rats were anaesthetised (35 mg/kg ketamine, 4 mg/kg xylasine and 0.5 mg/kg acepromazine) and haemodynamics measured using a 3.5
French umbilical vessel catheter. The ratio of right to left
ventricular and septal weight was recorded (RV/LV+S).

Results: At day 28, the monocrotaline-alone rats had severe PAH with
mean pulmonary arterial pressure (mPAP) (40.8 ± 6.4 mm Hg vs
16.4 ± 1.5 mm Hg, p<0.001), right ventricular systolic pressure
(RVSP) (94.3 ± 7.8 mm Hg vs 35.2 ± 2.4, p<0.001) and RV/LV+S
(0.6 ± 0.1 vs 0.26 ± 0.06, p<0.001) compared with controls. PAH
was reversed in all the groups treated with dexamethasone with a
suggestion of a dose–response effect, with mPAP falling to 28.7 ± 11.9
(p = 0.07 compared with monocrotaline alone), 24.9 ± 4.7 (p<0.05)
and 23.1 ± 3.5 (p<0.01) in Dex1.25, Dex2.5 and Dex5, respectively
(fig A). RVSP was also significantly lower in all three groups. Right
ventricular hypertrophy as assessed by RV/LV+S was also reversed by
dexamethasone compared with monocrotaline alone (p<0.001 in all
groups, fig B). None of the measurements in the Dex5 group were
statistically different to controls. There was a significant improvement
in survival between all the dexamethasone groups when compared
with monocrotaline alone (log rank test p<0.001).

Conclusions: These results suggest that monocrotaline-induced
PAH can be reversed by steroids, raising the possibility that an anti-
inflammatory strategy may be beneficial in some cases of pulmonary hypertension.

Respiratory physiology

S64 CLINICAL VALIDATION OF THE SEVERINGHAUS OXYGEN DISSOCIATION CURVE

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Background: Severinghaus has described a widely used mathematical model to calculate the oxygen dissociation curve for human blood. (J Appl Physiol 1979;46:599). This model is based on the

Abstract S64 Figure (A) Saturation and oxygen tension of 3524 blood gas specimens; (B) Dissociation curve calculated from Severinghaus equation; (C) Clinical data compared with Severinghaus equation; (D) Clinical samples at normal, low and high PH.
The mean SaO₂ was 94.98% (SD 5.9%) using the oximeter was compared with the calculated value derived from the specimen, the oxygen saturation obtained by the laboratory co-performed using 10 mmol glucose with radiolabelled [3H]-D-glucose. Insulin was added (0–7 H441 monolayers were cultured on porous filters at air.

Methods: We audited 3524 anonymised blood gas results from patients treated at this university hospital (2255 specimens with normal pH (7.35–7.45), 588 acidic specimens with pH < 7.35 and 711 alkalotic specimens with pH > 7.45). For each blood gas specimen, the oxygen saturation obtained by the laboratory co-oximeter was compared with the calculated value derived from the Severinghaus equation.

Results: The mean SaO₂ was 94.98% (SD 5.9%) using the laboratory co-oximeter and 94.82% (SD 5.3%) using the Severinghaus equation. The mean difference was only 0.16%, which is not clinically relevant. The raw clinical data are shown in panel A of the figure and the Severinghaus curve is shown in panel B. Panel C shows that the mean of the clinical values is almost identical to the Severinghaus result throughout the clinically relevant saturation range at normal pH. Panel D shows the effect of pH on clinical specimens, confirming the Bohr effect of rightward shift with acidosis and leftward shift with alkalosis.

Conclusion: The mathematical equation of Severinghaus predicts the oxygen saturation of human blood from patients with a range of diseases with remarkable precision. We believe this to be the first large-scale clinical validation of this equation.

