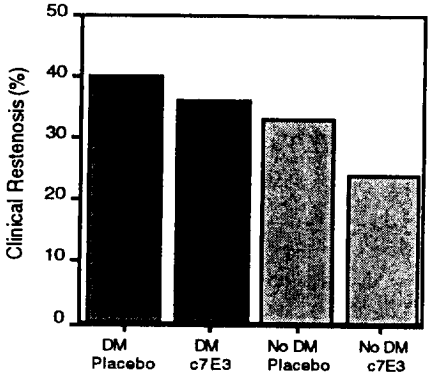
bolus and infusion had a 36% rate of clinical restenosis (CR). Patients without diabetes had a lower rate of restenosis whether receiving placebo (CR = 33%) or c7E3 (CR = 24%). In regression analysis, diabetes was the only baseline clinical feature associated with an increased event rate (hazard ratio 1.44, p = 0.001). Among patients without diabetes, the relative risk of major bleeding events was 2.6 times higher for those receiving c7E3 compared to placebo (9.9% vs. 3.7%, respectively). This effect was doubled among diabetics (12.9% vs. 2.2%, relative risk = 5.8). In conclusion, these data importantly confirm the higher clinical restenosis among diabetics and demonstrate a marked propensity to major bleeding events among diabetics treated with potent platelet antagonists.



935-35 Results of Stent Implantation for Diffuse Coronary Disease Assisted by Intravascular Ultrasound

Luigi Maiello, Patrick Hall, Shigeru Nakamura, Simonetta Blengino, Leo Finci, Giovanni Martini, Antonio Colombo. *Columbus Hospital, Milan, Italy*

The long term benefit of elective Palmaz-Schatz stent implantation for focal lesions in large vessels has been clearly delineated. The elective use of stents in diffuse disease, however, has not been fully evaluated. This study reports on the use of stents in 89 pts with 108 lesions (les) with diffuse disease. Diffuse disease was defined as a lesion length longer than 20 mm. After a successful angiographic result was obtained, intravascular ultrasound (IVUS) was performed to confirm optimal stent expansion and lesion coverage and to guide further balloon dilation and stent implantation. The mean age was 57 ± 10. Mean lesion length was 32 ± 6 mm. Vessel distribution was 51 LAD (47%), 45 RCA (42%), 10 LCX (9%), and 2 vein graft (2%). Lesion location was 49 proximal (45%), 52 mid (48%), and 7 distal (7%). 274 stents were implanted (139 Palmaz-Schatz, 34 short (7 mm) Palmaz-Schatz, 48 Gianturco-Roubin, and 53 Wiktor) for an average of 2.4 ± 1.4 stents/lesion. Procedure success was achieved in 83 patients (93%). Procedure associated complications included 3 myocardial infarction (3%) and 3 emergency bypass (3%) and 1 elective bypass (1%). Following the procedure, 77 pts (93%) with 94 les were treated only with antiplatelet therapy and no anticoagulation. Angiographic follow up at 4–6 months was performed on 49 of the eligible 65 lesions (71%). Baseline, final and follow up angiographic (AG) results are below:

AG Results	Reference (mm)	MLD (mm)	% Stenosis
Baseline	3.11 ± 0.47	0.66 ± 0.58	79 ± 19
Post Stent	3.09 ± 0.50	3.01 ± 0.47	3 ± 12
Follow Up	3.01 ± 0.48	1.80 ± 0.91	40 ± 28

There was 1 acute stent thrombosis event (1.2%). Restenosis by 50% diameter stenosis criteria was present in 17 of 49 lesions (35%) and 13 of 39 patients (34%).

Conclusions. (1) Stent Implantation in diffuse disease that is assisted by IVUS is associated with acceptable procedure complication rate and a low stent thrombosis rate despite the absence of post stent anticoagulation in the majority of patients. (2) The restenosis rate of 35% appears to represent an improvement over the reported restenosis rates for diffuse disease after angioplasty or other devices.

935-36 Mechanism of Benefit of Stenting in Failed PTCA. Final Results from the Trial of Angioplasty and Stents in Canada (TASC II)

Simon G. Ray, Ian M. Penn, Donald R. Ricci, Jacques Barth, G.B. John Mancini, Christopher E. Buller, Blair O'Neill, Christopher Foster, David Almond, Charles Lazzam, Louis Roy, Gerald Barbeau. *Vancouver Hospital and Health Sciences Centre, British Columbia, Canada*

TASC II is a randomised multicentre study comparing the strategies of stenting (n = 21) and prolonged perfusion balloon inflation (PPB; n = 22) as initial bail-out therapy in failed PTCA. Core lab qualitative and quantitative angiography analysis was possible in 40/43 patients.

Results.

