & Pelvis Roundup 1; Spine Roundup 6; Trauma Roundups 3, 7 & 8.*

### Vancomycin toxic to chondrocytes

■ There is a current trend of local delivery of topical vancomycin into at-risk wounds, or for treatment of localized musculoskeletal infection. Although there is emerging evidence surrounding the benefits of topical vancomycin from a wound infection perspective, here at 360, we have been somewhat concerned about the possibility of chondral toxicity when topical vancomycin is applied directly to the joint surface. The authors of this study from **Charleston, South Carolina (USA)** attempted to pinpoint the safe concentrations of vancomycin in a porcine model.<sup>1</sup> The authors harvested osteochondral samples from juvenile porcine knees, exposed them to vancomycin concentrations of 2 mg/ml, 5 mg/ml, and 10 mg/ml, and compared the viability of the harvest chondrocytes with those of saline. The authors undertook a predominantly histological study and graded the chondrocyte viability using the Mankin criteria and a live/dead stain to establish the viability of the chondrocytes with each of the solutions. This was then supplemented using calcein acetoxyethyl ester stain and confocal laser scanning microscopy. There were no differences

between the control and the 2 mg/ml group in terms of chondrocyte viability. However, there was a significantly higher rate of non-viable chondrocytes in the 5 mg/ml and 10 mg/ml groups. There is some evidence here that vancomycin should be treated with a certain amount of caution and there is clearly the potential, at least, for chondrocyte death. It is far from clear yet if the benefits outweigh the risks or vice versa. Infection is also chondrotoxic, and post-septic arthritis degenerative arthrosis can be challenging to treat. Although the arguments are currently being weighed up, a longitudinal study – or better still, a properly powered trial – is what is really needed here.

### Aspirin as good as rivaroxaban X-ref

■ In what can perhaps be considered a landmark paper, the *New England Journal of Medicine* yet again publishes game-changing research in orthopaedic surgery. This large clinical randomized controlled trial of 3424 patients (1804 undergoing total hip arthroplasty (THA) and 1620 undergoing total knee arthroplasty (TKA)) originates from across **Canada** and tests the efficacy of rivaroxaban and aspirin with the primary endpoint of symptomatic venous thromboembolism (SVTE).<sup>2</sup> All patients received oral rivaroxaban (10 mg) once daily until postoperative day 5, and were then randomly assigned to either continue rivaroxaban or switch to aspirin (81 mg

daily) for an additional nine days after TKA or for 30 days after THA. Follow-up was to 90 days and the trial was constructed as a double-blinded randomized controlled trial. Overall, there was a 0.64% event rate in the aspirin group and 0.70% in the rivaroxaban group. The trial was significant for non-inferiority but not significant for superiority. In terms of secondary outcomes, there was no difference in the major bleeding events (0.47% for aspirin vs 0.29% for rivaroxaban). Similarly, there were no significant differences in the clinically important bleeding events in the aspirin and rivaroxaban groups (1.29% for aspirin vs 0.99% for rivaroxaban). This trial does not give any insight into inpatient thromboprophylaxis; nevertheless, it is fairly compelling with regard to outpatient extended thromboprophylaxis. With no differences in the primary endpoint or subsequent secondary outcome measures in this large, well-conducted, randomized controlled trial, we can surmise that aspirin is equally as effective as rivaroxaban.

### Evidence synthesis: a better way?

■ As trials are becoming more and more commonplace, so is evidence synthesis, offering the opportunity to combine trials and increase the power of the studies such that more reliable conclusions can be reached. The major drawback of this approach is that the trials have to be published, and pairwise meta-analysis has to be

undertaken. This is a lengthy process and only allows consideration of simple questions. There are other approaches, with the network or Bayesian meta-analysis gaining popularity, that allow for more refined analysis using a network method to test several interventions against the 'central node'. Although this offers a more discriminating approach and multiple questions can be answered, these methods still lag behind the current trial data. A collaborative led by methodologists in **Bern (Switzerland)** have proposed a 'living' network meta-analysis approach, where the continuous updating of networks of prospectively planned randomized controlled trials (RCTs) is used.<sup>3</sup> The authors provide strong evidence against the null hypothesis in comparative effectiveness of medical interventions earlier than the updating of conventional, pairwise meta-analysis. The authors set out to establish the time period that meta-analyses reporting outcomes of medical interventions took to become positive – both as a network approach and a pairwise approach. They included all meta-analysis reporting the outcomes of at least 20 RCTs. The authors identified 49 comparisons reported in 44 networks. The comparisons were informed by both direct and indirect evidence (n=29), indirect evidence alone (n=13), or direct evidence alone (n=7). For seven comparisons, network and pairwise meta-analysis provided strong evidence; however,