S66 INSULIN STIMULATES GLUCOSE UPTAKE AND GLUCOSE TRANSPORTER EXPRESSION IN H441 HUMAN AIRWAY EPITHELIAL CELLS

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Background: Hyperglycaemia leads to elevated glucose levels in airway surface liquid (ASL) (Baker et al. J Appl Physiol 2007;102: 1969–75), increasing the risk of infection with bacteria such as methicillin-resistant Staphylococcus aureus (Philips et al. Thorax 2007;60:761–4). Inhaled insulin has been developed for the treatment of diabetes (Crotty and Reynolds. Pediatr Emerg Care 2007;23:903–5), but its effect on glucose transport in the airway is unknown. This study aimed to investigate the effect of insulin on glucose uptake by cultured human airway epithelial cells.

Methods: H441 monolayers were cultured on porous filters at air.

Results: The basal monolayer insulin concentration dose–response effect was fitted with a variable sigmoidal curve with an EC50 of 1.4 μmol. Basolateral glucose uptake was 52.14 ± 19.84 nmol/mg protein with no insulin. Maximal uptake was 484.46 ± 131.97 nmol/mg protein when 1.7 μmol insulin was added to the basolateral side of the monolayer (p<0.05, n = 5–9). In the presence of 1.7 μmol insulin, phloretin significantly reduced uptake to 55.74 ± 9.55 nmol/mg protein (p<0.001, n = 3). Apical glucose uptake in the presence of 1.7 μmol basolateral insulin was 31.6 ± 2.0 nmol/mg protein compared with 11.7 ± 1.2 nmol/mg with no insulin (p<0.001, n = 3). Western blotting detected a band for GLUT2 at 56 kDa. Increasing insulin concentration evoked the emergence of a second band at 46 kDa. Immunocytochemistry demonstrated the movement of GLUT2 to the cell membrane with increasing insulin concentrations.

Conclusions: Insulin stimulates glucose uptake across both apical and basolateral membranes, indicating the presence of insulin-sensitive transporter(s) in the membranes of airway epithelial cells. These transporters are probably GLUT, as phloretin inhibited insulin-induced glucose uptake and insulin stimulated GLUT2 expression and translocation to the cell membrane. Insulin stimulation of glucose uptake by airway epithelial cells could increase glucose uptake from ASL, potentially reducing the risk of infection.

S67 SNIF AND TWITCH TRANSDIAPHRAGMATIC PRESSURES IN HEALTH AND DISEASE

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Introduction and Objectives: Contractile function of the diaphragm is best quantified by measuring transdiaphragmatic pressure (Pdi), either during a maximum volitional effort such as a sniff (sniff transdiaphragmatic pressure: Pdi,Sn) or non-volitionally following supramaximal stimulation of the phrenic nerves (twitch transdiaphragmatic pressure: Pdi,Tw). However, normal values for these tests are not well established. The objective of this study was to obtain normal values for Pdi,Sn and Pdi,Tw, to determine whether gender, height, weight or body mass index influence these values and whether Pdi,Tw offers additional information over Pdi,Sn in the clinical evaluation of diaphragm strength.
Methods: Pdi,Sn and Pdi,Tw were measured in 91 and 101 healthy volunteers, respectively, to determine normal values, and in 453 patients referred for respiratory muscle assessment. Diaphragm weakness was defined as a Pdi,Sn and Pdi,Tw below the 5th centile.

Results: Mean (SD) Pdi,Sn was 131 cmH2O (27) for men and 114 cmH2O (24) for women. Mean (SD) Pdi,Tw was 27 cmH2O (6) for men and 25 cmH2O (5) for women. Age was negatively associated with Pdi,Sn (r² = −0.27) and Pdi,Tw (r² = −0.39). Height, weight and body mass index did not independently influence Pdi,Sn or Pdi,Tw. Taking into account age and gender, 204 patients were considered to have diaphragm weakness. The addition of the non-volitional Pdi,Tw to Pdi,Sn in the identification of diaphragm weakness improved specificity from 72% to 100% and positive predictive value from 82% to 100%.

Conclusions: Normal values for Pdi,Sn and Pdi,Tw have been established. The use of both tests of diaphragm function increases diagnostic precision.