	Pre randomisation		Post Randomisation			
	MLD (mm)	%	MLD (mm)	%	Success	Recoil (mm)
Stent n = 21	1.1 ± 0.5	59 ± 17	2.2 ± 0.4	20 + 11	90% 19/21	0.32 ± 0.35
PPB n = 19	1.2 ± 0.6	60 ± 18	1.5 ± 0.3	46 + 23	42% 8/19	0.96 ± 0.54
P	ns	ns	<0.001	<0.001	0.002	<0.001

1) *Stenting was more effective as bail-out therapy* (90% vs 42% p < 0.002), especially in treating dissections of grade C or above: stent 11/12 (91%) vs PBB (0/5 (0)% p < 0.0001).

2) *Angiographic results with successful PPB were inferior to stenting:* % stenosis: 30.6 ± 20.2; MLD 1.9 ± 0.3 (p < 0.05 cf stent MLD) due to greater recoil in the PPB group: PPB 0.66 ± 0.34 mm (p < 0.05 cf stent recoil).

3) *Stenting following failed PPB was successful in 9/10 attempts with equivalent angiograms results to primary stent bail-out:* % stenosis 24.8 ± 8.2; MLD 2.5 ± 0.4 mm, but procedure time was longer 152.6 ± 53.0 mins v 114.8 ± 31.3 mins (p < 0.05).

Summary. This randomised multicentre study of bailout therapy in failed PTCA confirms the benefit of stenting in improving immediate results by reducing elastic recoil and sealing complex dissections. Crossover to stenting following failed PPB gives angiographic results comparable to primary bail-out stenting at the expense of increased lab time.

935-37 The Trial of Angioplasty and Stents in Canada: Clinical Outcome

Ian M. Penn, Robert I. Brown, Donald R. Ricci, David Almond, Jean F. Marquis, John Webb, Blair O'Neill, Brendon Foley, Cindy Wong, Stephanie Monkman, TASC Investigators. *University of British Columbia, Vancouver, B.C., Canada*

The trial of angioplasty and stents in Canada (TASC I) compared the strategy of coronary artery stenting (S) to PTCA in de novo (de N = 149) and restenosis (R = 121) lesions with a 1° end point of angiographic restenosis and 2° end point of event free survival at 6 months.

Results:

	De novo		Restenosis		Total	
	S (76)	PTCA (73)	S (61)	PTCA (60)	S (137)	PTCA (133)
Death	0 (0%)	1	0	0	0	1
MI	7	1	3	0	10	1
CABG	2	1	0	2	2	3
Repeat Interven.	3	5	1	5	4	10
Event free Survival	64 (84%)	65 (89%)	57 (93%)	53 (88%)	121 (88%)	118 (89%)

There was a reduction of clinical events in patients with restenosis lesions treated by stenting as compared to de novo lesions: 6.6% vs 15.8% p = 0.094. There was an increased early (less < 40 days) infarct rate in the stented patients due to stent thrombosis and a trend towards decreased intervention in target lesions at 6 months (p = 0.088).

Conclusion: The strategies of coronary artery stenting in this study had equivalent of event free survival to STRESS and Benestent in de novo lesions. Patients who underwent stenting for restenosis lesions had an improved outcome with only a 7% cardiac event rate at 6 months.

935-38 Restenosis After Coronary Angioplasty is Associated with the Activation Status of Circulating Phagocytes Before Treatment

Patrick W. Serruys, Anneke Pietersma, Marcel Kofflard, L. Elly A. de Wit, Theo Stijnen, Johan F. Koster, Wim Sluiter. *Erasmus University, Rotterdam, NL*

Background. The purpose of this study was to identify biological risk factors for restenosis after PTCA, in order to predict the long-term outcome of PTCA before treatment.

Methods and Results. To investigate whether blood granulocytes and monocytes could determine luminal renarrowing after PTCA, several characteristics of these phagocytes were assessed before angioplasty in 32 patients who underwent PTCA of one coronary artery and who had repeat angiograms at six months follow-up. The plasma levels IL-1β, TNF-α, IL-6, fibrinogen, C-reactive protein and LP(a) before angioplasty were assessed as well. We found that the expression of the membrane antigens CD64, CD66 and CD67 by granulocytes was inversely associated with the luminal renarrowing normalized for vessel size (relative loss) at six months after PTCA, while the production of IL-1β by stimulated monocytes was positively associated with the relative loss. Next, these univariate predictors were corrected

for the established clinical risk factors, dilation of the LAD, current smoking and angina class.

Multiple linear regression analysis showed that luminal renarrowing could be predicted reliably ($R^2 = 0.65$; $P < 0.0001$) in this patients group on the basis of the vessel dilated and only two biological risk factors that reflect the activation status of blood phagocytes, i.e., the expression of CD66 by granulocytes and the production of IL-1β by stimulated monocytes.

