Correspondence

Impaction grafting

Sir—I read with pleasure the excellent prize winning article in the December issue by Lars Linder about cancellous impaction grafts in the human femur (Linder 2000). Lars Linder's work has been important for our experiments in bone grafting. I was puzzled by the clinical success of impaction grafting and our group performed a series of animal experiments trying to understand why impaction grafting works so well. When planning those studies, we jumped to the false conclusion that clinical success must be related to successful osseous incorporation of the graft. We therefore tried to find out which aspect of impaction grafting promoted bone ingrowth in the bone-chamber experiments mentioned by Lars Linder. It was only when he presented some of the data of his article at a meeting, that we realized that bony incorporation of the graft and clinical success might not be related, and that necrotic bone granula in a fibrous stroma might constitute an excellent biomaterial for hip revision.

However, in some of our earlier work we also tried to improve graft incorporation by adding growth factors to the graft. This was successful in the bone chamber model in rats (Wang and Aspenberg 1996, Tägil et al. 2000), but has so far failed in a larger animal model with a loaded prosthesis (unpublished). At the end of his article Lars Linder concluded that one principal line of thought now is to use bone-stimulating substances together with bone grafts in the hope of achieving more complete and consistent bone regeneration. Although he did not state this, I am afraid it could be misinterpreted as a recommendation to proceed along that line.

BMP preparations will probably be available to the clinician in the near future, and might become valuable in fracture treatment. However, it will then be possible to mix this substance with cancellous bone grafts during revision surgery. I would like to warn against such use for 2 reasons: 1. BMPs can also stimulate bone resorption, which has been observed both in vivo (Laursen et al. 1999) and in vitro (Kaneko et al. 2000). There is a risk of a transition phase of increased resorption in the graft, which could be detrimental to the mechanical stability. 2. Even if complete osseous remodeling is achieved, this will not necessarily lead to a better clinical result; the composite of necrotic bone and fibrous scar tissue might be preferable. In a study with impacted grafts in goat acetabuli, the mechanical properties of the construct were excellent, until the bone remodeling frontier had reached the cement, when the prosthesis loosened (Schimmel et al. 1998). This might also happen in humans if graft remodeling increases with the help of growth factors.

Per Aspenberg
Department of Orthopedics, Lund University Hospital, SE-221 85 Lund, Sweden

Sir—Dr. Aspenberg has raised an important question. That his fears are not unfounded is shown in a recent study by Höstner et al. (2000). Comparing impaction-grafted cases with or without the addition of OP-1, the authors noted 2 failures in the OP-1 treated group versus none in the control. They therefore discontinued the study.

I wish to emphasize that the wording in my article should not be interpreted as a recommendation to use growth factors; it was intended as a presentation of research lines, not as an approval of them.

Dr. Aspenberg's letter highlights the fact that at present, our view of how or when to use bone-stimulating substances is a simplistic one. It also points out the difference between animal research and clinical work and our lack of standardized, preclinical, high-quality methods to evaluate biological phenomena in humans. However, a proto-

col for preclinical testing in humans has been proposed (Linder 2000), which might serve as a first step in this direction.

Lars Linder
Deptartment of Orthopedics, Gävle Hospital, SE-801 87 Gävle, Sweden

Höstner J, Kärrholm J, Hultmark P. Early failures after femoral revisions using milled allograft bone mixed with OP-1. Poster presentation, 56th meeting of the Swedish Orthopaedic Association, 5-8 September 2000 (www.pi.se/actaorthopscand).

Kaneko H, Arakawa T, Mano H, Kaneda T, Ogasawara A, Nakagawa M, Toyama Y, Yabe Y, Kumegawa M, Hakeda Y. Direct stimulation of osteoclastic bone resorption by bone morphogenetic protein (BMP)-2 and expression of BMP receptors in mature osteoclasts. Bone 2000; 27 (4): 479-86.

Laursen M, Hoy K, Hansen E S, Gelineck J, Christensen F B, Bunger C E. Recombinant bone morphogenetic protein-7 as an intracorporal bone growth stimulator in unstable thoracolumbar burst fractures in humans: preliminary results. Eur Spine J 1999; 8 (6): 485-90.

Linder L. Cancellous impaction grafting in the human femur: Histological and radiographic observations in 6 autopsy femurs and 8 biopsies. Acta Orthop Scand 2000; 71 (6): 543-52.

Linder L. CHIP - Comparable Human Implants Protocol. Poster presentation, 56th meeting of the Swedish Orthopaedic Association, 5-8 September 2000 (www.pi.se/actaorthopscand).

Schimmel J W, Buma P, Versleyen D, Huiskes R, Slooff T J. Acetabular reconstruction with impacted morselized cancellous allografts in cemented hip arthroplasty: a histological and biomechanical study on the goat. J Arthroplasty 1998; 13 (4): 438-48.

Tagil M, Jeppsson C, Aspenberg P. Bone graft incorporation. Effects of osteogenic protein-1 and impaction. Clin Orthop 2000; 371: 240-5.

Wang J S, Aspenberg P. Basic fibroblast growth factor enhances bone-graft incorporation: dose and time dependence in rats. J Orthop Res 1996; 14 (2): 316-23.

Low-molecular-weight heparin as prophylaxis against thromboembolism after total hip replacement—The never-ending story?

Sir—We would like to add some information to the ongoing debate on thromboembolism in your Journal and, in particular, comment on the recent correspondence from Björn M Persson (Acta Orthop Scand 2000; 71: 215–216), whose fundamental question is whether the benefit of prophylaxis with low-molecular-weight heparin (LMWH) offsets the asserted increased risk of impaired primary wound healing and prosthetic fixation.

We should begin by answering Persson's first question: whether LMWH is worth its price in view of its higher monetary cost than that of warfarin or unfractionated heparin when, according to the meta-analysis by Murray et al. (1996) and Freedman et al. (2000), it has no advantage concerning mortality. The true cost of a management strategy can be assessed only by means of a complete health-economic analysis taking account total costs of care and not just drug costs. It has been convincingly shown that in-hospital prophylaxis with LMWH is cheaper than unfractionated heparin and warfarin (Anderson et al. 1993, Drummond et al. 1994, O'Brien et al. 1994, Menzin et al. 1995, Bergqvist et al. 1996a, Hull et al. 1997). Most of these health-economic evaluations use venographic data from clinical trials to estimate the risk of deep venous thrombosis (DVT) and pulmonary embolism (PE) using comparative prophylactic management strategies. This may be criticized, as the proportion of subclinical DVT that develops into symptomatic DVT or PE is not known. A retrospective study, however, has compared the cost savings of LMWH and warfarin, and shown that the savings are due to a reduced rate of DVT and PE, less bleeding, and lower laboratory and monitoring costs with LMWH (Saunders and Grant 1998). The cost-effectiveness of prolonged prophylaxis as compared to in-hospital prophylaxis has also been shown (Detournay et al. 1998, Bergqvist and Jönsson 1999), and a recent study showed LMWH to maintain a cost-effective advantage over warfarin