Animal coronaviruses: what can they teach us about the severe acute respiratory syndrome?

L.J. Saif

Food Animal Health Research Program, Ohio Agricultural Research & Development Center (OARDC), Ohio State University, Wooster, OH 44691, United States of America

Summary

In 2002, a new coronavirus (CoV) emerged in the People’s Republic of China, associated with a severe acute respiratory syndrome (SARS) and mortality in humans. The epidemic rapidly spread throughout the world before being contained in 2003, although sporadic cases occurred thereafter in Asia. The virus is thought to be of zoonotic origin from a wild animal reservoir (Himalayan palm civets \( \textit{Paguma larvata} \) are suspected), but the definitive host is unknown. There is concern about possible transmission of SARS CoV to rodents or domestic cats (as proven experimentally) with perpetuation of the disease in these species. In livestock and poultry, CoVs are recognised causes of enteric and respiratory infections that are often fatal in young animals. Although the emergence of SARS surprised the medical community, veterinary coronavirologists had previously isolated CoVs from wildlife and documented their interspecies transmission to livestock. Furthermore, scientists were aware of compelling evidence pointing to the emergence of new CoV strains and the mutation of existing strains resulting in new disease syndromes in animals, but the evolution and disease impact of CoVs was not widely appreciated before SARS. This review focuses on the comparative pathogenesis of CoV infections, including the factors that accentuate CoV respiratory disease, with emphasis on livestock and poultry. The goal is to provide insights into CoV transmission and disease mechanisms that could potentially be applicable to SARS, highlighting the contributions of veterinary scientists to this area of study. Such examples illustrate the need for communication and collaboration between the veterinary and medical communities to understand and control emerging zoonotic diseases of the 21st Century.

Keywords


Introduction and chronology of severe acute respiratory syndrome

Severe acute respiratory syndrome (SARS) emerged in Guangdong Province, the People’s Republic of China, in 2002 and within months, spread globally. A clinically ill physician from the People’s Republic of China sparked a super-sparing event at the Metropole Hotel in Hong Kong in February 2003. This episode triggered the spread of SARS to Vietnam, Singapore and Canada, thereby affecting both developing countries lacking a good public health infrastructure and developed countries with modern public health systems. The rapid global spread of a new disease of unknown aetiology with no available diagnostic tests or treatments resulted in the World Health...
Organization (WHO) issuing the most stringent travel advisory in its history in March 2003 (53).

Lacking the research and investigative capacity to control the epidemic, the WHO elicited public health service partners from countries such as the United States of America (USA) (52), the United Kingdom, the Netherlands, Germany and France. The Global Alert and Response Network of the WHO, which includes a virtual network of eleven leading and well-equipped infectious disease laboratories in nine countries, previously established to address mainly influenza outbreaks, was instrumental in spearheading laboratory efforts (53). These laboratories were connected by secure websites and teleconferences to identify the causative agent of SARS, develop diagnostic tests and collect and analyse clinical and epidemiological data on the disease. Similarly, the USA Centers for Disease Control and Prevention (CDC) established other virtual interdisciplinary teams in the USA, eliciting help from both medical and veterinary coronavirus (CoV) experts (52). Both the WHO and the USA CDC provided factual information on SARS through updated websites, hotlines and frequent presentations to the news media to educate the public.

In spite of recent rapid advances in molecular virology and biotechnology, classical virology methods (electron microscopy, cell culture isolation, immunofluorescence) were instrumental in first identifying this unknown agent as a CoV, in adapting the organism to cell culture and then in developing initial assays for its detection and for antibody detection (47, 65, 66). Thus, exceptional international laboratory efforts led to the rapid genetic sequencing and identification of a new CoV as the causative agent of SARS by April 2003, only about one month after the initial WHO global alert (18, 47, 55, 66, 68, 69). Although vaccines or antivirals to prevent or control SARS infections were lacking, the epidemic was countered by classical infection control and containment methods. On 5 July 2003, the WHO reported that the global SARS epidemic was contained after over 8,000 cases and about 800 deaths in 29 countries. However, since then and into 2004, new cases of SARS have emerged sporadically in Singapore, Taiwan and the People’s Republic of China, most of which were associated with laboratory-acquired exposure to the disease. These cases did not spread by contact, with the exception of the most recent cases (March/April 2004) from the People’s Republic of China in which multiple contacts were infected and at least one died. The laboratory-acquired exposure to SARS CoV demonstrates that adherence to the strict laboratory safety procedures required for work with Biosafety Level 3 (BSL-3) pathogens is vital. The widespread distribution of SARS CoV samples in international laboratories highlights the need for vigilance in the inventory and use of these virus stocks. In addition, adequate laboratory supervision and facilities are required to avoid future laboratory-acquired infections as a possible source of a new SARS epidemic.

In summary, the unprecedented SARS super-spreading events precipitated the transmission of the disease, even within modern, well-equipped hospital environments (79), secondarily infecting and incapacitating health care workers and compromising the health care system. International air travel also facilitated the rapid worldwide spread of the disease (64, 100), thereby contributing to the global SARS epidemic. Countries such as Vietnam, which rapidly implemented and enforced control measures and sought international guidance, were able to effectively contain the epidemic. Other countries with delayed responses or a lack of transparency in reporting disease cases, such as the People’s Republic of China, experienced a more devastating and widespread epidemic (41). Finally, implementation of effective surveillance and control measures, definitive identification of the causative agent of SARS as a CoV and containment of the epidemic can largely be attributed to an unparalleled level of global cooperation in combating the newly emerged global disease.

The origin of severe acute respiratory syndrome: is severe acute respiratory syndrome a zoonosis?

Wildlife reservoirs

Approximately 75% of emerging infectious diseases are of zoonotic origin (87). Epidemiological and genetic data have been presented postulating that SARS evolved from a wild animal host, but no definitive evidence yet exists to prove this hypothesis. Epidemiological observations supporting the theory include the following: the index patient in Guangxi Province was a wild animal trader, two of seven index patients were restaurant chefs, food handlers were over-represented in early-onset cases with no contact history and early-onset patients were more likely to live near agricultural live animal markets (but not on or near farms) (101). This temporal and spatial clustering of index cases is consistent with the classical emergence of new agents from animal reservoirs.

