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RCEM COVID-19 CPD Journal club
Weekly top 5 papers
Dr Charles Reynard, Dr Anisa Jafar, Dr Mina Naguib, Professor Simon Carley and the RCEM COVID-19 CPD team

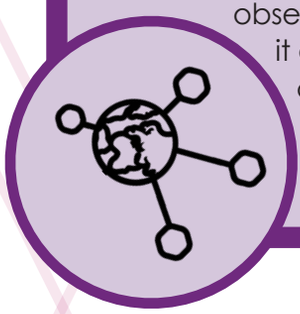
This week's flash update is the distilled outputs of a global output of more than 1,700 papers a week. Here we present the top 5 papers that deserve your attention. If you have the head-space for ten more hot-off-the-press papers check out the Director's Cut. If an interactive live journal club captures your interest then checkout the webinar Tuesdays at 11:00, click here to register.

The following papers have been split into 3 categories that will allow you to focus on those that are most vital to your practice.

- Worth a peek: interesting, but not yet ready for prime time
- Head Turner: new concepts
- Game Changer: this paper should change practice

International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC) COVID-19 Report: 27 April 2020 from ISARIC [1]
Topic: Epidemiology
Rating: Head turner
Scout: Professor Simon Carley

The ISARIC project is a pre-Covid project designed to provide surveillance on respiratory diseases. This is the first report from ISARIC during Covid-19 and reports on 27,424 individuals from 278 sites across 30 countries. They applied a 14-day rule (as that group does not have a reliable outcome yet), and so there are 19,463 patients in the main data set. There is a huge amount of observational data here, and you'll need some time to get through it all. Key points for me were the high mortality amongst admitted patients (20%) and very high mortality amongst patients admitted to the ICU at least a third of them die (and this number may rise as many are still in hospital/ ICU at the time of reporting). Age seems to be the most obvious factor in prognosis with a mortality of 78% in those aged over 70 at the time of admission.



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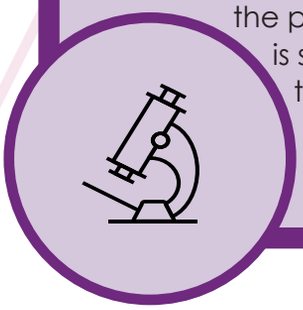
Hyperinflammatory shock in 6 children by Riphagen et al [2]
Topic: Pathophysiology
Rating: Head turner
Scout: Dr Mina Naguib

Thus far, one of the few sources of reprieve in the COVID-19 pandemic is that children have largely been spared serious disease. A myriad of reasons have been hypothesised; from a lack of ACE-2 receptor expression, to lacking co-morbidities associated with increased mortality. This case series sheds light on a worrying trend. Eight children were identified by the South Thames Retrieval Service in London to have Kawasaki disease shock syndrome; a significant jump from the one or two they usually see. Presentation involved rash, refractory fever, third spacing, and predominance of gastrointestinal symptoms. Biochemical aberrations included elevated CRP, procalcitonin, ferritin, and D-dimer. All developed vasoplegic shock, indicative of an underlying cytokine storm - consistent with that seen in COVID-19. Mechanical ventilation was due to cardiovascular shock rather than respiratory failure, and both inotropic and vasopressor support was required. One, sadly, died after attempted resuscitation on ECMO. All were treated with immunoglobulin alongside usual care. Interestingly, they reflected some of the higher-risk patterns seen in adults; a majority were male (five), Afro-Caribbean (six), and above the 75th centile for weight (seven). However, given all tested negative, it is possible that these demographic associations go beyond SARS-CoV-2, representing wider socioethnographic predispositions which the pandemic has brought to light and should be explored. Overall numbers are low; we cannot yet make the jump from correlation to causation, and regardless, we lack any cure for such patients. However, awareness of possible complications is important in the assessment of febrile children.