Conclusions. The results of the present study indicate that activated blood granulocytes prevent luminal renarrowing after PTCA, while activated blood monocytes promote restenosis. To validate this new finding further study in an independent patients group is required.

936 Cardiac Allograft Vasculopathy

Tuesday, March 21, 1995, 9:00 a.m.–11:00 a.m.
Ernest N. Morial Convention Center, Hall E
Presentation Hour: 10:00 a.m.–11:00 a.m.

936-83 Chronic Estradiol Treatment of Rabbits with Cardiac Allografts Attenuates Graft Vascular Proliferation Induced by Insulin-like Growth Factor-I (IGF-I) and Interleukin-6 (IL-6)

Hong Lou, Teruaki Kodama, Nevin Katz, Marie Foegh. *Georgetown University Medical Center, Washington, DC*

Male New Zealand White rabbits fed a 0.5% cholesterol diet (n = 13) received a heterotopic cardiac allograft and cyclosporine (10 mg/kg/day) until sacrifice 6 to 7 weeks later, at which time both the native and transplanted hearts and aorta were harvested. Six of the rabbits were treated with estradiol 100 μg/kg/day i.m., beginning 7 days prior to transplantation and continuing until sacrifice; the remaining seven rabbits served as controls and received placebo. The native aorta as well as the aorta from the grafted hearts were isolated and used for *in vitro* studies involving cytokine and growth factor stimulated cell proliferation. Tritiated thymidine incorporation is expressed as CPM/mg protein and the changes in cell proliferation are expressed as % changes from the control (the unstimulated vessel). IGF-I and IL-6 but not interferon-γ (INF-γ) significantly increased cell proliferation, measured as ^{3}H-thymidine incorporation, in explants from both native and allograft vessels and significantly more so in the graft ($p < 0.05$). The mitogenic effect of both IGF-I and IL-6 in the graft aorta, but not in that associated with the native heart, was abrogated by chronic treatment with estradiol ($p < 0.02$).

% Change in Vascular Wall Cell Proliferation

	IGF-I (20 μg/ml)	INF-γ (50 U/ml)	IL-6 (50 U/ml)
Native			
– Estradiol	175 ± 32	189 ± 43	162 ± 28
+ Estradiol	167 ± 42	143 ± 79	159 ± 36
Allograft			
– Estradiol	328 ± 66	197 ± 56	366 ± 101
+ Estradiol	64 ± 12	116 ± 41	72 ± 14

Mean ± SEM

This inhibitory effect of estradiol treatment on the mitogenic effect of IGF-I and IL-6 on the vascular wall of the allograft supports previous studies showing that accelerated coronary transplant arteriosclerosis in this model is inhibited by estrogen. These data speak to the use of hormone replacement therapy in post menopausal women receiving a cardiac transplant.

936-84 Efficacy of Endothelin A Receptor Antagonist (FR139317) for Long-term Heart Preservation

Kenji Okada, Chojiro Yamashita, Morihito Okada, Masayoshi Okada. *Kobe University, Department of Surgery, Division II*

Prolonged heart preservation by simple cold storage in University of Wisconsin solution (UWs) and its deteriorative effect on endothelial function have been problematic. We have studied whether continuous coronary microperfusion (CCMP) technique with oxygenated UWs improves post-ischemic functional recovery and addition of endothelin (ET) A receptor antagonist (FR139317) reduces damaged endothelium-dependent vasoconstriction. Twenty three isolated hearts of Japanese white rabbits were divided into four groups according to preservation methods or modification of UWs. Group I (control non-preserved), Group II (with original UWs), Group III (with oxygenated UWs) and Group IV (with oxygenated UWs contained 10 mg/l of FR139317). Cardiac functions of isolated hearts were evaluated by Langendorff apparatus. As pre and post-ischemic functional parameters, systolic aortic pressure (sAP), aortic flow (AF), coronary flow (CF) and cardiac output (CO) were serially measured. In Group II, III and IV, all hearts were preserved with CCMP technique in hypothermia for 24 hours. Initial perfusion pressure of CCMP was set to 5 mmHg with constant flow and the pressure was monitored during the preservation. After all experimental protocol, tissue water content (tWC) was measured. And ultrastructural findings of myocardium and endothelial cells were evaluated. Recovery rate (post/pre;%) of cardiac functions, CCMP pressure after 24 hours and tWC were as follows. In Group IV, ultrastructural findings showed minimal myocardial and endothelial injury among preservation groups.