Based on genetic and antigenic analysis, CoVs isolated from two clinically normal wild animal species (Himalayan palm civets, also referred to as masked palm civets or civet cats [Paguma larvata] and a raccoon dog [Nyctereutes procyonoides]) from wild animal markets in Shenzhen, the People’s Republic of China, have been assigned as members of the new SARS CoV group (24). All
the animal SARS CoV isolates possessed a 29 nucleotide sequence not found in most human isolates. Furthermore, the highest IgG antibody titres to SARS CoV were observed in traders of masked palm civets (72.7%) compared to traders of all live animals (13%) and healthy controls (1.2%) (8). However, the reservoir for SARS is still unknown and whether civet cats transmitted SARS CoV to humans or vice versa is undefined. Nevertheless, these data show that live animal markets (wet markets), which not only exist in the People’s Republic of China but throughout the world, are likely to have played a pivotal role in the emergence of SARS CoV. These live markets are acknowledged as breeding grounds for influenza virus outbreaks such as that which occurred in Hong Kong in February 2003. The unsanitary crowded conditions, co-mingling of or close contact among different species of animals and between animals and humans, the carryover of animals and the introduction of new animals and animal slaughter on the premises, with the dispersion of blood and secretions or offal, all foster an environment conducive to the emergence of new zoonotic diseases.

To date, only animals (mainly wild animals) in the SARS endemic areas have been tested for SARS CoV or antibodies; animals outside the endemic regions have not been tested. In addition, unless more stringent, but cumbersome (requiring BSL-3 facilities) virus neutralisation tests are conducted to confirm antibody seroprevalence in humans and animals, the results using intact SARS CoV or nucleocapsid (N) protein may be suspect. This is because of the documented antigenic cross-reactivity (enzyme-linked immunosorbent assay [ELISA], Western blots, immunofluorescence) observed between SARS CoV and animal group I CoVs (47) attributed to the N protein (26, 85). These issues hinder definitive analysis of animal reservoirs for SARS.

Between December 2003 and January 2004, several new cases of SARS re-emerged in humans in Guangdong Province, the People’s Republic of China (61). In most of these cases there was no link to known risk factors such as civet cats. Other postulated reservoirs including rats and cats were tested, but no final conclusions were drawn concerning the origin of this re-emergent case. However, based on sequence data suggesting that the re-emerged SARS strains were most similar to the civet cat isolates (61), the Government of the country ordered the destruction of large numbers of civet cats in the wildlife markets in the People’s Republic of China (98).

Other animal hosts or vectors for severe acute respiratory syndrome coronavirus

In addition to the Metropole Hotel outbreak, a second major outbreak of SARS occurred in 2003 in another location in Hong Kong at the Amoy Gardens apartments where 321 people were ultimately infected (9). This outbreak was clinically more severe and associated with more cases of diarrhoea (73%), higher intensive care unit admissions (32%) and mortality rates (13%) than the Metropole Hotel outbreak. Environmental factors (faulty sewage system) were postulated to have contributed to virus spread in the Amoy Gardens via aerosolised faecal material (39). However, an alternative hypothesis proposed was that an animal vector, such as roof rats, infected by the index patient, rapidly spread the disease among the 150 affected households (59). The authors further speculated that dual infections of rats with a rat CoV and SARS CoV may have been required to cause a productive SARS CoV infection in other rats. Indeed, CoV was detected in rodent droppings from the apartment complex, but since the rodents showed no disease, they were postulated to be mechanical viral vectors (39). It is also interesting to note that virus remnants were detected from throat or rectal swabs of five house cats, one of which had antibodies reactive with SARS CoV (59).

These data are consistent with SARS animal transmission studies which revealed that the respiratory tract of both mice and cats can be experimentally infected with SARS CoV, although infections in both species remained sub-clinical (56, 84). Moreover, both experimentally-infected cats and ferrets (Mustelo furo) transmitted virus to their contact-exposed cage mates (56). In the experimental animal transmission studies performed to date, only cynomolgous macaques (Macaca cynomolgus) (in some studies, but not others) and ferrets have been reported to develop variable disease expression after infection by SARS CoV, with SARS CoV shedding detected from nasal or pharyngeal swabs (22, 56). However, in neither species do the clinical signs completely mirror those of human SARS cases, which include the delayed onset of clinical disease and frequent diarrhoea with CoV shedding in stools (9, 47, 65, 68).

Attempts have been made to experimentally transmit SARS CoV to domestic livestock and poultry. Weingartl et al. (99) reported failure to transmit SARS CoV to six-week-old pigs that were seropositive for antibodies to porcine respiratory CoV (PRCV) (a group I animal CoV). However, the authors detected SARS CoV ribonucleic acid (RNA) in the blood by reverse transcriptase-polymerase chain reaction (RT-PCR) and noted that the pigs seroconverted with neutralising antibodies to SARS CoV. This study should be repeated in pigs seronegative for PRCV or other CoV antibodies because several investigators have noted that antibodies to PRCV and other animal group I CoVs cross-react with SARS CoV (26, 47, 85). Whether such pre-existing antibodies to group I CoV interfere with SARS CoV infection is unclear. Both Weingartl et al. (99) and Swayne et al. (86) also reported lack of SARS CoV transmission to specific pathogen-free chickens, turkeys, ducks or quail, although again some RT-PCR positive samples were detected among the exposed poultry.
Classification and evolution of severe acute respiratory syndrome and animal coronaviruses

Within months of the emergence and global spread of SARS, the causative agent was identified as a new CoV, only distantly related to known CoVs of humans or animals (18, 47, 55, 66, 68, 69). The existing animal CoVs comprise three groups based on high levels of antigenic or genetic relatedness of species within a group and lower relatedness among CoV species of the different groups (Table I). The SARS CoV and two wild animal SARS-like CoVs (24) have been tentatively assigned to group IV (Table I), based on phylogenetic analysis (18, 47, 55, 66, 68, 69). Alternatively, SARS CoVs may comprise a subgroup of group II CoVs based on rooted tree phylogenetic analysis (78). Additional phylogenetic analysis suggests that SARS CoV may have evolved from a distant recombination event between ancestral mammalian-like and avian-like parental CoV strains (80).

