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# Highlights from this issue

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*The Triumvirate*

## THE OLD MAN AND THE CCR2

Idiopathic Pulmonary Fibrosis is a disease that affects predominantly elderly men and, at the current time, their fate, much like that of Santiago the marlin fisherman, is sealed on the first page. Similarly the sea and the immune system are complex and often hostile environments. To better understand the role of CCR2 signalling in pulmonary fibrosis Milger and colleagues performed studies in experimental models of fibrosis and measured levels of CCR2<sup>+</sup> lymphocytes in patients with pulmonary fibrosis (see page 1007). While they found high levels of CCR2<sup>+</sup> cells in patients with IPF, the studies in models of disease suggest these lymphocytes have protective functions in developing lung fibrosis. While Santiago tried valiantly to kill all the sharks feeding on his fish, the consequence, should he have succeeded, may not have delivered the outcome he hoped for, and we should take heed before trying to therapeutically destroy CCR2<sup>+</sup> CD<sup>+</sup> T cells.

## FOR WHOM THE BELL TOLLS

Lung transplant is often the only treatment for people with progressively fatal diseases although it is unlikely to have helped Robert Jordan in his quest against Franco's Fascists. However, before his operation to blow up a bridge, Pilar read his palm and foresaw his demise. Faust and colleagues adopt a more scientific approach to predicting survival following operations to transplant lungs (see page 1052). They measured donor telomere length and found shorter telomeres were associated with increased chronic lung allograft dysfunction, a major risk factor for death post transplant. While Pilar refused to tell Mr Jordan her prediction, Faust and colleagues suggest telomere length could be used to stratify for whom the bell tolls post lung transplant?

## A FAREWELL TO ARMS

Ernest Hemingway was not, strictly speaking, volunteering for a study when he suffered severe bomb inflicted injuries as a Red Cross volunteer in Italy in 1918. However, it took him 6 months to recover and his recollections were famously immortalised in his semi-autobiographical novel *A Farewell to Arms*. While less romantic, the study by Hamid *et al* tests the hypothesis that aspirin reduces inflammation in human models of ARDS, a major consequence of severe trauma (see page 971). They undertook a placebo-controlled study using two doses of aspirin measuring a variety of endpoints in 33 healthy volunteers as well as EVLP analysis from donor human lungs. These preliminary data suggested that aspirin at either low or high dose was able to reduce neutrophilia and tissue

damage. While these intriguing results need to be confirmed in a clinical trial, one can but wonder whether, had aspirin been considered in 1918, which of the 47 endings Hemingway considered for his novel, he would have chosen?

## ON THE COST OF (WAR AND) INFLATION

War and hyperinflation are two predisposing factors that promote the development of ARDS, and were famously linked by Hemmingway when he stated that "The first panacea for a mismanaged nation is inflation of the currency; the second is war. Both bring a temporary prosperity; both bring a permanent ruin. But both are the refuge of political and economic opportunists." Similarly inflation of the lung can bring temporary relief but permanent ruin if ARDS develops. In the study by Cereda *et al* the investigators use inspiratory and expiratory CT scans to develop a metric of injurious inflation (see page 981). Using both an experimental model in rats and patients with ARDS they were able to identify areas of 'unstable' inflation, which predicted the development of ARDS. It is hoped that using this imaging strategy will avoid mismanagement, ensure that ruin is temporary but that prosperity is permanent.

## OPIUM SMOKING THEN AND NOW...

Set in the cathedral town of 'Cloisterham', 'The Mystery of Edwin Drood' was Dickens' last novel and he died before completing it. The eponymous hero disappears in suspicious circumstances. The villain of the story is John Jasper - choirmaster and smoker of opium. The epidemiological study of opium smoking reported by Rahmati and colleagues comes not from an English cathedral town but from Iran (Editors' choice, see page 1028). The Golestan Cohort Study (northeastern Iran) included over 8000 opium smokers. The authors conclude that smoking opium is associated with a more than threefold increase in the risk of respiratory disease (malignant and non-malignant). A greater effect is seen with greater exposure. So, as John Jasper '...lights his pipe, and delivers himself to the Spectres it invokes at midnight...' he should add to these Spectres the increased risk of respiratory disease.

## A TALE OF TWO CONTINENTS

Although not necessarily a 'Tale of Two Cities', Peter Castaldi and colleagues report the tale of two continents (see page 998). The authors investigated 10 cohorts of COPD patients in North America and Europe to assess the patterns and clustering of COPD-related characteristics. 17, 146 patients with COPD were enrolled and common factors, such as FEV1, FEV1/FVC, FVC, body mass index, Modified

Medical Research Council score, asthma and cardiovascular comorbid disease, were identified. Interestingly, identical clustering analyses across multiple COPD cohorts showed only modest reproducibility. The authors suggest that COPD heterogeneity is characterised by continuous disease traits coexisting within the same individual rather than separate identifiable COPD subtypes. Doctor Manette possibly considered all of this during his time in the Bastille...

## DICKENS TWINS

Charles and Ned Cheeryble were twin brothers and the kind-hearted employers of Nicholas Nickleby. They may have been considered eligible for the Nordic Twin Study of Cancer if it was not that they lived in London. Jacob Hjelmborg and colleagues led the Nordic study, the aim of which was to determine the genetic and environmental causes of lung cancer (see page 1021). 43 512 monozygotic (MZ) and 71 895 same sex dizygotic (DZ) twins were enrolled with smoking history collected before lung cancer diagnosis. During 28.5 years of follow-up, 30 MZ and 28 DZ pairs were observed to develop lung cancer. All were current smokers at baseline. Interestingly, among ever smokers the concordance of lung cancer was increased. The relative recurrence risk decreased with age for MZ but was the same for DZ pairs with inheritable risk of lung cancer at 41% for current smokers and 37% for ever smokers. We would have to go back in fictional history to check Charles' and Ned's smoking history and outcome, but it is fair to say that discordant pair analysis confirms that smoking does cause lung cancer.

## PLASTIC FANTASTIC...

Is it an octopus or perhaps some bizarre shoreline crustacean? See page 1056 of this month's Thorax to test your diagnostic skills (or knowledge of marine biology)?



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