Comment

SARS coronavirus: in context

The rapid emergence and spread of an apparently untreatable new infectious disease – SARS – has caused consternation around the world. The cause was quickly identified as a coronavirus. Dave Cavanagh counsels that in developing strategies to deal with the SARS virus the medical profession has much to learn from experience of coronaviruses gained in a veterinary context.

The pace of progress with SARS coronavirus has been – is – breathtaking. From the index case in Hong Kong to the sequence of the whole genome (29·7 kb) took only 2 months. The structural proteins of the SARS virus have only 20–40 % identity with those in the previously known three coronavirus groups, sufficient to warrant that it be assigned to a new group, number 4. Novel though the virus is, we should look back at what we have learned with coronaviruses of veterinary importance whilst rushing forwards to combat SARS coronavirus.

Virus has been isolated in Guangdong Province from apparently healthy Himalayan palm civet cats and raccoon dogs, the virus' surface spike protein having 99 % identity to that of the human SARS isolates. Should we be surprised at the existence of such similar coronaviruses in several mammalian species? No. The fastidiousness exhibited by many coronaviruses when it comes to growth in the laboratory is not reflected *in vivo*. For example, the Group 1 Canine coronavirus can infect pigs, albeit asymptomatically. This virus, and porcine transmissible gastroenteritis coronavirus and feline coronavirus have > 90 % identity in their spike protein, a determinant of host range and pathogenicity. The Group 2 bovine coronavirus has > 98 % spike protein identity with a virus isolated from a child with diarrhoea, and 96 % identity with the recently discovered Group 2 respiratory coronavirus. Turkeys experimentally infected with bovine coronavirus replicated the virus, resulting in enteritis. The Group 3 coronaviruses from chickens, turkeys and pheasants differ from each other to an extent no greater than that exhibited by serotypes of the chicken coronavirus, infectious bronchitis virus (IBV).

One fear that has been voiced regarding SARS, even supposing that transmission ceases over the next few months and the link with the reservoir is not reconnected, is that it might survive in asymptomatic carriers. After inoculation with IBV at one day of age, chickens excreted virus again, detected in respiratory and faecal swabs, at 4 months of age. The trigger, it would seem, was the stress of coming into lay. About 10 % of cats become persistently infected, asymptomatic chronic shedders (for more than a year) of feline coronavirus following natural infection.

It should really come as no surprise that the SARS virus has been recovered from faeces, and for a longer period than from the respiratory tract. This happens in chickens with IBV (which is able to replicate in many alimentary tract tissues, asymptomatically, and in oviduct and kidney, sometimes causing lethal nephritis) and other coronaviruses, including human ones. If it is demonstrated that the SARS virus is growing and directly causing pathology in both the respiratory tract and the gut then that would be a first; given strains of coronaviruses, although possibly growing in both regions, cause disease in one rather than both areas.

A feature of coronaviruses that prompted speculation in the early SARS days was recombination. This has happened frequently with IBV, whilst type II feline coronaviruses are recombinants of canine and feline type I coronaviruses. Might SARS coronavirus recombine with human coronaviruses, of which there are species in coronavirus groups 1 and 2? Fortunately, the dozen or so coronaviruses of which we are aware indicate that recombination has not occurred between viruses of different groups, only within a group.

The coronavirus surface spike protein (S) is the most variable. Is the SARS virus S protein likely to mutate in man? One would imagine so, if it were to establish itself in the human community. This might be partly in response to immunity, and partly, perhaps, as it adapted to its new host, e.g. in respect of receptor specificity, as observed with murine coronavirus. Isolates of the 229E species of human coronavirus differ by 7 % in the amino-terminal (S1) half of S. Avian IBV strains differing by less than 5 % of their S1 amino acids can behave as different serotypes and can exhibit poor cross-protection, a concern for vaccine developers. There is a wealth of experience from the development of coronavirus vaccines for chickens, cattle, pigs, cats and dogs – though not all of it is encouraging. On the whole, inactivated vaccines have induced protection only poorly. Although widely used in egg-laying chickens, their purpose is to boost immunity induced by prior application of live attenuated vaccine. The spike protein alone can induce immunity, most recently demonstrated by expression from a fowl adenovirus; a single oral application protected 90–100 % of chickens. Whilst the spotlight is likely to be on the spike protein, it should not be overlooked that the internal nucleoprotein has been reported to induce protective immunity. The WHO has recommended that SARS vaccines be developed. The quickest and probably safest to develop would be an inactivated or subunit vaccine. Even if its immunogenicity were to prove less than desired, it might induce protection against the worst outcome of infection – life-threatening pneumonia.

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Further reading

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