Although CoVs generally do not cross-react antigenically across groups, an interesting but unexplained observation is the cross-reactivity between several animal members of group I CoVs (transmissible gastroenteritis virus [TGEV], PRCV, feline infectious peritonitis virus [FIPV], canine coronavirus [CaCoV]) and SARS CoV (47), probably at the inner N protein level (26, 85). This suggests that although the genetic divergence between SARS CoV and other CoVs is high, a conserved epitope on the N protein may exist.

The emergence of SARS in healthy adults surprised the medical community, but veterinary coronavirologists have long recognised the potential of CoVs to produce lethal infections in young animals. Coronaviruses cause a broad spectrum of diseases in domestic and wild animals, poultry and rodents ranging from mild to severe enteric, respiratory or systemic disease, as well as minor colds in humans (7, 14, 15, 48, 51, 67, 70, 71, 72, 73, 74) (Table I). In livestock and poultry, CoVs cause mainly localised

### Table I

Animal coronaviruses: groups, target tissues and types of diseases

<table>
<thead>
<tr>
<th>Genetic group</th>
<th>Virus</th>
<th>Host</th>
<th>Disease/Infected tissue</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Human coronavirus-229E</td>
<td>Human</td>
<td>Respiratory</td>
</tr>
<tr>
<td></td>
<td>Transmissible gastrointestinal virus</td>
<td>Pig</td>
<td>x (upper)</td>
</tr>
<tr>
<td></td>
<td>Porcine respiratory coronavirus</td>
<td>Pig</td>
<td>x (upper)</td>
</tr>
<tr>
<td></td>
<td>Porcine epidemic diarrhoea virus</td>
<td>Pig</td>
<td>x (upper/lower)</td>
</tr>
<tr>
<td></td>
<td>Feline enteric coronavirus</td>
<td>Cat</td>
<td>x (SI)</td>
</tr>
<tr>
<td></td>
<td>Feline infectious peritonitis virus</td>
<td>Cat</td>
<td>x (upper)</td>
</tr>
<tr>
<td></td>
<td>Canine coronavirus</td>
<td>Dog</td>
<td>x (SI)</td>
</tr>
<tr>
<td></td>
<td>Rabbit coronavirus</td>
<td>Rabbit</td>
<td>x (SI)</td>
</tr>
<tr>
<td>II</td>
<td>Human coronavirus-OC43</td>
<td>Human</td>
<td>Respiratory</td>
</tr>
<tr>
<td></td>
<td>Mouse hepatitis virus</td>
<td>Mouse</td>
<td>x (upper)</td>
</tr>
<tr>
<td></td>
<td>Rat coronavirus (sialodocryadenitis)</td>
<td>Rat</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Haemagglutinating encephalitis virus</td>
<td>Pig</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Bovine coronavirus</td>
<td>Cattle</td>
<td>x (upper, lung)</td>
</tr>
<tr>
<td>III</td>
<td>Infectious bronchitis virus</td>
<td>Chicken</td>
<td>Respiratory</td>
</tr>
<tr>
<td></td>
<td>Turkey coronavirus</td>
<td>Turkey</td>
<td>x</td>
</tr>
<tr>
<td>IV?</td>
<td>Severe acute respiratory syndrome</td>
<td>Human</td>
<td>Respiratory</td>
</tr>
<tr>
<td></td>
<td>Civet cat coronavirus</td>
<td>Himalayan palm civet</td>
<td>x</td>
</tr>
<tr>
<td></td>
<td>Raccoon dog coronavirus</td>
<td>Raccoon dog</td>
<td>x</td>
</tr>
</tbody>
</table>

a) if no specific information is provided in parentheses, the entire respiratory/gastrointestinal tract is affected or the specific site of infection is not known
b) bovine coronavirus-like coronavirus from a child (102)
SI: small intestine
?: unknown or unreported
CNS: central nervous system
enteric or respiratory infections, although infectious bronchitis virus (IBV) of poultry causes both upper respiratory and systemic infections targeting the kidney (interstitial nephritis) and oviduct (decreased egg production) (7, 15). Coronaviruses are enveloped and possess four major proteins, i.e. the nucleocapsid (N) protein surrounding the RNA genome and three membrane proteins: the surface spike (S) glycoprotein, the membrane (M) glycoprotein and the envelope (E) protein (48). In addition, some group II CoVs can be distinguished from other CoVs by a surface haemagglutinin (HE), apparent as a shorter layer of projections on the virion surface compared to the longer S projections. Typical group I CoV particles (TGEV) that clearly display the surface S protein spikes are shown in the immune electron micrograph in Figure 1a, while Figure 1b presents group II CoV particles (bovine CoV [BCoV]) displaying the dense outer surface projections consisting of both the longer spike and shorter HE proteins. The S protein appears to be a critical determinant for viral attachment and fusion, cell tropism, species specificity, pathogenicity and induction of neutralising antibodies (1, 58, 75). The CoV genome consists of linear, single-stranded RNA of positive polarity and ranges from 28 kb-32 kb in length (48). For CoVs, the large size of the RNA genome, the replication strategy (nested set of sub-genomic RNAs) and the lack of proof-reading enzymes for RNA replication (analogous to other RNA viruses), all contribute to the recognised propensity of CoVs to recombine or mutate and for new strains to emerge.