SARS-CoV-2 viral spike G614 mutation exhibits higher case fatality rate by Becerra-Flores et al [3]
Topic: Pathophysiology
Rating: Worth a peek
Scout: Dr Anisa Jafar

Viruses mutate and virulence fluctuates, but has this happened with the novel coronavirus? It has been found that a mutation on the viral envelope spike protein, which is more commonly found in European variants than those infecting Chinese patients, coincides with a higher case fatality rate. This was based on regional case fatality rates being compared to the prevalence of the particular mutation (whose mechanism of increased fatality is suggested to be immunologic). The authors are tentative in conclusions as there are lots of confounding factors to consider. Interestingly UK data was not included in the standard linear regression due to "unusually low number of cases due to an unusually low level of testing/diagnosis and an unusually high level of death reporting" which is a story of its own...



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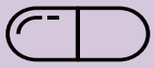
The COVID-19 vaccine development landscape by Le et al [4]
Topic: Treatment
Rating: Head Turner
Scout: Dr Charles Reynard

The way out of this pandemic is through immunity; for this we need a vaccine. Le et al map out the status of development globally. There are a huge 115 total candidates, 78 confirmed as active, 73 are at preclinical stages but we only need one to work. The authors comment on the range of technologies being assessed, the heterogeneity is a strength, not only increasing the chances of success but also allowing the vaccine to be better matched to different populations such as the elderly. There are five candidates currently in phase I clinical trials, excluding the University of Oxford's efforts. Two are from the United States and three from China, vaccine types range from mRNA to artificial antigen-presenting cells. If the logistical challenges of mass production can be overcome, the authors speculate that it may be ready for early 2021. Vaccines used to take 10 years to develop, we might be about to get them in just over a year.



Occurrence, prevention, and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-analysis by Kisely et al [5]
Topic: Epidemiology
Rating: Worth a peek
Scout: Dr Anisa Jafar

Since the beginning of the pandemic, there has been a significant response from employers and training bodies to provide psychological support to healthcare staff. This timely study looks at the available literature on those healthcare workers involved in outbreaks and finds a greater level of acute and post-traumatic stress as compared to those considered to be lower risk controls. It is useful to be aware of specific risk factors in colleagues which include younger age, being more junior, having dependent children at home, having family who have been infected, enduring longer quarantine and having poorer practical support. We must also remember that stigma plays a role, and therefore being aware of this in the workplace is important. To mitigate these risk factors, potentially useful interventions include: clear communication, access to appropriate PPE, ensuring adequate rest and access to both practical and psychological support.

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In summary

ISARIC describe the largest international cohort of COVID-19 cases [1]
Riphagen et al warned us of a potential new paediatric presentation [2]
Becerra-Flores et al correlate a mutation with increased virulence [3]
Thanh Le et al map the vaccines that might return normality [4]
Kisely et al emphasised the psychological protective measures for staff [5]

References

1) International Severe Acute Respiratory and Emerging Infections Consortium (ISARIC), COVID-19 Report: 20 April 2020, https://media.tghn.org/medialibrary/2020/04/ISARIC_Data_Platform_COVID-19_Report_20APR20.pdf [accessed 10/05/2020]

2) Riphagen, S. Gomez, X. Gonzalez-Martinez, C. Wilkinson, N. Theocharis, P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. Correspondence. doi.org/10.1016/ S0140-6736(20)31094-1

3) Becerra-Flores, M. and Cardozo, T. (2020), SARS-CoV-2 viral spike G614 mutation exhibits higher case fatality rate. Int J Clin Pract. Accepted Author Manuscript. doi:10.1111/ijcp.13525

4) Le, T.T., Andreadakis, Z., Kumar, A., Roman, R.G., Tollefsen, S., Saville, M. and Mayhew, S., 2020. The COVID-19 vaccine development landscape. Nat Rev Drug Discov.

5) Kisely, S., Warren, N., McMahon, L., Dalais, C., Henry, I. and Siskind, D., 2020. Occurrence, prevention, and management of the psychological effects of emerging virus outbreaks on healthcare workers: rapid review and meta-analysis. bmj, 369.

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