JOURNAL CLUB SUMMARIES

May Journal club summaries

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MUC5B IS IN MUCUS REGULATION

Muc5b is known to be involved in mucus regulation though its specific role is unknown. An American group developed a Muc5b deficient mouse (*Nature* 505:412–16). Muc5b deficiency caused material to accumulate in the upper airway. This subsequently led to chronic infection by multiple bacterial species including *Staphylococcus aureus*, with associated impaired resolution of inflammation. There was accumulation of apoptotic macrophages, impaired phagocytosis and a reduction in interleukin 23 production. In mice who had oversecretion of Muc5b, macrophage function improved as did airway clearance. This could provide a target for therapy to control the secretion of mucin and restore mucociliary clearance.

B BLOCKERS IN ASTHMA?

Traditionally β blockers have been avoided in asthma due to concerns about acute bronchoconstriction. There is increasing evidence that cardioselective β blockers can now be used though they seldom are. In this trial stable patients with asthma on <1000 μg/day of beclometasone dipropionate equivalent dose were randomised to propranolol or placebo (*Heart* 2014;100:219–23). Tiotropium was given concurrently to propranolol throughout the trial. Prior to randomisation a subgroup underwent a safety visit and received a single dose of intravenous esmolol. The trial looked at the effect of these drugs on spirometry and total airway resistance (R5%). There was no significant change in FEV_1 or total airway resistance (R5%) following esmolol infusion at 2 min, 8 min, 16 min and 32 min. However there was a significant decrease in heart rate and blood pressure. For those treated with propranolol and tiotropium there was a non-significant rise in FEV_1 predicted 30 min post 10 mg dose, this continued to 3 h. For total airway resistance there was a fall in the mean difference, this also persisted to 3 h. There was no significant difference to the matched controls. These results were maintained after uptitration of propranolol to 80 mg. The authors suggest that this indicates that intravenous esmolol does not worsen asthmatic function and that lung function is not impaired when propranolol is administered in conjunction with tiotropium.

ANOTHER ROLE FOR CHEST ULTRASOUND?

Portable ultrasound is increasingly available and can be carried out by trained operators. In this study 144 patients with presumed pneumonia were seen in the emergency department (ED) (*AJEM* 2014;32:115–18). They all had a chest ultrasound performed by one of five trained ED physicians and a chest x-ray which was interpreted by a radiologist. The primary end point was the diagnosis of pneumonia at hospital discharge. There was a sensitivity of 0.95 for the ultrasound examination against 0.6 for radiography ($p < 0.05$). The negative predictive value was 0.67 against 0.25 for radiography ($p<0.05$). This indicates that ultrasound done by trained personnel could be used in the diagnosis of pneumonia in the ED.

MOLECULAR DIFFERENCES IN NON-SMALL CELL CANCER BETWEEN SMOKER AND NON-SMOKERS

Around 15% of men with lung cancer and up to 50% of women have never smoked. Therefore it is important to look for differences in the tumour cells. This study compared the differences in 21 genes expressed in non-small cell lung cancer samples between smokers and non-smokers (*Adv Med Sci* 1;58:196–206). Tumour gene expression was higher for five genes including ER2 ($p=0.002$) in non-smokers. Tumour gene expression was lower for a further six genes including PR ($p<0.0001$). These genes are involved in sex hormone receptor signalling which is thought to be important in lung cancer signalling pathways. This information could lead to targeted treatment for those who have never smoked, with non-small cell lung cancer.

LONG PENTRAXIN 3 (PTX_3) DEFICIENCY AND ASPERGILLOSIS IN RESPIRATORY PATIENTS

Long pentraxin 3 (PTX_3) is involved in the modulation of effector pathways providing immune resistance to *Aspergillus fumigatus*. This study looked at those receiving haematopoietic stem cell transplants, to see if single nucleotide polymorphisms of the donor's PTX_3 affected the risk of the transplant recipient getting *A fumigatus* infection (*N Engl J Med* 2014;370:421–32). Four single nucleotide polymorphisms were affected. Receipt of a transplant from a donor with the homozygous haplotype (h2/h2) was associated with an increased risk of *A fumigatus* infection (cumulative incidence, 37% vs 15%, adjusted HR 3.08, $p=0.003$). Could this explain why some people are more prone to *A fumigatus* infection in the respiratory population?

THE IMPACT OF PREMATURITY ON LUNG FUNCTION

Prematurity has been shown to have a long-term impact on pulmonary function (*N Engl J Med* 2014;370:584–5). This group looked at the ventilatory responses in 13 adults who were born prematurely (gestational age <32 weeks) to 5 min of isocapnia, isobaric hypoxia (fraction of inspired oxygen 0.12) and hyperoxia (fraction of inspired oxygen 1.0). Measurements were recorded using a pulse oximeter. They were age matched with adults born at term. The two groups had similar pulmonary function and exercise capacity. The hypoxic ventilator response was reduced in preterm adults ($p=0.008$). Two preterm adults hypoventilated causing an increase in the partial pressure of end tidal CO_2; this caused presyncopal symptoms. Hyperoxia induced respiratory depression in only 8 of the 13 preterm adults compared with all 13 of the controls. However the mean response to hyperoxia was also reduced in the preterm adults ($p=0.01$). This study shows that there are abnormal ventilator responses to hypoxia and hyperoxia in adults with a history of preterm birth.

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