Numerous examples illustrate the emergence of new animal CoV strains or the mutation of existing strains to produce natural variants or host range mutants. In the late 1970s and into the 1980s, a new group I porcine CoV, the porcine epidemic diarrhoea CoV (PEDV), appeared in Europe and rapidly spread to Asia (67). The disease resembled TGEV of swine and caused severe diarrhoea with major losses of piglets, before becoming enzootic in swine. The disease is still absent from the USA. It is interesting to note that PEDV is genetically more similar to human CoV-229E (229E) than to the other animal group I CoVs (19) and antibodies to PEDV fail to neutralise TGEV or PRCV, although a shared antigen in Western blot is reported (67). Unlike other group I CoVs, but like SARS CoV (47, 65), PEDV grows in Vero cells (38), which raises intriguing questions about the origin of the disease.

Alternatively, new CoV strains with altered tissue tropisms and virulence may also arise from existing strains. For example, the less virulent PRCV evolved as an S gene deletion mutant of the highly virulent TGEV (TGEV-V) (51, 74). Size differences in the 5' end S gene deletion region (621-681 nucleotides) of European versus American strains of PRCV support their independent origin on two continents within a similar time-frame (1980s). Deletion of this region (or in combination with deletions in open reading frame 3a) presumably accounted for altered tissue tropism from enteric to respiratory and reduced virulence of the PRCV strains (1).

Fig. 1
Electron micrograph showing immune electron microscopy of coronavirus particles
Coronaviruses were incubated with diluted hyperimmune antiserum to the respective coronavirus
Another example of an animal CoV that has evolved with altered tissue tropism and virulence from the less virulent feline enteric CoV (FCoV) (37, 97) is FIPV, a virulent systemic variant, which probably evolved as a persistent infection of cats with FCoV. This ability of certain CoVs to persist in their host also provides a longer opportunity for new mutants to be selected with altered tissue tropisms and virulence from among the viral RNA quasispecies (or swarm of viruses).

In addition, animal CoVs may acquire new genes via recombination, as demonstrated by the acquisition of an influenza C-like HE by BCoV or an ancestral CoV (2). Recombination among CoVs may also generate new strains with altered tissue or host tropisms. Experimental targeted recombination between feline and mouse S protein genes enables FCoV to infect mice (27). Recent phylogenetic analysis suggests that SARS CoV may have evolved from a distant past recombination event between mammalian-like and avian-like parent strains, with the S gene representing a mammalian (group I)-avian (group III) origin mosaic (80). This recognition that CoVs can further evolve in a host population to acquire new tissue tropisms or virulence via mutations or recombination suggests that similar events may occur if SARS CoV infections persist in humans.

**Interspecies transmission of coronaviruses**

The likelihood that SARS CoV is a zoonotic infection potentially transmitted from wild animals to humans is not unprecedented based on previous veterinary research on interspecies transmission of animal CoVs and wildlife reservoirs for CoV. For example, the group I porcine CoV (TGEV and PRCV), CaCoV and FCoV are antigenically and genetically closely related CoVs that appear to be host range mutants of an ancestral CoV (40, 57, 74). They cross-infect pigs, dogs and cats with variable disease expression and levels of cross-protection in the interspecies (winter) epidemics, although only virus excreted by dogs was infectious for pigs (74). Serological evidence for a CoV cross-reactive with TGEV was reported in minks (33). Wild birds (Sturnus vulgaris) and flies (Musca domestica) have been proposed as mechanical vectors for TGEV (74).

Captive wild ruminants from the USA including Sambar deer (Cervus unicolor), white-tailed deer (Odocoileus virginianus), waterbuck (Kobus ellipsiprymnus) and elk/wapiti (Cervus elaphus) harbour CoVs antigenically (cross-neutralising) closely related to BCoV (54, 89). The deer and waterbuck isolates were from animals with bloody diarrhoea resembling winter dysentery (WD) in cattle (89). They infected and caused diarrhoea in oronasally-inoculated gnotobiotic calves, thereby demonstrating that wild ruminants may serve as a reservoir for CoV strains transmissible to cattle. Unfortunately, these CoVs have not been sequenced to assess their genetic similarity to BCoV.

The promiscuousness of BCoV is evident by infection of dogs and humans by genetically similar (> 97% nt identity) CoV strains (21, 102). Bovine CoV can also experimentally infect and cause disease (diarrhoea) in phylogenetically diverse species such as avian hosts including baby turkeys, but not baby chicks (43). The latter study notably showed that BCoV-infected baby turkeys also transmitted the viruses to unexposed contact control birds. These data raise intriguing questions such as whether wild birds (e.g. wild turkeys) could also be a reservoir for CoVs transmissible to cattle or conversely, whether cattle (or ruminants) can transmit CoVs to wild birds or poultry. The reasons for the broad host range of BCoVs are unknown, but may be related to the presence of an HE on BCoV and the possible role of the protein in binding to diverse cell types.

Recent data suggest that SARS CoV may also have a broad host range in addition to humans. Genetically similar CoVs were isolated from civet cats and racoon dogs (24). Experimental infection with the SARS CoV caused clinical disease in macaques and ferrets and sub-clinical infection in cats (22, 56). In the latter two species, the SARS CoV was further transmitted to exposed contacts, demonstrating transmission within a new host species. Consequently, although previous data document the emergence of new animal CoV strains and the broad host range of several CoVs, the determinants for host range specificity among CoVs are undefined. In addition, little is understood about CoVs circulating in wildlife and relatively few animal CoV strains have been fully sequenced for comparative phylogenetic analysis to trace their evolutionary origins.

**Pathogenesis of enteric and respiratory coronaviruses in livestock and poultry**

Given that both pneumonia and diarrhoea occur in SARS patients, an understanding of the tissue tropisms and pathogenesis of respiratory and enteric animal CoVs should contribute to the understanding of similar parameters for SARS. Veterinary research on respiratory...
and enteric CoV infections in the natural animal host (swine, cattle, poultry) has provided important information on CoV disease pathogenesis, possible potentiators for increased disease severity and vaccine strategies potentially applicable to SARS CoV. Enteric CoV infections alone frequently cause fatal infections in young animals (73, 74). A notable difference between SARS CoV and most fatal animal CoV infections is the unexplained propensity of SARS to cause more severe disease in adults than children. However, in adult animals, respiratory CoV infections are more severe or often fatal when combined with other factors including stress and transport of animals (shipping fever of cattle), high exposure doses, aerosols, treatment with corticosteroids and other respiratory co-infections (viruses, bacteria, bacterial lipopolysaccharides). Similarly, such variables may influence the severity of SARS or contribute to the phenomenon of super-spreading of the disease. The following sections provide a perspective on the pathogenesis of selected group I, II and III enteric and respiratory CoV infections of livestock and poultry and the role of the various above co-factors in disease potentiation.

