autopsy). Causes were idiopathic in 43 (32%), pericarditis in 24 (18%), cardiac surgery in 23 (17%), irradiation in 19 (14%), collagen disease in 7 (5%), infective in 5 (4%, 3 post-tuberculous), malignancy in 3 (2%) and miscellaneous in 11 (8%). There was a 24% mean annual increase in the incidence from 1990 onwards compared to 1985–1989, and a significant relative increase in incidence of idiopathic (39% vs. 20%, p = 0.02), but not other causes of CP. Clinical presentation was congestive heart failure in 90 pts (67%), gastrointestinal in 13 (10%), cardiac tamponade in 7 (5%), arrhythmic in 6 (4%) and miscellaneous in 19 (14%). Most pts were severely symptomatic (69% in NYHA class III–IV); median duration of symptoms was 10 months. Atrial fibrillation or flutter was noted in 22 pts (16%). Pericardial calcification on chest X-ray was seen in 34 pts (25%). Prior investigative procedures included liver biopsy in 13 pts (10%), gastrointestinal endoscopy in 10 (7%), bronchoscopy in 8 (6%), thoracotomy or thoracoscopy in 6 (4%) and laparotomy in 5 (4%). The diagnosis was suspected elsewhere in 42 pts—in the remaining 93, a de novo diagnosis was first suspected by a clinician in 56 cases (60%), echocardiography in 28 (30%), following computed tomography in 3 (3%) and at catheterization in 1 patient (1%). In 5 pts (3 with post-surgical CP), the diagnosis was discovered only at thoracotomy for non-pericardial surgery.

Conclusions: (1) The commonest cause of CP in the current era remains idiopathic, (2) Despite the decline of tuberculosis, calcific CP was present in 25% of pts, (3) Clinical suspicion and echocardiography are the primary means (90%) of detecting unsuspected CP.

901-99 Modified Left Ventricular Mechanical Restitution Plots During Atrial Fibrillation in Humans: The Effect of Interval Dependent Changes in Contractile State

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In atrial fibrillation (AF), beat-to-beat changes in left ventricular (LV) systolic performance are caused by variations in 1) LV filling (preload), 2) aortic pressure (afterload), and 3) myocardial inotropic or contractile state. These interdependent factors are influenced by the preceding diastolic or R-R interval ($R\text{-}R_1$), but the impact of variations in the pre-preceding R-R interval ($R\text{-}R_2$) is not defined. This latter effect was studied in 13 patients with AF by measuring LV peak ejection velocity (V_{pe}, Doppler echocardiography) in 50–100 consecutive cardiac cycles. V_{pe} was plotted against $R\text{-}R_1$ for beats with a short $R\text{-}R_2$ and for beats with a long $R\text{-}R_2$. Such modified mechanical restitution plots indicate a direct relation between V_{pe} and $R\text{-}R_1$ (for $R\text{-}R_1$ = 500–1000 ms). The slope (linear fit) of V_{pe} versus $R\text{-}R_1$ was similar for short and long $R\text{-}R_2$ (slopes ≈ 0.06 and 0.05 sec_{-1}). V_{pe}, calculated from best linear fit and a common $R\text{-}R_1$, was consistently higher when $R\text{-}R_2$ was short (e.g., < 700 ms) when compared to long (e.g., > 800 ms).

	$R\text{-}R_1$ = 500	$R\text{-}R_1$ = 750	$R\text{-}R_1$ = 1000
V_{pe} (% of max) at Short $R\text{-}R_2$	70 ± 2	86 ± 2	102 ± 3
V_{pe} (% of max) at Long $R\text{-}R_2$	60 ± 3*	72 ± 3*	84 ± 3*

Data are mean ± SEM. *p < 0.05.

By comparing V_{pe} at a common $R\text{-}R_1$, the effects of time dependent changes in LV preload and afterload are minimized if not abolished. Thus, differences in V_{pe} (at a common $R\text{-}R_1$) reflect changes in contractile state.

Data confirm a positive inotropic effect of an abbreviated pre-preceding interval ($R\text{-}R_2$). In AF, beat-to-beat changes in myocardial contractile state (which occur as a consequence of variable $R\text{-}R_2$) have a significant effect on LV mechanical restitution plots.

