Results: The 2 groups were age matched. 67% fractured indoors with peak incidence in winter (Dec-Feb). Mean weight and BMI in FC were lower than CC (p<0.001). The FC showed several lifestyle differences from CC (p<0.004). Routine laboratory results were consistent with acute phase response. BMD was reduced in the FC compared to CC at both the Lspine (0.918 vs 1.082; p<0.05) and all 4 sites of the femur (p<0.05). Vitamin D was lower (mean 10.94ng/ml vs 19.28ng/ml; p<0.001) in the FC at baseline and 6 mths compared to CC. In FC initial Vit D status had significant correlations with BMD at Femoral neck (r=0.9). Testosterone (TT) and free androgen index (FAI) declined with age in both groups, were significantly lower in FC (p<0.001) initially, at 6 mths & 1yr. The quality of life using SF36 showed a poorer premorbid health status in FC compared to CC (p<0.001). Cumulative survival is only 60% censored at one year in FC.

Conclusion: Osteoporosis & subclinical hypogonadism are important risk factors for hip fractures in men.

Y35 AN INVESTIGATION INTO NEW MATERIALS FOR EXTRACORPOREAL MEMBRANE OXYGENATION (ECMO)

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Introduction: ECMO can result in activation of coagulation and inflammation. Also tubing wear in the pump can result in thrombin, SEM and spallation. In-Vitro Biocompatibility: pigs

Methods: I) Mechanical: Destruction testing with roller pump and test rig, SEM and spallation. II) In Vivo Biocompatibility: 15 pigs 48 hours of veno-venous perfusion, 5 for each material samples: FBC, ABG, PT, TT, APPT, Lactoferrin, C3adesarg and Thromboxane B2. Lung biopsies; neutrophil Staining, H & E, and lung water. Other organs; H & E. III) In-Vitro Biocompatibility: a) 5 circuits of each material recirculated for 6 hours with human blood. Samples as above plus fibrinogen, Csh-9 instead of C3adesarg. b) H2O2Fibrinogen uptake with and without albumin washing.

Results: I) Mechanical: Tygon was the best. II) In-Vivo: LVA; increased Cardiotoxicity, Inflammation and Coagulation, equal haemolysis, reduced pneu-mo-nephrotoxicity. SRT; increased cardiotoxicity, coagulation and inflammation, equal haemolysis and pneumotoxicity, reduced nephrotoxicity. III) In-Vitro: a) SRT and LVA, increased coagulation. SRT, lower Csh-9. b) Untreated Tygon, lower fibrinogen uptake, no differences after albumin.

Conclusion: Neither SRT or LVA are safe for ECMO use.

Y36 THE FUNCTION OF THE DIAPHRAGM IN COPD

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In chronic obstructive pulmonary disease (COPD) compensatory diaphragm sarcemere adaptation is thought to occur but its importance remains unclear. The present studies used novel techniques (Polkey et al Thorax 1995;50:1131-5) to investigate diaphragm function in COPD both statically and under conditions of increased ventilation. At functional residual capacity (FRC) diaphragm strength, measured as transdiaphragmatic pressure (Pdi) during phrenic nerve stimulation and a maximal sniff, was substantially reduced in COPD patients who were also poorly able to translate Pdi into negative intrathoracic pressure. Paired bilateral phrenic nerve stimulation further showed that diaphragm strength was reduced over a range of stimulation frequencies, but, nevertheless that diaphragm adaptation was present. During exhaustive treadmill exercise inspiratory muscle relaxation rate slowed indicating excessive inspiratory muscle loading. Nevertheless, by phrenic nerve stimulation, overt diaphragm fatigue was shown to be absent, suggesting a predominant contribution from extradiaphragmatic muscles. Finally during 2 minutes of maximal isocapnic hyperventilation diaphragm pressure generation was poor, even allowing for the diminished strength demonstrated at FRC. It is concluded that although compensatory diaphragm adaptation occurs in COPD its functional importance has been previously overestimated.

Y37 REGULATION OF IL-8 FUNCTION BY THE HEPARIN/HEPARINASE BALANCE IN THE AIRWAYS

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Inflammatory cell recruitment into tissue sites of inflammation is determined by a number of chemoattractants, including the chemokine family of heparin binding proteins. The extracellular matrix is no longer perceived to play a passive role in this process. The glycosaminoglycans (GAGs) heparin and heparan sulphate (HS), bind chemokines and are believed to maintain a non-diffusible gradient within tissues. This study tests the hypothesis that, heparin and HS modify inflammatory cell responses to the chemokine interleukin-8 (IL-8), in asthma and cystic fibrosis (CF).

Ex vivo immunohistochemical analysis demonstrated co-localisation of extracellular IL-8 and HS in lung tissue from patients with CF and significantly more HS in alveolar basement membranes in CF compared to normal lung. This supports the concept that the interaction of IL-8 with HS is physiologically relevant and that neotrophils migrate in response to a chemokine (IL-8) bound to a matrix component (HS). In vitro models demonstrated spontaneous protease and heparanase-dependent loss of GAGs and IL-8 binding sites on the endothelium in culture.

Further, heparin at concentrations pertaining to those found in respiratory tissue, significantly inhibited the in vitro binding and chemotactic response of neutrophils to IL-8. Contrary to previous reports HS had no significant effect on binding or function. Mast cells are the sole source of heparin and degranulation is central to the pathophysiology of allergic Airways disease. However, in bronchial lavage fluid from patients with allergic asthma, there was no significant increase in heparin levels from saline-challenged sites compared to allergen-challenged sites. This indicated that, following its release heparin may be bound by proteins of the tissue matrix.

To test the theory that catabolism of heparin has an important regulatory role in inflammation, a novel zymographic technique was developed to quantify and characterise heparin degrading enzymes in the airways. Significantly increased levels of heparanase activity were detected in the sputum of patients with asthma and CF compared to normal subjects. Heparin concentrations in the sputum correlated negatively with the level of heparanase activity, being highest in normal subjects and undetectable in CF patients. This indicated that the heparin/heparanase balance may influence the pathology of inflammatory diseases characterised by increased expression of IL-8 including allergic asthma and CF. Further, a clinical trial of heparin inhalation therapy is indicated in CF.

Y38 THE SIGNAL TRANSDUCTION PATHWAYS INVOLVED IN THE ACTIVATION AND ProliferATION OF HEPATIC STELLATE CELLS - THE PRINCIPAL EFFECTORS OF LIVER FIBROSIS

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Fibrosis of the liver leading to cirrhosis is a major cause of death in many parts of the world. The principal cell type responsible for the development of liver fibrosis is the hepatic stellate cell (HSC). In normal liver these cells are quiescent and relatively sparse. In response to liver injury or inflammation they transform ("activate") into highly