



Highlights from this issue

doi:10.1136/thoraxjnl-2021-218295

The Triumvirate

“Remember, remember the 5th of November: gunpowder, treason and plot!” As this issue of *Thorax* drops on your doormat, UK readers are preparing for Guy Fawkes night, when we remember a foiled attempt to blow up parliament and we burn an effigy of Guy Fawkes on bonfires around the country. Treason is still to be found in the UK respiratory landscape with a plot by the tobacco giant, Phillip Morris, to take over the inhaler manufacturer Vectura. The plot seems unlikely to be foiled at the last minute and we are not aware of any plans to burn effigies of the CEO of Phillip Morris this year...

EARLY LIFE INTERVENTIONS

Children love Guy Fawkes night and have traditionally wheeled an effigy of Guy Fawkes door to door, before the bonfire, collecting a “penny for the guy”. The idea of encouraging children to celebrate the execution of Guy Fawkes is likely to be to discourage each generation from future sedition. The childhood origins of an adult condition are explored in this month’s *Thorax*. Sadiyah Hand and colleagues (see page 1072) describe 23 year follow-up from the Merthyr Allergy Prevention Study. This trial randomised high risk infants to cow’s milk avoidance (with soya formula, if not breast feeding) vs an unrestricted diet, to determine whether cow’s milk exclusion for the first 4 months of life reduced the risk of asthma and allergic disease. The authors report the surprising finding that early cow’s milk exposure was associated with a decreased risk of wheeze and asthma at age 23 years. Conversely, early exposure to soya was associated with increased risk of atopy and asthma. There was a low prevalence of breast feeding overall (around one third of infants at 1 week). An accompanying editorial (see page 1067) discusses the problems of selection and attrition bias and recommends directed acyclic graphs to visualise confounders. Guy Fawkes fell off the scaffold and broke his neck before he could be hanged and so did not receive his assigned intervention - as often happens to a proportion of patients in clinical trials.

PREDICTING MORTALITY IN ARDS AND IMMORTALITY FOR GUY FAWKES

Guy Fawkes and his co-conspirators were motivated by their manifest religious and ideological differences with the state, which set in train a series of events leading to their downfall. In contrast, the differences which lead to acute respiratory distress syndrome (ARDS) may be potential rather than manifest. In the journal this month, Mac Sweeney and colleagues (see page 1099) study the role of transepithelial nasal potential difference (NPD) in the pathogenesis of ARDS. The authors measured NPD in ventilated patients at risk of ARDS and in ventilated patients who had developed ARDS. They also studied patients recovering from ARDS and

healthy controls. They conclude that maximum NPD predicts ARDS but not death. The failure of the gunpowder plot could perhaps have been predicted when the plotters broke cover and warned their allies to stay away from parliament. However, the immortality, achieved by Guy Fawkes through the 5th of November, celebrations could not have been so easily predicted.

I THOUGHT I SAW FIREWORKS

The 5th of November is traditionally associated with fireworks in the UK. While the study into the epidemiology and prognosis of pleural empyema by Bobbio *et al* (see page 1117) is unlikely to have us reaching for the cordite it may well provoke an emotional response similar to that we get when listening to the haunting song of this name by First Aid Kit. It is a tragedy that the incidence of empyema is increasing and has such a high mortality rate, with 17.1% of the whole population. There were three broad sub-groups of patients spontaneous empyema, post-surgical empyema and cancer associated empyema. It is no surprise, but still heart breaking to see that the factors associated with increasing mortality include cancer (almost 30% mortality), hypertension, atherosclerosis and atrial fibrillation. To quote First Aid Kit, “Why do I do this to myself every time? I know the way it ends, Before it’s even begun”. I think the respiratory community needs more than a first aid kit to deal with the rising tide of empyemas.

AFTER A HURRICANE COMES A RAINBOW,

Katy Perry’s Firework is more upbeat than the fireworks described above. It is more motivational anthem than haunting harmony, which is probably required when thinking about starting chemotherapy. The study by Visser and colleagues (see page 1150) describes the genetic relationship between toxic hurricane and rainbow response to pemetrexed for non-small cell lung cancer. Somewhat surprisingly they found that a polymorphism in the target gene *ATIC*, that encodes the enzyme 5-Aminoimidazole-4-Carboxamide Ribonucleotide Formyltransferase, was associated with both worse adverse effects and better response to therapy. Although chemotherapy is unlikely, in the immortal words of Katy Perry, “to open one (door) that leads you to the perfect road” it does suggest that the adverse and therapeutic effect of pemetrexed may be genetically linked, so hang on in there.

WHITE NOISE

Fireworks on the 5th of November result in a late-night cacophony of explosive noise that impacts on both sleep quality and quantity. However, there is increasing evidence that white noise could improve sleep by masking loud sounds and reducing the difference between background

levels and peak sounds. Although drug induced sleep in the ICU serves a different purpose, it has postulated that light sedation has improved benefit in terms of clinical outcomes. Aitken and colleagues (see page 1089) performed a systematic review and meta-analysis to determine the effect of the depth of sedation on intensive care mortality, duration of mechanical ventilation, and other clinically important outcomes. From the 25 studies (8 RCTs and 18 cohort studies), lighter sedation in the cohort studies improved time to extubation, intensive care and hospital length of stay and ventilator-associated pneumonia but no effect on hospital mortality, delirium or adverse events. There was no such effect observed in the RCTs. The evidence to support light sedation is limited and perhaps we should not consider light sedation with white noise for our ICU patients.

SUGAR AND SPICE...

Exploding fireworks are made up of all things not nice. Toxic elements such as gun powder, heavy metals, ozone, carbon dioxide, nitric oxide and sulphur dioxide are required. Gupta and colleagues (see page 1142) used the nitric oxide component of the firework (thankfully a non-flammable gas, although it accelerates combustion) and observed that inhaled nitric oxide improved partial pressure of oxygen by 1.7kPa, without deleterious effects on cardiac output, in 26 pre-transplant liver patients. Perhaps nitric oxide can be considered off the naughty list after all, although the mechanism of action in hepatopulmonary syndrome needs more work.

BEWARE OF WHAT LIES IN CAVITIES

Guy Fawkes and his associates hid the explosives in an undercroft (cavity) beneath parliament. The destructive contents of a pulmonary cavity are described in a case based discussion (see page 1163) from Abbas and colleagues.



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