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Because of the Canterbury earthquakes, this was the only scientific meeting held by the Health Research Society of Canterbury in 2011.

## Intermittent hypoxic exposure has a positive effect on heart rate variability in a sedentary population

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Increased heart rate variability (HRV) is associated with increased physical fitness (1) while lower HRV indicates cardiac disease (2). Intermittent hypoxic exposure (IHE) is a technique used to simulate altitude exposure, and may enhance exercise tolerance in unhealthy adults (3). We aimed to explore the effects of IHE on HRV in a sedentary population.

Sixteen participants (5 male, 11 female, aged 56.3±5.1 years, BMI 28.9±6.2, mean±SD) were exposed to 16 IHE sessions [IHE: 5min normobaric hypoxia ($F_IO_2$=0.16 at week 1, decreasing to $F_IO_2$=0.10 at week 4):5min ambient air, repeated for 1hour, *n*=8] and [Control (C): 5min placebo ($F_IO_2$=0.21):5min ambient air, repeated for 1 hour; *n*=8]. Arterial blood pressure (BP), HRV and oxygen uptake ($VO_2$) were monitored during lying, standing, sub-maximal exercise and recovery pre- and post- intervention.

Relative to the control group the IHE group decreased lying HR by 9.1±8.3% (mean±90% confidence limits) [IHE: 59.2±6.1 to 56.8±6.2, mean±SD beats/min; and C: 64.6±11.0 to 66.2±9.2 beats/min for the pre and post groups respectively]. HRV (rMSSD) increased in the IHE group relative to the C group during lying (76.8±67.0%; IHE: 32.51±15.12 to 35.95±12.07 rMSSD; C: 21.04±8.75 to 20.35±9.54 rMSSD), and exercise (23.2±27.7%; IHE: 4.13±1.86 to 5.08±2.96; C: 4.64±3.84 to 4.06±2.58 rMSSD; mean±SD beats/min for pre- and post-measurements). There were no beneficial BP or VO2 changes between groups, or in standing or recovery HRV measures.

These findings suggest 16 IHE sessions in a sedentary population may improve resting HRV and HR, but has little effect on BP or $VO_2$. As HRV is generally associated with improved health, this may prove beneficial for patients unable to engage in physical activity such as those with spinal injuries or musculoskeletal conditions. More research with a larger population is needed to test these findings.

**References:**

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## How testicular salvage data may influence future management of perinatal torsion of the testis

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The incidence of testicular torsion peaks in neonates and puberty. Animal models have demonstrated loss of spermatogenesis at 4-6 hours following torsion, and of hormonal function at 10 to 12 hours (1) – findings which have shaped management of this condition. While there is consensus about the management of torsion in older children, the best management of perinatal torsion has been less certain.

For a long time, it was believed that all neonatal testicular torsion resulted in death of the testis, such that neonates with testicular torsion warranted no surgical intervention. Recent observations, however, have distinguished between two apparently separate entities within torsion of the testis affecting neonates: pre-natal and post-natal. Increasingly, evidence is pointing towards a different prognosis and consequent management for each condition. Torsion occurring after birth, if picked up and managed promptly by surgical exploration may achieve testicular salvage in a few instances, unlike testicular torsion occurring before birth. The distinction can be made clinically, in that prenatal testicular torsion is evident at the time of birth with an indurated and enlarged scrotum, whereas postnatal torsion becomes evident some days later (2). Moreover, improvements in the safety of neonatal anaesthesia makes emergency surgery, in selected circumstances, a safe prospect (2).

**References:**

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2. Pinto KJ, Noe HN, Jerkins GR. Management of neonatal testicular torsion. J Urol 1997;158:1196–7.

## Model-based diagnosis of acute pulmonary embolism and septic shock in porcine trials

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Acute pulmonary embolism (APE) and septic shock (SS) are prevalent dysfunctions in the intensive care unit (ICU) and are associated with high rates of mortality. The aim of this research is to test the ability of a model-based technique to diagnose and track disease-dependent hemodynamic changes resulting from these forms of shock.

In two porcine studies, APE (N=5) and SS (N=4) were induced using autologous blood clot injections and endotoxin infusions, respectively. In both studies hemodynamic measurements were recorded every 30 minutes. Subject-specific cardiovascular system (CVS) models were fitted to each pig from a minimal set of typically available ICU measurements. Identified parameters and outputs were compared to experimentally derived indices, measurements not used in the identification, and trends from the literature to validate the subject-specific models.

The models accurately predicted the maximum ventricular pressures and end diastolic ventricular volumes to mean absolute errors of less than 7.1% and 6.7%, in both studies. Modelled pulmonary vascular resistance (PVR) compared well (R=0.68 for APE and R=0.73 for SS) to the experimentally derived values. Importantly, in the APE study a large rise in PVR, a major hemodynamic consequence of APE, was identified in all five pigs as expected. In response to endotoxin infusion a drop in systemic vascular resistance of 26% (on average) was identified by the model, in contrast to an increase seen in the APE pigs. In addition, hyperdynamic states were observed in two of the pigs, consistent with known trends for septic shock.

These results indicate that subject-specific CVS models can be used to diagnose APE and SS. Furthermore, the identified models can accurately monitor acute hemodynamic changes resulting from these two common forms of shock, indicating the potential for the model to be used as assistive tool for therapy decisions.

## Intracellular antioxidant activity of 7,8-dihydroneopterin protects macrophages from oxidised low-density lipoprotein.

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Immune system activation and the oxidative modification of lipoprotein are considered the key processes in atherosclerosis. Reactive oxygen species generation in response to actual or perceived damage is a defense mechanism of the immune cells. However, if excessive or unresolved, the oxidative stress can lead to further cellular damage, dysfunction and death. Oxidative stress and cellular death in response to oxidised low-density lipoprotein (oxLDL) may contribute to the formation of a necrotic core region in an atherosclerotic plaque.

Interferon-activated macrophages are known to produce 7,8-dihydroneopterin and its oxidised form neopterin, both of which have been detected in atherosclerotic plaques. We have shown 7,8-dihydroneopterin can protect human monocyte-derived macrophages (HMDM) and monocyte-like cell lines from a variety of oxidative stress. 7,8-Dihydroneopterin prevents the oxLDL-induced loss of glutathione but also decreases the uptake of DiI-labeled oxLDL and causes the down regulation of scavenger receptor for oxLDL, CD36[1]. We investigated which of these effects of 7,8-dihydroneopterin protect the HMDM cells from acute oxLDL-induced death.

7,8-Dihydroneopterin down-regulates CD36 protein level over 12h. Measurement of intracellular 7-ketochoesterol also showed that 7,8-dihydroneopterin significantly decreased the uptake of oxLDL. 7,8-dihydroneopterin incubated with oxLDL-treated

HMDM reduced intracellular reactive oxygen species generation (detected using dihydroethidium fluoroprobe) as early as 3h. 7,8-Dihydroneopterin was oxidised in the process suggesting direct scavenging of the oxidants. Pre-incubation of HMDM with 7,8-dihydroneopterin to reduce the CD36 levels, followed by exposure to oxLDL in the absence of 7,8-dihydroneopterin, failed to significantly inhibit the cell death.

This suggests that it is the antioxidant activity of 7,8-dihydroneopterin rather than reduced uptake of oxLDL that prevents acute oxLDL-induced cell death in macrophages.

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