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ABSTRACTS IN CARDIOLOGY

Restenosis and myointimal hyperplasia

Restenosis caused by intimal vascular smooth muscle hyperplasia after coronary angioplasty or bypass surgery is a major problem, both clinically and economically. There is therefore considerable interest in the mechanisms controlling intimal smooth muscle proliferation. Heparin is an inhibitor of smooth muscle cell proliferation both in vitro and in vivo. Chan *et al* describe an abnormal growth regulatory response to heparin in vascular smooth muscle cells cultured from patients with restenotic lesions.

Chan *et al* had to face the usual difficulties of investigators trying to obtain normal human control tissue. Their controls therefore comprised various arteries from two organ donors and saphenous vein and internal mammary artery from patients undergoing primary revascularisation procedures. They used saphenous vein as the normal vessel control for patients with restenosis.

Two caveats apply to the interpretation of these results and their clinical application. Chan *et al* isolated smooth muscle cells from the whole vessel wall including medial smooth muscle cells. Medial smooth muscle cells greatly outnumber those in the intima, particularly in the veins and normal arteries. These results could therefore be a consequence of comparing smooth muscle cell populations in the intima and the media. In

addition, up to 40% of the control patients undergoing primary bypass surgery will develop restenoses; their smooth muscle cells may already have been showing abnormal growth regulatory behaviour. This may explain the overlap in growth inhibition by heparin seen in the study.

Chan *et al* found that heparin inhibited growth in smooth muscle cells derived from patients with restenosis significantly less than those from controls. This aberrant response was not confined to cells derived from restenotic lesions: it was also found in smooth muscle cells cultured from apparently normal vessels from the same patient.

As the validity of animal models of restenosis is increasingly questioned, the importance of studying the disease in humans increases. Chan *et al*'s data suggest that patients liable to restenosis have a generalised abnormality of smooth muscle cell proliferation in response to heparin, which may reflect a wider abnormality in the control of the growth of smooth muscle cells.

Prospective studies of the behaviour of human intimal smooth muscle cells might help to identify those at risk of restenosis and lead to therapeutic interventions to prevent restenosis.

SA THORNE

Abnormal growth regulation of vascular smooth muscle cells by heparin in patients with restenosis

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Proliferation of vascular smooth muscle cells (VSMC) underlies myointimal hyperplasia, which can lead to restenosis after angioplasty and vascular surgery. We propose that some individuals have an intrinsic capacity for this exaggerated response to vascular injury, partly through decreased sensitivity to the physiological growth inhibitor heparin. We investigated the effect of heparin on VSMC from restenotic lesions and from apparently normal vessels of the same patients, and VSMC from control patients undergoing primary bypass procedures. Cells from patients with restenosis (both restenotic lesion and undiseased vein) showed much lower sensitivity to growth inhibition by heparin than the controls (median inhibition 8 (95% CI-2 to 25) v 22 (15-44)%, $p < 0001$); this finding suggests aberrant growth regulation in these cells. (*Lancet* 1993;341:341-2.)