	% sAP	% AF	% CF	% CO	CCMPpress.	% tWC
Group I	99.7 ± 0.5	99.7 ± 0.5	99.7 ± 0.5	99.7 ± 0.5	(–)	82.2 ± 0.3
Group II	78.0 ± 8.2	52.8 ± 26.5	62.6 ± 17.7	56.0 ± 21.2	11.3 ± 2.2	88.3 ± 21.2*
Group III	87.1 ± 6.8	83.5 ± 10.7†	82.3 ± 12.0†	82.8 ± 8.9†	8.2 ± 1.3†	83.2 ± 2.9
Group IV	91.5 ± 4.2	89.2 ± 9.2‡	96.5 ± 11.7‡	91.5 ± 5.4‡	5.2 ± 0.2‡	84.7 ± 1.7

*$p < 0.05$ Group I vs II, †$p < 0.05$ Group II vs III, ‡$p < 0.05$ Group III vs IV

Conclusions: 1) CCMP with oxygenated UWs improved post-ischemic cardiac functions and suppressed tissue edema in prolonged heart preservation. 2) Addition of ETA antagonist suppressed damaged endothelium-dependent vasoconstriction and also showed excellent functional recovery and minimal myocardial injury.

936-85 Intrathymic Injection of Donor Splenocytes Prolongs Rat Cardiac Allograft Survival but Does not Inhibit Graft Arteriosclerosis

Yong T. Shin, David H. Adams, Lauri R. Wyner, Enver Akalin, Mohamed H. Sayegh, Morris J. Karnovsky. *Harvard Medical School, Boston, MA*

Chronic rejection, manifested by the development of graft arteriosclerosis, remains the leading cause of late death in cardiac transplant recipients. Immunologic mechanisms have been implicated in both experimental and clinical studies, yet the pathogenesis of chronic allograft rejection remains poorly understood. Recent studies have shown that intrathymic (i.t.) injection of donor cells or processed allo-MHC antigens with or without transient immunosuppression induces specific systemic T cell tolerance and prevents acute allograft rejection in several experimental transplantation models. In this study we examined the effects of i.t. injection of donor cells with or without systemic anti-lymphocyte serum (ALS) on the development of *chronic rejection* in the Lewis-to-F344 rat cardiac allograft model. Recipients were divided into 4 groups: control group A was pre-treated with saline i.t., group B was pre-treated with a one-time dose of ALS (1 ml) via intraperitoneal injection (i.p.), group C received donor (Lewis) splenocytes i.t. (2×10^6), and group D received both the splenocytes i.t. and a one-time dose of ALS i.p. two weeks prior to transplantation. Allografts were followed by daily palpation and graded from 0–4 (grade 0 = rejection, grade 4 = normal heartbeat). Graft survival on post-op day 90 for all three experimental groups was 100% vs. 33% for the control (n = 6/group). Moreover, mean heartbeat grade for the three experimental groups (B = 2.83 ± 0.17, C = 2.0 ± 0.41, D = 2.67 ± 0.21) was significantly higher ($p < 0.01$) than that of the control group (A = 0.4 ± 0.24). Histologic and immunocytochemical analysis of 90-day old grafts revealed the following results:

GROUPS	Inflammation	% Vessels Diseased	% Luminal Occlusion	Intima:Media Ratio
Control (A)	severe	89 ± 1	64 ± 5	0.97 ± 0.33
Splenocyte only (C)	moderate-severe	79 ± 8	57 ± 7	0.68 ± 0.16
ALS only (B)	minimal	25 ± 7**	8 ± 3**	0.09 ± 0.04*
Splenocyte + ALS (D)	minimal	27 ± 4**	8 ± 3**	0.07 ± 0.03*

*$p < 0.02$, **$p < 0.003$ vs. Control

Conclusions: (1) The induction of systemic unresponsiveness with donor splenocyte i.t. plus ALS i.p. or ALS i.p. alone markedly reduced inflammation and inhibited graft arteriosclerosis indicating that the immune response and graft inflammation play a critical role in the pathogenesis of chronic allograft rejection. (2) The donor cells i.t. alone significantly prolonged graft survival and prevented rejection as measured by functional criteria but did not significantly inhibit graft inflammation or graft arteriosclerosis. These results suggest that partial suppression of the immune response without significant inhibition of graft inflammation prolongs rat cardiac allograft survival but does not prevent graft arteriosclerosis.

936-86 Plasma Fibrinogen Level Predicts Severity of Intimal Thickening After Cardiac Transplantation

Clyde R. Meckel, Todd J. Anderson, Gilbert H. Mudge, Peter Ganz, Daniel I. Simon. *Brigham and Women's Hospital, Boston, MA*

Diffuse atherosclerosis is the primary reason for late graft failure after cardiac transplantation. Because there is increasing evidence that imbalances in the hemostatic and fibrinolytic pathways are associated with allogeneic re-