Group I transmissible gastroenteritis virus and porcine respiratory coronaviruses: comparative pathogenesis of enteric and respiratory infections

The emergence in the 1980s of a naturally occurring S gene deletion mutant of TGEV with an altered tissue tropism, the PRCV, provided a unique opportunity for comparative studies of these two CoVs in the same host species (pigs). Transmissible gastroenteritis virus and PRCV exemplify localised enteric (TGEV) or respiratory (PRCV) infections most severe in neonatal (less than two weeks) or young adult (one to three months) pigs, respectively (51, 74). Transmissible gastroenteritis virus targets small intestinal epithelial cells, leading to severe villous atrophy, malabsorptive diarrhoea and potentially fatal gastroenteritis (Table 1). The virus also infects the upper respiratory tract with transient nasal shedding (95), but infection or lesions in the lung are less common. In adults, TGEV is mild with transient diarrhoea or inappetence, but pregnant or lactating animals develop more severe clinical signs and agalactia (74).

Porcine respiratory coronavirus, an S gene deletion mutant of TGEV, presents altered tissue tropism (respiratory) and reduced virulence (51, 74). Like SARS, PRCV spreads by droplets and has a pronounced tropism for the lung, replicating to titres of $10^7$ to $10^8$ tissue cell infective dose (TCID)$_{50}$ and producing interstitial pneumonia affecting from 5% to as high as 60% of the lung (17, 28, 34, 51, 74). Although many uncomplicated PRCV infections are mild or sub-clinical, lung lesions are almost invariably present. Like SARS, clinical signs of PRCV include fever with variable degrees of dyspneoa, polynehoa, anorexia and lethargy, and some coughing and rhinitis (17, 28, 34, 51, 74). Further resembling SARS (13, 60), PRCV replicates in lung epithelial cells and antigen is detected in type I and II pneumocytes and alveolar macrophages. In the lungs, bronchiolar infiltration of mononuclear cells, lymphohistiocytic exudates and epithelial cell necrosis leads to interstitial pneumonia. Like SARS, porcine respiratory CoV induces transient viraemia with virus also detected from nasal swabs and in the tonsils and trachea (18, 47, 65). The disease further replicates in undefined cells in the intestinal lamina propria, but without inducing villous atrophy or diarrhoea and with limited faecal shedding (17, 28, 34, 74). Recently however, faecal isolates of PRCV were detected with consistent, minor (point mutations) changes in the S gene compared to nasal isolates from the same pig (16). No diarrhoea and limited faecal shedding were observed in pigs inoculated with the faecal PRCV isolates, suggesting their possible lack of intestinal stability. Such observations suggest the presence of CoV quasispecies in the host with some strains more adapted to the intestine, a potential corollary for the faecal shedding of SARS CoV (9, 18, 47, 65). Of further relevance to SARS, was the displacement of the TGEV-V infections by widespread dissemination of the clinically milder PRCV in Europe and the disappearance of PRCV from swine herds in summer with re-emergence of the disease in older pigs in winter (51, 74).

The emergence of PRCV also permitted comparative immunological studies of the immune responses and protection to the enteric TGEV versus the respiratory PRCV in the porcine host. Both passive immunity targeting maternal vaccination to provide passive antibodies in milk to suckling pigs and active immunity have been evaluated for the two CoVs. VanCott et al. (95, 96) and Brim et al. (3, 4) compared B cell (antibody-secreting cells [ASC]) and T cell (lymphoproliferative [LP] responses) immune responses to TGEV-V and PRCV in young pigs to assess the interrelationships among components of the common mucosal immune system (gut-associated lymphoid tissue [GALT] and bronchus-associated lymphoid tissue [BALT]) and induction of protective immunity to TGEV challenge. Only TGEV-V primed for high numbers of IgA ASC and LP responses in the intestine (GALT) and induced almost complete protection against TGEV challenge. A single PRCV infection of the respiratory tract (BALT) induced few IgA ASC and low LP responses in the intestine, but higher numbers of IgG ASC and higher LP responses in the lower respiratory tract (bronchial lymph nodes). Importantly, PRCV infection primed for anamnestic IgG and IgA intestinal antibody responses after TGEV challenge, leading to partial protection against diarrhoea and virus shedding. Similarly, a single infection of the respiratory tract of pregnant swine with PRCV induced only partial passive immunity to TGEV (5, 74), but interestingly, repeated PRCV infections of the mother induced higher IgA antibody responses in milk and protection rates to TGEV (76). This finding suggests that repeated PRCV exposure is needed to stimulate adequate
numbers of IgA memory cells in the intestine for subsequent transit to the mammary gland and secretion of protective levels of IgA antibodies in milk. These data show that compartmentalisation exists within the common immune system whereby stimulation at one mucosal site does not necessarily evoke complete reciprocity in immune responses or protection at other distant mucosal sites. The analogy to SARS is that respiratory vaccines for SARS may not completely prevent the diarrhoeal disease or faecal shedding if, like TGEV, SARS CoV also infects the intestine, thereby permitting the continued circulation of SARS CoV in a population.

