



Highlights from this issue

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The Triumvirate

As we write this month's *Airwaves* citizens, scientists and politicians around the world are preparing for a second wave of COVID-19 cases while hoping their fears are groundless. This month's airwaves takes the "second wave" as its theme and we explore reappearances and recurrences - both welcome and unwelcome. We bring you chimpanzees, off-target effects and dental extractions.

CHIMPANZEES, RSV AND CEACAM3

As the nights draw in and the months of November, December and January approach, every paediatrician knows that the season for respiratory syncytial virus (RSV) is approaching. RSV, originally named "chimpanzee coryza agent", causes regular winter epidemics, resulting in the hospitalisation of around 2% of infants with acute bronchiolitis as well as episodes of wheezing in older children. One of the enduring puzzles of RSV is why some children have a more severe respiratory illness than others. In this month's *Thorax*, Tsai and colleagues (*see page 725*) describe a meta-analysis to investigate differentially expressed genes (DEGs) of RSV infection from Gene Expression Omnibus (GEO) datasets. Using their findings from both a training and a validation dataset, the authors report that CEACAM3 mRNA expression is reduced in subjects experiencing asthma exacerbations. CEACAM3 (Carcinoembryonic antigen-related cell adhesion molecule 3) is an adhesion molecule which is used by pathogens to bind and invade host cells. We all hope that coronavirus does not follow the example of RSV and go from a second wave to a regular season. Sixty-five years after the discovery of RSV, a vaccine for RSV still proves elusive. Let's hope that developing a vaccine to coronavirus does not become an equally intractable problem.

OFF-TARGET EFFECTS OF COVID-19 AND TOBRAMYCIN

In the UK, senior doctors have expressed concerns that the Autumn will bring intense pressure on the National Health Service. Part of the problem could be winter infections such as a second wave of COVID-19 and seasonal influenza. However there are also the off-target effects of COVID-19: the backlog of procedures delayed by the pandemic lockdown (particularly for patients with cancer). Off-target effects of inhaled tobramycin are discussed in this month's journal. This antibiotic is widely used for chronic pulmonary infection with *Pseudomonas aeruginosa* in cystic fibrosis (CF). However, there is a disconnect between the benefits of inhaled tobramycin (reduced mortality) and its proposed mechanism (reducing the quantity of *P. aeruginosa* in sputum). Nelson *et al* (*see page 780*)

conducted a careful study of the sputum microbiota in 30 patients with CF receiving inhaled dry powder tobramycin on a 28 day cycle. The biggest change in the microbiota was seen in the first week and primarily affected non-dominant, low abundance, taxa: an off target effect. Back in the world of the coronavirus pandemic, the off-target effects of COVID-19 may yet be more lethal than the infection itself.

'THE GREATEST ERROR IS NOT TO MOVE'

This was a statement from Mike Ryan, WHO health emergencies programme executive director, on March 16. Heeding this advice, it was during the early phase of the pandemic, clinicians moved quickly to report patient characteristics and the response to treatments and the scientists focused on the pathophysiology of SARS-Cov-2 and identifying potential targets for future treatment. This observation science is important in all aspects of medicine and Marjan Kerkhof and colleagues (*see page 744*) used this approach to investigate the association between COPD exacerbations and lung function decline during maintenance therapy. Of 12178 COPD patients included in the study 74% were receiving ICS therapy. The authors observed that patients not receiving ICS with blood eosinophil level ≥ 350 cells/ μ L had greater decline in FEV1 after each exacerbation. This loss in lung function was reduced in those with $\text{BEC} \geq 350$ cells/ μ L currently treated with ICS. A more targeted approach to prevention of exacerbations using ICS in such patients may prevent excess loss of lung function. A similar approach to Sars-COV-2 infection is clearly warranted and we must continue to follow Dr Ryan's sage words.

ENHANCING CIVILITY BY REDUCING ZINC

Fang Fang wrote in her Wuhan Diaries that "the true test of a country's level of civility... is how you treat the weakest and most vulnerable members of your society." Min Zhou and colleagues (*see page 771*) present data from their own research diaries which details the association between urinary zinc and lung function over a 3 year period in 3917 adults from Wuhan. The authors showed that urinary zinc was associated with a restrictive ventilation defect with systemic inflammation as an underlying mechanism for the lung damage. To protect our weakest and most vulnerable in society and enhance civility, we must protect them from both infectious and non-infectious toxic agents.

SAY HELLO, WAVE GOODBYE

Many of us have had the opportunity to say hello to COVID-19 and we are all desperate to

say goodbye to it to. However, this was surely not Soft Cell's intended message. Similarly, the intended target of nintedanib was almost certainly not the Mast Cell, however this not so Soft Cell does have a role in pulmonary fibrosis which is often forgotten. However, Dr Overed-Sayer and colleagues (*see page 754*) identified high numbers of Mast Cells in the lungs of patients with IPF and demonstrated the presence of Mast Cell-fibroblast cross talk. They demonstrated that nintedanib, but not pirfenidone, could inhibit Mast Cell survival, growth and signalling and reduced mast cell accumulation and fibrosis in rats. So, as we stand at the door of the Pink Flamingo crying in the rain, maybe we need to make sure the Mast Cell is not forgotten again.

THE POLICY OF TRUTH

As eye tests in Barnard Castle demonstrate, people's discrete choices don't always lend themselves to a policy of truth. Understanding people's discrete choices may however help design better policies and treatments. Tervonen and colleagues (*see page 735*) provided almost 2000 patients with airways disease some discrete choice about inhaled medication and found the feature most valued by patients was a short onset of action! As Depeche Mode might have said "It's not too late to change events, it is time to face the consequence" of asking questions about inhaled therapy!

SELF-EXTRACTION OF TEETH: FROM CORONAVIRUS TO FUSOBACTERIUM NECROPHORUM

Self-extraction of teeth has been practiced by some desperate patients during lockdown but beware the death-bearing fusobacterium! The teaser image shown here is laid bare on *page 815*.



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