MYOCARDIAL INFARCTION – BASIC

901-100 Overexpression of Inducible Heat Shock Protein (HSP)72 in Transgenic Mice Decreases Infarct Size

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Previous studies have demonstrated that induction of HSP72 by whole body hyperthermia reduces infarct size in an in vivo model of ischemia and reperfusion. Furthermore, hearts obtained from transgenic mice that overexpress HSP72 demonstrate improved functional recovery and decreased infarct size in vitro after global ischemia and reperfusion. To test the hypothesis that overexpression of HSP72 reduces infarct size in vivo, transgenic mice that were heterozygote for a rat HSP70i gene ([+]HSP72) and transgene negative litter-mate controls ([–]HSP72) were subjected to 30 minutes of left coronary artery occlusion followed by 120 minutes of reperfusion. Core body temperature was monitored with a rectal thermometer and maintained between 36.5° C and 37.0° C with a heating pad. Infarct (inf) size, determined by dual staining with triphenyltetrazolium chloride and phthalocyanine blue dye, was lower in [+]HSP72 mice compared to [–]HSP72 mice:

Group	N	Inf size/LV	Risk area/LV	Inf size/Risk area
[–]HSP72	6	18.4 ± 2.9	56.5 ± 7.1	33.4 ± 4.5
[+]HSP72	7	5.8 ± 0.8*	52.3 ± 6.2	12.7 ± 2.8*

All values expressed as % (mean ± SEM), *p < 0.01 vs [–]HSP72 mice

Thus, overexpression of HSP72 reduces infarct size in this in vivo transgenic mouse model of myocardial ischemia and reperfusion.

901-101 Rabbit Ventricular Myocytes Can Be Preconditioned by Activation of Protein Kinase C-Coupled Receptors

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We have shown that protein kinase C (PKC)-coupled receptors such as adenosine A_1, muscarinic M_2, angiotensin II AT_1, adrenergic α_1 and endothelin ET_1 mimic ischemic preconditioning (PC) in intact rabbit heart. We tested whether similar protection could be achieved in isolated heart cells devoid of endothelial or other cells. Adult rabbit myocytes were isolated by enzymatic dissociation. Ischemia was simulated by centrifuging the myocytes into an oxygen-free pellet for 120 min. Cells were exposed to the agonist for 10 min before ischemia. Cell viability was evaluated with hypotonic trypan blue every 30 min. The area under the plot of % dead cells vs time was used to describe the rate of cell death. Death of myocytes with 100 μM of the A_1 agonist phenylisopropyl adenosine (30.2 ± 1.8 hr %) was 37% slower than that in untreated myocytes (49.8 ± 1.8 hr %, $p < 0.05$) and protection was comparable to that caused by PC. Stimulation of α_1 receptors with 100 μM phenylephrine, M_2 receptors with 10 μM carbachol, and AT_1 receptors with 10 μM angiotensin II delayed cell death by 33%, 47% and 37%, respectively. However, no protection was seen with endothelin up to 1 nM (40.4 ± 1.6 hr % vs 37.6 ± 2.8 hr % in untreated cells). With the exception of endothelin these data not only support the PKC theory of PC but also indicate that protection derives from activation of PKC within the cardiomyocyte rather than another cell type such as the mast cell.

901-102 In Vivo Evidence That Neutrophils Become Activated and Generate Oxygen Radicals in Reperfused Hearts

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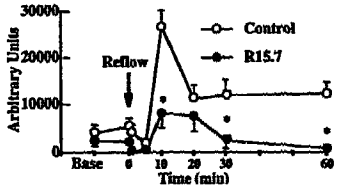
Direct demonstration that postischemic reperfusion may stimulate oxygen radical (OR) production from activated neutrophils (PMNs) has been hindered by difficulties in measuring ORs in vivo. To address this issue, blood was simultaneously drawn from the aorta (A) and the coronary sinus (CS) in dogs undergoing 90 min of coronary artery occlusion at baseline, during ischemia and after reflow. Samples were mixed with the spin-trap PBN (17 mM), extracted with toluene, and measured in an electron paramagnetic resonance (EPR) spectrometer. Control dogs received no treatment (C; n = 12); a second group was injected at reflow with 1 mg/kg bolus of R15.7, a monoclonal antibody against the PMN adhesion protein CD18 (R15; n = 7). The two groups had similar hemodynamic variables and collateral flow during ischemia (15 ± 5% of baseline in C, versus 11 ± 2% in R15). Time course of CSA-differences in EPR signal is shown (* = $p < 0.05$).



Marked increase in OR concentration was observed after reflow, which peaked at 10 min and was still elevated after 60 min. This phenomenon was largely blunted by administration of anti-PMN antibodies. Validation experiments showed that 91 ± 8% of EPR signal was accounted for by superoxide radicals. Thus, ORs can be measured in blood draining from the coronary sinus in vivo. Activation of PMNs is a major source of ORs during reperfusion after prolonged myocardial ischemia.