**Group II bovine coronavirus: pneumoenteric infections**

The shedding of SARS in the faeces of many patients and the occurrence of SARS in 10% to 27% of patients (65), but with a higher percentage (73%) in the Amoy Gardens, Hong Kong outbreak (9) suggest that SARS may be pneumoenteric like BCoV. Bovine coronavirus causes three distinct clinical syndromes in cattle (73), i.e. calf diarrhoea (14, 73), WD with haemorrhagic diarrhoea in adults (70, 88, 90, 91) and respiratory infections in cattle of various ages including cattle with shipping fever (Table 1) (10, 14, 29, 30, 31, 32, 35, 36, 49, 50, 73, 81, 82, 83). The virus is ubiquitous in cattle worldwide based on BCoV antibody seroprevalence data. All BCoV isolates from both enteric and respiratory infections are antigenically similar, comprising a single serotype, but with two to three subtypes identified by neutralisation tests or using monoclonal antibodies (14, 29, 30, 73, 90). In addition, genetic differences (point mutations but not deletions) have been detected in the S gene, differentiating between enteric and respiratory isolates, including those from the same animal (12, 32). Nevertheless, inoculation of gnotobiotic or colostrum-deprived calves with calf diarrhoea, WD or respiratory BCoV strains led to both nasal and faecal CoV shedding and cross-protection against diarrhoea after challenge with a calf diarrhoea strain (11, 20). However, sub-clinical nasal and faecal virus shedding detected in calves challenged with the heterologous BCoV strains (11, 20) confirmed field studies showing that sub-clinically infected animals may be a reservoir for BCoV (35, 36). Cross-protection against BCoV-induced respiratory disease has not been evaluated.

**Calf diarrhoea and calf respiratory bovine coronavirus infections**

Calves under three weeks of age infected with BCoV develop a severe, malabsorptive diarrhoea resulting in dehydration and often death (14, 73). Concurrent faecal and nasal shedding often occurs. Calf diarrhoea BCoV strains infect the epithelial cells of the distal small and large intestine and superficial and crypt enterocytes of the colon, leading to villous atrophy and crypt hyperplasia (73, 92). Bovine coronavirus is also implicated as a cause of mild respiratory disease (coughing, rhinitis) or pneumonia in two to twenty-four-month-old calves and is detected in nasal secretions, the lungs and often the intestines and faeces (14, 35, 36, 73). In studies of calves from birth to twenty weeks of age, Heckert et al. (35, 36) documented both faecal and nasal shedding of BCoV with repeated respiratory shedding episodes in the same animal, with or without respiratory disease, and subsequent transient increases in their serum antibody titres consistent with these re-infections. These findings suggest a lack of long-term mucosal immunity in the upper respiratory tract after natural CoV infection, confirming similar observations for human respiratory CoV (6) and PRCV (5).

**Winter dysentery bovine coronavirus infections**

Winter dysentery occurs in captive wild ruminants (89) and adult cattle during the winter months and is characterised by haemorrhagic diarrhoea, frequent respiratory signs and a marked reduction in milk production in dairy cattle (70, 73, 92). Intestinal lesions and BCoV-infected cells in the colonic crypts resemble those described for calf diarrhoea (92). The BCoV isolates from WD outbreaks at least partially reproduced the disease in BCoV seropositive non-lactating cows (91) and in BCoV seronegative lactating cows (88). Interestingly, in the later study, the older cattle were more severely affected than similarly exposed calves, mimicking the more severe SARS cases observed in adults compared to children (45).

**Shipping fever bovine coronavirus infections**

Since 1995, BCoVs have been associated with respiratory disease (shipping fever) in feedlot cattle (49, 50, 81). Bovine coronavirus was isolated from nasal secretions and lungs of cattle with pneumonia and from faeces (29, 30, 31, 49, 50, 81, 82, 83). In a subsequent study, a high percentage of feedlot cattle (45%) shed BCoV both nasally and in faeces as evidenced by ELISA (10). Application of nested RT-PCR detected higher BCoV nasal and faecal shedding rates of 84% and 96%, respectively (31). Co-factors contributing to the severity of shipping fever are discussed in the subsequent sections.

**Group III infectious bronchitis virus: upper respiratory coronavirus infection with other tissue targets**

Infectious bronchitis is a highly contagious respiratory viral disease of chickens, which, like SARS, is spread by aerosol or possibly faecal-oral transmission and distributed worldwide (7, 15). Genetically and antigenically closely related CoVs have been isolated from pheasants and turkeys (25, 42), but in young turkeys, they mainly cause enteritis. Respiratory infections of chickens are
characterised by tracheal rales, coughing and sneezing, with the disease most severe in chicks (7, 15). Infectious bronchitis virus also replicates in the oviduct, causing decreased egg production. Nephropathogenic strains can cause mortality in young birds. Infectious bronchitis virus is recovered intermittently from the respiratory tract for about 28 days after infection and from the faeces after clinical recovery, with the cecal tonsil being a possible reservoir for IBV persistence in the same way as the intestines of cats are a reservoir for the persistence of FCoV (37). Infectious bronchitis virus was recovered from both tracheal and cloacal swabs in chickens at onset of egg production, suggesting re-excretion of IBV from chronically infected birds, as also demonstrated for faecal shedding of FCoV or BCoV after induction of immunosuppression (62, 63, 91).

Infectious bronchitis virus replicates in epithelial cells of the trachea and bronchi, intestinal tract, oviduct and kidney causing necrosis and oedema with small areas of pneumonia near large bronchi in the respiratory tract and interstitial nephritis in the kidney (7, 15). Of interest for SARS, is the persistence of IBV in the kidney and the prolonged faecal shedding of the virus, because SARS CoV is detected in the urine and shed for longer in the faeces. However, it is unclear whether SARS CoV shedding in urine is a consequence of viraemia or a kidney infection like IBV. Both diagnosis and control of IBV are complicated by the existence of multiple serotypes and the occurrence of IBV recombinants (7, 15). This is unlike the scenario for most group I or II respiratory CoVs in which only 1 or 2 (FCoV) serotypes are known. Also relevant to SARS CoV is the finding that IBV strains also replicate in Vero cells, but only after passage in chicken embryo kidney cells (7).

Co-factors that exacerbate coronavirus infections, disease or shedding

Underlying disease or respiratory co-infections, dose and route of infection and immunosuppression (corticosteroids) are all potential co-factors related to the severity of SARS. These co-factors can also exacerbate the severity of BCoV, TGEV or PRCV infections. Additionally, they may also play a role in the super-spreader cases observed with the SARS epidemic (46) by enhancing virus transmission or host susceptibility.

