with antibodies to PKC-β1 and -β2 was slight in NF myocyte, but intense in the myocytes of failed LV. *In situ* hybridization revealed increased expression of PKC-β1 and β2 mRNA in cardiomyocytes of failed human heart tissue. Total PKC activity was increased in membrane fractions from failed hearts (1219 ± 188 vs. 609 ± 171 pmol/min/mg protein; failed vs. NF; $P < 0.05$). LY333531, a selective inhibitor of PKC-β, significantly decreased PKC activity from failed hearts by 24%.

Conclusions: PKC-β1 and -β2 are elevated in failed human heart, and inhibition of PKC-β may represent a novel therapeutic approach to heart failure.

2:30

851-3 Growth Hormone Resistance in Chronic Heart Failure

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Acquired growth hormone (GH) resistance occurs in severe illness and cachexia, and may explain the different responses to GH in recent studies of patients with chronic heart failure (CHF).

In 72 CHF patients (age 61 ± 1y, peak VO_2 16.5 ± 0.7 ml/kg/min) and 20 healthy controls ([Con] 58 ± 2y, $p = 0.07$) the GH - IGF-I axis was studied in relation to IGF binding protein 3 (IGFBP-3) and GH-binding protein (GH-BP) (controls vs CHF: differences = NS). The CHF patients were sub-devided according to cachectic ([c], >7.5% weight loss over >6 months) or non-cachectic (nc) state. The logIGF-I/GH ratio (9 AM) was calculated as index of GH sensitivity, and was found to correlate well with mean GH overnight levels (11 CHF patients: blood samples for 8 hrs, every 20 min, $r = -0.60$, $p = 0.05$), and mean overnight logIGF-I/GH ratio ($r = 0.72$; $p = 0.01$).

	Con n = 20	ncCHF n = 51	cCHF n = 21	ncCHF vs Con (p)	cCHF vs Con (p)	cCHF vs ncCHF (p)
total GH (ng/ml)	1.2±0.3	1.2±0.3	5.3±1.3	NS	<0.0001	<0.0001
intact GH (ng/ml)	0.5±0.1	0.4±0.1	1.6±0.5	NS	0.0073	0.0017
IGF-I (ng/ml)	151±9	150±8	124±9	NS	0.09	0.06
log IGF-I/GH	2.7±0.2	2.0±0.1	1.7±0.2	NS	0.0002	0.0001
IGFBP-3 (μg/ml)	3.8±0.1	3.7±0.1	3.1±0.2	NS	0.012	0.012
GH-BP (pmol/l)	852±83	950±84	607±64	NS	0.06	0.0047

mean ± SEM; NS = p > 0.20. Sample time: 9 AM

Correlations: log IGF-I/GH *vs* %ideal weight (Con: $r = 0.23$, p = NS; CHF: $r = 0.54$, $p < 0.0001$), and *vs* GH-BP (Con: $r = 0.79$; CHF: $r = 0.61$, both $p < 0.0001$; nc: $r = 0.50$, $p < 0.01$; c: $r = 0.68$, $p < 0.001$).

Cachectic patients with CHF show the biochemical features of acquired GH resistance possibly due to a down regulation of GH receptors. The presence of GH resistance may influence the response to GH therapy and should be assessed prior to treatment.

2:45

851-4 The Growth Hormone Secretagogue Hexarelin Improves Cardiac Function in Rats After Experimental Myocardial Infarction

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Background: Accumulating evidence indicate that growth hormone (GH) can enhance cardiac performance both in rats after experimental myocardial infarction (MI) and in patients with congestive heart failure. Hexarelin is one of several synthetic compunds with capacity to stimulate GH secretion in animals and humans. The aim of the present study was to investigate if administration of Hexarelin could improve cardiac function in rats after experimental MI.

Methods: Male rats were treated for two weeks with either Hexarelin in a dose of 5 or 50 $\mu g \cdot kg^{-1}$, recombinant human GH (rhGH) in a dose of 1 $mg \cdot kg^{-1}$ or saline injected s.c twice daily four weeks after ligation of the left coronary artery. Intact rats were used as controls. Transthoracic echocardiography was performed before and after the treatment period.

