RCPE: John W. Ballantyne Lecture: "From genes to therapy in COVID-19 – a template for translational genomics in critical care"

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"From genes to therapy in COVID-19 – a template for translational genomics in critical care" Dr Kenneth Baillie

Q. Why has there been a spectacular failure in developing any herd immunity against the virus? Do you foresee a substantial burden of morbidity related to vaccine related adverse effects in the near future?

A. I'm not an epidemiologist so I'll be careful not to say too much on this. I don't think we've had enough vaccination yet to reach the threshold for herd immunity. Vaccine side effects are tragic for those who are affected by them, but they are thankfully very rare so at a population level I don't think a substantial burden of disease is likely.

Q. Is liver disease as a risk factor related to poor IgM production or other identified cause?

A. That's an interesting idea and plausible, along with many other consequences of chronic liver disease for immune function. I only used neutralising IgM in my talk as an example of something that is probably, on balance, beneficial.

Q. Do the current multi centre research studies include children's multi system response pattern to SARS2 corona virus? Does the vasculitis pattern mimic Henoch Schonlein syndrome and link to the antiplatelet conditions?

A. Yes we are actively recruiting patients with PIMS-TS UK-wide and sharing data and samples with researchers who can help understand that condition. With regard to vasculitis, I don't know.

Q. As the long term effects of SARS COV-2 infection become more evident, Is there any scientific basis to suggest that these effects may be genetically determined?

A. Yes I think there are good reasons to predict that is true – PHOSP Covid study will hopefully answer this.

Q. Is sufficient genetic and clinical data available from all patient subgroups in RECOVERY that can be used to look for genetic variation in patient response to Dex (within and beyond effects on the immune system)? Might this help predict patient-specific value of GCs in a range of conditions?

A. Great question – the straight answer is sadly not, but we're linking the data to do what we can with this.

Q. Dimethyl fumarate also activates the nrf2 anti-inflammatory pathway - could this be beneficial?

A. Any anti-inflammatory effect could certainly be a plausible mechanism of action. When we choose genes to predict drug effects we have to be quite stringent about including only those genes where we have good reason to expect (perhaps hope is a better word) that a genetic effect might predict the effect of treatment. For DMF, rightly or wrongly, we didn't include NRF2, but I appreciate the suggestion and I'll have a look at it later.