Impact of respiratory co-infections on coronavirus infections, disease and shedding

Shipping fever is recognised as a multifactorial, polymicrobial respiratory disease complex in young adult feedlot cattle with several factors exacerbating respiratory disease, including BCoV infections (49, 50, 81, 82, 83). The disease can be precipitated by several viruses, alone or in combination (BCoV, bovine respiratory syncytial virus [RSV], parainfluenza-3 virus, bovine herpesvirus), including viruses similar to common human respiratory viruses and viruses capable of mediating immunosuppression (bovine viral diarrhoea virus, etc.). The shipping of cattle over long distances to feedlots and the co-mingling of cattle from multiple farms create physical stresses that overwhelm the defence mechanisms of the animals and provide close contact for exposure to high concentrations of new pathogens or strains not previously encountered. Such factors are analogous to the physical stress of long aeroplane trips with close contact among individuals from diverse regions of the world, both of which may play a role in enhancing the susceptibility of travellers to SARS or the transmission of SARS (64, 100). For shipping fever, various predisposing factors (viruses, stress) enable commensal bacteria of the nasal cavity (Mannheimia haemolytica, Pasteurella sp., Mycoplasma sp., etc.) to infect the lungs, leading to fatal fibrinous pneumonia (49, 50, 81, 82, 83) such as that seen in SARS patients (13, 60, 65). In broiler chickens, severe disease or death ensues from systemic Escherichia coli co-infections after IBV damage to the respiratory tract or Mycoplasma sp. co-infections with IBV (15).

Antibiotic treatment of such animals (or SARS patients) co-infected with CoVs and bacteria, with the massive release of bacterial lipopolysaccharides (LPS), may precipitate induction of pro-inflammatory cytokines, which may further enhance lung damage. For example, Van Reeth et al. (94) showed that pigs infected with PRCV then given a sub-clinical dose of E. coli LPS within 24 h developed enhanced fever and more severe respiratory disease compared to animals infected with each agent alone. They concluded that the effects were probably mediated by the significantly enhanced levels of pro-inflammatory cytokines induced by the bacterial LPS. Therefore, both LPS and lung cytokine levels need to be examined in SARS patients as possible mediators of the severity of SARS. Bacteria (Chlamydia sp.) that have been isolated from SARS patients, but their role in enhancing the severity of SARS is undefined (68).

Interactions between PRCV and other respiratory viruses may also parallel the potential for concurrent or pre-existing respiratory viral infections to interact with SARS CoV (such as metapneumoviruses, influenza, reoviruses, RSV, human coronavirus-OC43 [OC43] or 229E). Hayes (34) showed that sequential dual infections of pigs with the arterivirus porcine respiratory reproductive syndrome (PRRSV) (order Nidovirales, like CoV), followed ten days later by PRCV, significantly enhanced lung lesions and reduced weight gains compared to animals infected with each virus alone. The dual infections also resulted in more pigs shedding PRCV nasally for a prolonged period and...
surprisingly, to faecal shedding of PRCV. The lung lesions observed resembled those in SARS victims (13, 60).

In another study, Van Reeth and Pensaert (93) inoculated pigs with PRCV then two to three days later, with swine influenza A virus (SIV). They found that SIV lung titres were reduced in the dually-infected pigs, but paradoxically, the lung lesions were more severe in the dually-infected pigs. They postulated that the high levels of interferon (IFN)-alpha induced by PRCV may mediate interference with SIV replication, but might also contribute to enhanced lung lesions. Such studies are highly relevant for possible dual infections by SARS CoV and influenza virus and for the potential treatment of SARS patients with IFN-alpha.

Impact of route (aerosols) and dose on coronavirus infections

Experimental inoculation of pigs with PRCV strains showed that administration of PRCV by aerosol compared to the oronasal route, or in higher doses, resulted in higher virus titres shed and longer shedding (95). In other studies, high PRCV doses induced more severe respiratory disease. Pigs given $10^{9.5} \text{TCID}_{50}$ of PRCV developed more severe pneumonia and more deaths were observed than in pigs exposed by contact (44). Furthermore, higher intranasal doses of another PRCV strain (AR310) induced moderate respiratory disease whereas lower doses produced sub-clinical infections (28). By analogy, hospital procedures that could potentially generate aerosols, or exposure to higher initial doses of SARS CoV may enhance SARS transmission or lead to enhanced respiratory disease (46, 79).

Impact of treatment with corticosteroids on coronavirus infections of animals

Corticosteroids are known to induce immunosuppression and reduce the numbers of cluster of differentiation antigen (CD) 4 and CD 8 T cells and certain cytokine levels (23). Many hospitalised SARS patients were treated with steroids to reduce lung inflammation, but there are no data to assess the outcome of this treatment on virus shedding or respiratory disease. A recrudescence of BCoV faecal shedding was observed in one of four WD BCoV-infected cows treated with dexamethasone (91). Similarly, treatment of older pigs with dexamethasone prior to TGEV challenge led to profuse diarrhoea and reduced LP responses in the treated pigs (77). These data raise issues for corticosteroid treatment of SARS patients related to possible transient immunosuppression, resulting in enhanced respiratory disease or increased and prolonged CoV shedding (super-spreaders). Alternatively, corticosteroid treatment may be beneficial in reducing pro-inflammatory cytokines if found to play a major role in lung immunopathology (23).

Future research

The following unanswered questions regarding SARS pathogenesis are highly relevant to the design of prevention and control strategies. What is the initial site of viral replication? Is SARS primarily targeted to the lung like PRCV with faecal shedding of swallowed virus and with undefined sequelae contributing to the diarrhoea cases? Alternatively, is SARS CoV pneumoenteric like BCoV, with variable degrees of infection of the intestinal and respiratory tracts and is disease precipitated by the co-factors discussed or by unknown variables? Does SARS CoV infect the lung directly or via viraemia after initial replication in another site (oral cavity, tonsils, upper respiratory tract) and does the virus productively infect secondary target organs (intestine, kidney) via viraemia after replication in the lung?