**THE RELATIONSHIP BETWEEN NEURAL RESPIRATORY DRIVE AND HYPERCAPNIA IN PATIENTS WITH NEUROMUSCULAR DISEASE**

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Background: Although respiratory muscle strength is a better predictor of hypercapnic ventilatory failure than poor spirometry in neuromuscular disease (NMD), more reliable tests to monitor progression to hypercapnic ventilatory failure are required. If the respiratory muscles are weak, neural respiratory drive must increase to maintain the balance between the capacity of the respiratory muscles and the load on the respiratory muscle pump. Neural respiratory drive can be measured by quantifying the diaphragm electromyogram (EMGdi) and carbon dioxide retention measured in a non-volitional Pdi,Tw manoeuvre.

Aims and Hypothesis: The aim of the study was to investigate the relationship between neural respiratory drive, measured by quantifying the diaphragm electromyogram recorded using a multipair oesophageal electrode.

Methods: 11 patients with NMD were studied (four neuralgic amyotrophy, two amyotrophic lateral sclerosis, one muscular dystrophy, one phrenic nerve trauma, one myotonic dystrophy, one polymyositis, one polynuropathy; eight men; mean (SD) age 53.9 years (10.1); vital capacity 76.8% predicted (20.0); pH 7.43 (0.04); pO2 11.0 kPa (1.5); pCO2 5.1 kPa (1.0); HCO3 24.9 mmol/l (3.5)). Sniff nasal pressure (SNIP), and mouth inspiratory pressure (PImax) were measured. EMGdi was recorded at rest using a multipair oesophageal electrode. Resting EMGdi was normalised by expressing EMGdi as a percentage of peak EMGdi recorded during maximum inspiratory manoeuvres. Normalised EMGdi activity/minute was then calculated ("EMGdi%index"). The maximum inspiratory manoeuvres were inspiration from FRC to TLC, PImax manoeuvres, maximum sniff manoeuvres and sprint maximum inspiratory manoeuvres.

Results: Correlations between EMGdi%index and each variable measured are shown in the table. There were significant correlations between EMGdi%index and pCO2 (r = 0.67, p = 0.03) and HCO3 (r = 0.68, p = 0.04) only. Mean (SD) PImax and SNIP were 63.1 cmH2O (33.0) and 51.0 cmH2O (35.7), respectively, and mean (SD) EMGdi%index was 575.6 au/min (312.6).

Conclusions: The significant correlations between EMGdi%index, pCO2 and HCO3 suggest that the EMGdi%index could potentially be used to monitor progression towards hypercapnic ventilatory failure in NMD. The value of the EMGdi%index over other respiratory muscle function tests requires further study.

**THE DEVELOPMENT OF THE BRONCHIAL SUBEPITHELIAL RETICULAR BASEMENT MEMBRANE**

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Background: Abnormal thickening of the bronchial subepithelial reticular basement membrane (RBM) is a recognised feature of airway remodelling. However, even although the RBM is present in the airways of healthy children and adults, nothing is known about its normal development. We hypothesised that the RBM is first visible at birth and subsequently thickens normally with age for the first 3 years, when final adult thickness is reached.

Methods: Cartilaginous airways were studied in lungs obtained postmortem from 87 infants and children (22 weeks gestation to 17 years old) who had died from non-respiratory causes and had no history of asthma. RBM thickness was measured in haematoxylin and eosin stained paraffin wax sections using computer aided image analysis and a method previously validated in endobronchial biopsies.

Abstract S68 Table Correlations between EMGdi%index and anthropometric/physiological variables

<table>
<thead>
<tr>
<th>r</th>
<th>p Value</th>
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<td>Age</td>
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<tr>
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<td>HCO3</td>
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<td>Vital capacity %</td>
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<tr>
<td>Sniff nasal pressure</td>
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<tr>
<td>PImax</td>
<td>−0.61</td>
</tr>
</tbody>
</table>

BMI, body mass index; PImax, mouth inspiratory pressure.

Abstract S69 Figure

Reticular basement membrane (RBM) thickness vs age

+ : females △ : males

Thorax 2008;63(Suppl VII):A4–A73

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