Results: Stroke volume (SV) was increased 49% ± 10% by rhGH, 53% ± 16% by Hexarelin 10 $\mu g\,kg^{-1} \cdot day^{-1}$, and 55% ± 21% by Hexarelin 100 $\mu g \cdot kg^{-1} \cdot day^{-1}$, ($p < 0.05$ vs baseline). Cardiac output (CO) was increased 62% ± 21% by rhGH, 48% ± 19% by Hexarelin 10 $\mu g \cdot kg^{-1} \cdot day^{-1}$ and 51% ± 13% by Hexarelin 100 $\mu g \cdot kg^{-1} \cdot day^{-1}$. There were no effects on SV and CO in the saline treated groups.

Conclusion: Hexarelin improves cardiac performance to a similar extent as exogenously administered rhGH in rats after experimental myocardial infarction. This may have clinical implications if beneficial effects can also be obtained in patients with congestive heart failure.

3:00

851-5 Renal and Hemodynamic Effects of Growth Hormone Treatment in Experimental Heart Failure

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Chronic growth hormone (GH) treatment is a new approach for the therapy of heart failure. We analyzed whether cardiac and renal function could be improved by chronic application of GH in experimental heart failure. Manifest heart failure was induced by a large aortocaval shunt in male Wistar rats which were treated with recombinant human GH (2 mg/day s.c.) for 30 days. We anylazed renal excretory function by using metabolic cages and measured cardiac pressures and contractility.

Rats treated with GH developed a significant higher body weight already after 6 days of treatment. After 30 days, the GH treated rats weighed 333 ± 9 vs. 305 ± 6 g in placebo treated shunted rats ($p < 0.01$). The relative heart weight increased in shunted rats from 319 ± 7 to 583 ± 40 mg/100 g, compared to sham operated controls, but was not influenced by GH treatment. Cardiac enddiastolic pressures were elevated in shunted rats compared to sham-operated controls, but were not modified by GH. Similarly, cardiac contractility (dP/dt) was lower in shunted rats (4820 ± 210 vs. 5400 ± 433 mmHg/sec, $p < 0.05$) and was not improved by GH therapy. Water intake was not different between GH- and placebo treated shunted animals. Water and sodium excretion, however, was enhanced by GH: natriuresis increased from 1.54 ± 0.06 to 2.01 ± 0.10 mmol/d ($p < 0.05$) and diuresis from 17.4 ± 2.0 to 23.1 ± 3.0 ml/d ($p < 0.05$).

Our results suggest that chronic treatment with growth hormone might not improve cardiac function in this model of heart failure but seems to have a beneficial effect on water and sodium homeostasis.

3:15

851-6 17β-Estradiol Protects Against the Development of Pressure Overload Cardiac Hypertrophy in Rats

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Cardiac hypertrophy shows gender-based differences with markedly higher mortality in men. The influence of estrogens on cardiac hypertrophy is poorly understood. This study examined the protective effect of 17β-estradiol (E2) against the development of cardiac hypertrophy induced by abdominal aortic banding for 6 weeks. One hundred 8-wk old male (M) and ovariectomized female (F) Sprague Dawley rats were randomized to sham-operated (S), banding + placebo (P) and banding + E2 (E2, 10 mg slow release pellets implanted 48 h before surgery) groups. We measured carotid and left ventricular systolic (CSP, LVSP, mmHg) and diastolic pressure (CDP, LVDP), ratio of left ventricular weight to body weight (LVW/BW, mg/g), LV ± dp/dt (mmHg/s) and LV wall thickness (LVW-T, mm), and cardiac myosin heavy chain (MHC) mRNAs by Northern blot analysis.

Group	LVW/BW	CSP	LVSP	LV ± dp/dt	LVW-T
P (M)	2.8 ± 0.1	177 ± 11	127 ± 7	4573 ± 169	4.4 ± 0.2
E2 (M)	2.3 ± 0.1*	117 ± 4*	95 ± 4*	3372 ± 201*	3.6 ± 0.1*
P (F)	3.0 ± 0.1	155 ± 3	99 ± 5	4406 ± 232	5.1 ± 0.2
E2 (F)	2.5 ± 0.0*	118 ± 3*	79 ± 3*	3624 ± 148*	3.7 ± 0.1*

Mean ± SEM. * $p < 0.05$ compared with group P

E2 significantly attenuated hypertension and reduced left ventricular muscle mass in both male and ovariectomized female rats. Further, E2 but not P decreased expression of β-MHC mRNA. (14.3% in male; 15.2% in female; both $P < 0.05$) but increased α-MHC mRNA (9.8% in male; 11.3% in female; both $P < 0.05$).

Conclusions: 17β-Estradiol prevents the development of hypertension and cardiac hypertrophy in rats with experimental hypertension.

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