EFFECT OF BALLOON INFLATION ON SMOOTH MUSCLE CELL PROLIFERATION IN THE PORCINE CAROTID ARTERY.

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Arterial stretch at the time of coronary angioplasty may contribute to smooth muscle cell (SMC) proliferation and the subsequent development of restenosis. We evaluated this in a porcine model of carotid arterial injury using a standardized balloon dilatation procedure (5 inflations for 30 sec, 60 sec between inflations). Eight 4-month-old pigs (25-35 kg) underwent dilatation at 6 atmospheres (atm) in the left and 3 atm in the right carotid artery. Dilated region sections were compared with non-dilated segments either totally or minimally denuded of endothelium.

Bromodeoxycytidine (BDC), 25 mg/kg/day, was infused by implantable pump for 48 hours, from the time of dilatation until sacrifice. BDC is incorporated into nuclei of dividing cells during the S-phase; positive (proliferating) SMC are detected using a double antibody immunohistochemical technique. Unlabeled nuclei were counterstained with propidium iodide, a fluorescent dye. Quantitation of dividing-SMC was performed with the IBAS computerized system. ^{111}In autologous platelet deposition was quantitated. Results are mean ± SE.

	Minimally Denuded	Totally Denuded	Dilated 3 atm	Dilated 6 atm
SMC nuclei (% positive)	2.3 ± 0.6	4.8 ± 1.3	25.5 ± 5.1*	37.6 ± 5.7*
Platelet deposition (x10^6/cm^2)	1.9 ± 0.6	3.5 ± 0.5	4.8 ± 1.4	459 ± 205*

*p<0.01 paired t-test, compared with nondilated segments

Arterial dilatation at 3 atm, which did not injure below the subendothelium, produced little more platelet deposition than endothelial denudation alone but caused marked SMC proliferation. Although the proliferative response to 6 atm was probably greater than 3 atm (p=0.08), 6 atm frequently caused more vascular injury with increased platelet deposition and thrombus formation. The proliferative response to 6 atm may be mediated by stretch, thrombus or both.

Arterial dilatation is a potent stimulus for SMC proliferation 48 hours after injury in this animal model.

A PRACTICAL PORCINE MODEL OF HUMAN CORONARY ARTERY RESTENOSIS POST PTCA

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Restenosis at the site of interventional procedures for coronary artery disease remains a major, unsolved clinical problem. This problem has been compounded by the lack of an animal restenosis model which could be used to test new therapies, and also by the limited availability of human restenosis tissue for direct evaluation.

We thus developed a model of human restenosis in the domestic crossbred swine fed a standard, non-atherogenic diet. Metallic foreign bodies (*.125 mm stainless steel or tantalum wire coils*) were implanted percutaneously in pig coronary arteries with oversized PTCA balloons inflated to high pressures (*14 atm*).

Pathologic lesions in 5 of 5 implanted animals (*at 11 days to 63 days*) included a severe proliferative response of medial smooth muscle cells with significant luminal compromise (*mean area stenosis 70% ± 24% SD*). Disruption of the internal elastic lamina was present in all vessels showing the proliferative response, as was mild chronic inflammation surrounding the wire itself. One animal died spontaneously at 11 days from a tight, proliferative LAD stenosis. In all animals, histopathologic features of the proliferative neointimal tissue were identical to those of human restenotic tissue post PTCA obtained in 38 patients by atherectomy.

This model produces a response identical to human restenosis, and is simple, inexpensive, and practical for studying preventive therapies. It furthermore supports the concept that restenosis is a healing phenomenon resulting from arterial injury, and is likely independent of the atherosclerotic process.

LONG-TERM PATHOLOGIC FINDINGS AFTER IN VIVO PLACEMENT OF PERCUTANEOUS BALLOON EXPANDABLE TANTALUM STENTS.

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Balloon expandable endovascular stents (S) represent a potential solution to certain complications of balloon angioplasty, namely restenosis and abrupt closure. We examined pathologic findings to assess tissue reactivity and biocompatibility of Medtronic-Wiktor annealed tantalum S, placed percutaneously in 58 peripheral arteries of 25 normal dogs (treated with 325 mg aspirin q.d.) and 42 peripheral and coronary arteries of 16 cholesterol-supplemented Yucatan miniswine (no drug therapy). All 100 S, were 15 mm in length; implant sites included iliac artery in 57 cases brachiocephalic in 22, carotid in 7, brachial in 4 and coronary in 10. Sequential angiography performed at 1 day in 5 arteries, 2 wk in 21, 6 wks in 29, 3 mo in 18, 6-8 mo in 27 showed 100% patency of S segments. Histologic exam of S at 1 day post-implant revealed irregular intimal surface with thrombus covering the S struts. Within 6 wks, complete covering of the S wire with neointima resulted in "smoothing" of the intimal surface. At 6-8 months, a thin, atrophic, and fibrotic neointima covered the S wires. Thickness of the neointima varied from 78-331 um; peak neointimal growth (239 µm) developed at 6 wks post-implant; by 8 mo, maximum neointimal thickness measured <169 µm. The pathologic exam was notable for the absence of giant cell or other rigorous inflammatory response to the tantalum. These histologic findings complement the angiographic findings in these animal models regarding the biocompatibility of this endovascular prosthesis.

Wednesday, March 21, 1990
10:30AM–12:00NOON, Room 43
The Signal-Averaged Electrocardiogram

REPRODUCIBILITY OF ANALYSIS OF THE SIGNAL AVERAGED ELECTROCARDIOGRAM

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We measured variation in signal averaged ECGs recorded from 17 normals, ages 27-47 years. The changes exceeding spontaneous variation were expressed as 95% confidence intervals of the % difference in measurements between recordings. We measured high frequency (HF) QRS and low amplitude signal (LAS) duration, terminal root mean square (RMS) voltage, HF area (60-120 Hz) beginning with the LAS and % HF. Window onset changed by only 1.3-1.9 ms. Short-term (24 hrs) changes in HFQRS, LAS and RMS using 40 Hz highpass were within 5.4%, 13.2% & 30.9% respectively. Changes were greater using 25 and 80 Hz highpass, but not significantly so. Short-term changes in HF area and % HF were within 47.0% and 54.2%, and were highly variable in each lead. Unlike ectopic beat frequency, long-term (6-15 mos) variation in all measurements was never appreciably greater than short-term. Immediate recordings with unchanged electrodes also showed suprising variation (within 7.4% for HFQRS, 10.3% for LAS, 20.1% for RMS, 42.6% for HF area and 42.7% for % HF). The variation in measurements at all time frames must be accounted for and confidence intervals must be determined, as when testing for drug efficacy. The immediate data suggest that neither biologic variation nor lead placement explain the changes.