



# Highlights from this issue

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## THE GOOSE THAT LAYS THE GOLDEN EGG

Jak and the beanstalk is a confusing and conflicted tale. Jack is rewarded for disobeying his mother, stealing from a giant, and ultimately killing the giant from whom he stole. JAK2 is also somewhat conflicted as described by Dr Milara and colleagues in this issue of *Thorax* with high levels of JAK2 being found in the pulmonary arteries of patients with IPF with and without associated pulmonary hypertension (see page 519). In this story however, inhibiting JAK2 either with JSI-124 or siRNA prevented endothelial and smooth muscle transition, promoted relaxation of pulmonary arteries and ameliorated bleomycin induced lung fibrosis and pulmonary hypertension. So maybe blocking JAK2 will actually be the goose that lays the golden egg in IPF?

## MAYBE TOMORROW

As the Stereophonics mused in the early naughties “*I look around at a beautiful life; Been the upperside of down; Been the inside of out; But we breathe; We breathe*”. However patients with IPF struggle with this last bit, but they may have similar aspirations to “*I wanna breeze and an open mind; I wanna swim in the ocean; Wanna take my time for me; All me; So maybe tomorrow*”. In this issue Richeldi and colleagues describe the open label extension of the TOMORROW trial (see page 581). Patients who received nintedanib during the TOMORROW trial and the subsequent extension period lost 125 mL/yr of FVC compared with of a loss of 190 mL/yr in patients who received placebo during the trial and nintedanib in the extension period. While these results are promising it look like we will still have to wait until tomorrow to reverse or halt fibrosis.

## THE LAND OF NOD

“*The strangest things are there for me; Both things to eat and things to see*”. However, of all the things described by Robert Louis Stevenson as he described his dreamtime, we expect he didn't imagine the effect of influenza infection on macrophages in the lung. The macrophage is the first responder and dampens dangerous immune responses but calls for reinforcements following infection. Peiro and colleagues describe how ‘influenza infection leads to NOD-like receptor

protein –3 (NLRP-3) upregulation and pro-IL-1 $\beta$  which in turn leads to neutrophil release of mCRAMP that commit macrophages to produce large amount of IL-1-B (see page 546). Or as Lux Interior and Poison Ivy may have said the Cramps help macrophages stay sick.

## MABEL

The context of these lyrics “*I'm bad for you love, but I'm your cigarette*” by Mabel are clear. These sorts of lyrics are frustrating and could ultimately promote COPD by promoting the perception of cigarettes as ‘cool’. The effect of MBL (Mannose Binding Lectin) on the development of COPD was assessed in a study by Dicker *et al* (see page 510). They found that COPD patients with MBL deficiency had fewer moderate or severe exacerbations, lower markers of inflammation more diverse airway microbiota and less haemophilus colonisation than those without. Putting this all together suggests that Mabel is probably bad for people with COPD.

## EXIT MUSIC

“*Breathe; Keep breathing; Don't loose; Your nerve*” may sound like a motivational speech but these lyrics from Radiohead would not be recommended as a treatment of lung cancer and would not explain the regional variation in outcomes described by Dr Moller and colleagues (see page 530). However, there is considerable variation in proven therapies including surgical resection, with 9%–17% rates, radical radiotherapy, 4%–13% rates, and chemotherapy, 22%–35% rates around the UK. The authors suggest the variation is due to management decision and not patient, or tumour, characteristics. The authors conclude there are approximately 550 avoidable deaths due to the conservative approach taken in some areas. ‘Now; they are one; in everlasting peace’ but ‘now; today; we escape; we escape’ this geographical variation an improve outcomes for all patients with lung cancer.

## OOMPA-LOOMPAS AND CHILDHOOD LUNG FUNCTION

In Roald Dahl's classic ‘Charlie and the Chocolate Factory’ Augustus Gloop is described as ‘...so enormously fat he looked as though he had been blown up with a powerful pump.’ Augustus is the first to be

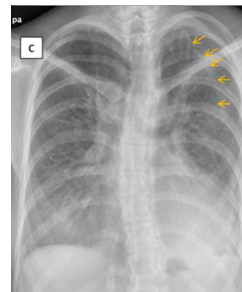
ejected from the Chocolate Factory, having fallen into the chocolate river in his enthusiasm to drink chocolate. The links between overweight, obesity and lung function are described in a paper in this month's journal (see page 538, Editors' choice). The outcome is less severe than befell Augustus. Ekström and colleagues report that overweight and obesity, at age 8 years, are associated with lower FEV1/FVC ratio at 8 and 16 years. The authors conclude that, with childhood obesity becoming increasingly common, these impairments in children's lung function may have implications their health as adults. One wonders what the Oompa-Loompas would have said...

## HOMOZYGOTE DISADVANTAGE

Traditional teaching says that sickle cell trait confers a heterozygote advantage through resistance to malaria. However, homozygous sickle cell anaemia has a considerable ‘homozygote disadvantage’ including painful crisis, stroke and chest syndrome (to name but a few). In this issue Greenough and colleagues describe a cluster analysis of over 100 children and young adults with sickle cell disease, determining pulmonary phenotypes (see page 575). These clusters were mixed obstructive/restrictive lung disease; older patients with restrictive lung disease; and younger patients with obstructive lung disease and bronchodilator reversibility. These clusters will require validation in a second population but offer a new insight into the pulmonary pathology of a neglected disease.

## DON'T FADE AWAY

Not a song by Whitesnake in this instance but our teaser image of the month. See page 595 to test your diagnostic skills.



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