Finally, the persistent, macrophage tropic, systemic FIPV infection of cats presents yet another CoV disease model and a dilemma for attempted control strategies. In this disease scenario, induction of neutralising IgG antibodies to the FIPV S protein, not only fails to prevent FIPV infections, but actually potentiates the immunopathogenesis of FIPV. This occurs via generation of immune complexes with activation of complement, or it may be the result of antibody-dependent enhancement of FIPV infection of macrophages, as has been observed in vitro (63).

The suspected zoonotic origin of SARS CoV (24, 101) and the recognised propensity of several CoVs to cross species barriers, illustrate the need for additional animal studies of the mechanisms of interspecies transmission of CoVs and their adaptation to new hosts. The possible animal reservoir for SARS remains undefined. At present, very little is understood about CoVs or other viruses circulating in wildlife or their potential to emerge or recombine with new or existing CoVs (80) as public or animal health threats.

Conclusions

In summary, studies of animal CoV infections in the natural host provide enteric and respiratory disease models which enhance the understanding of both the similarities and divergences of CoV disease pathogenesis and targets for control. Several reviews of animal CoV vaccines in the context of the development of vaccines for SARS have recently been made available or are in press (71, 72).
Certainly, SARS has highlighted the need for closer contact, communication and collaboration between veterinary scientists and the medical community to address emerging zoonotic public health threats. Hopefully, the SARS epidemic will generate new interest, collaborations and funding for these fundamental research questions applicable not only to SARS CoV, but also to the estimated 75% of newly emerging human diseases arising as zoonoses (87). A summary of the lessons learned from SARS and several strategies that should be implemented based on these lessons follows.

Lessons

a) Coronaviruses were long-recognised and studied by veterinary scientists as major causes of potentially fatal respiratory and enteric infections in animals. Moreover, such studies emphasised the potential of CoVs for interspecies transmission, but the medical research community was largely unaware of these findings or their implications for public health based on experiences with low impact human CoV infections. This knowledge base from research on animal CoVs contributed significantly to the rapid progress in the characterisation of SARS CoV and will enhance the future development and testing of vaccines and antivirals for SARS.

b) Given that an estimated 75% of newly emerging pathogens in humans are zoonotic and based on experiences with SARS CoV, veterinary scientists are essential partners for disease control and public health management. Their input and assistance should involve the identification and management of animal reservoirs for newly emerged zoonotic pathogens.

c) Local events in the People's Republic of China rapidly triggered a global epidemic within only a few weeks. International co-operation and collaboration, with established working relationships and access to modern communication tools (secure networks via the internet, teleconferences, electronic reporting systems, including non-governmental sources such as Pro-Med) were essential for the co-ordination and implementation of efforts required for the identification and control of SARS. Both the established international network for influenza virus surveillance initiated by the WHO, and the USA CDC played major roles in these efforts.

d) Few established mechanisms exist to promote interagency co-operation (animal and public health agencies, both national and international) in investigating and controlling outbreaks mediated by newly emerging or re-emerging zoonotic pathogens.

e) Containment of the SARS epidemic relied on traditional methods of initial disease identification (virus isolation, electron microscopy characterisation, serology) and containment (quarantine and trace-backs) adapted to the environments of the 21st Century (airports, aeroplanes, population centres, hospital intensive care units, etc.). Rapid global travel, 'super-spreaders' and infection of health care workers intensified the epidemic. Countries which rapidly implemented and enforced control measures managed to contain the epidemic; other countries with delayed responses experienced more devastating consequences. Even within the limited time-frame of the epidemic and the major foci of infections contained within a few countries, the cost of the SARS epidemic was extraordinary, estimated at US$40 billion in total or approximately US$5 million per infected patient.

Strategies

a) Veterinary scientists with appropriate expertise should be recruited in the initial stages of suspected zoonotic disease outbreaks to interact as partners with their medical counterparts at all stages of the outbreak investigation and control process, with the major emphasis placed on the studies and reagents needed to identify and control the animal host reservoir. There are several organisations which could be a source of information on experts in various fields, as follows:

– the World Organisation for Animal Health (OIE) has designated experts for various animal disease entities whose expertise could be sought by national and international agencies

– federal granting agencies, federal agencies and universities have lists of scientists with disease expertise based on grant and publication records who could be recruited to provide advice on a specific pathogen.

b) Closer research ties and interagency funding and co-operation are required to provide grants to academic researchers to promote collaborative infectious and zoonotic disease research between medical and veterinary scientists and to provide training funds for students in this area, as follows:

– to study disease pathogenesis in the most appropriate animal models, including the natural host, and to elucidate novel mechanisms of disease in animals, including diseases presently lacking a human counterpart

– to identify the animal reservoir of zoonotic pathogens and to develop and validate diagnostic assays targeted to detect such zoonotic agents in animals to study the chain of interspecies transmission. Species-specific reagents are lacking to conduct immunological tests for antibodies to the zoonotic pathogens in the various host species

– to enable teams of medical and veterinary scientists to assemble collections of zoonotic pathogens from human and animal sources and conduct comparative studies to assess pathogen evolution and the changes that occur upon adaptation to new hosts. Both historical and recent animal and human microbial collections should be maintained and be made available through reference centres such as the American Type Culture Collection in Manassas, VA, USA.
c) The failure to identify the animal reservoir for SARS CoV or to develop diagnostic tests for the disease, validated for use in diverse animal populations, remains a concern for the re-emergence of SARS from an animal reservoir. Consequently, there is a need to develop and validate assays and reagents and implement an integrated disease surveillance system encompassing wildlife, domestic animals and humans.

d) Co-operation and co-ordination of efforts among animal and public health agencies with input from international disease experts is essential to establish this system, as follows:

- collaborative funds must be provided to study the factors that promote interspecies transmission of pathogens and the mechanisms involved
- contingency funds must be provided to rapidly assemble interdisciplinary teams with the targeted disease and disciplinary expertise (i.e. in methods and strategies for detection, diagnosis, response, recovery and prevention in both the animal and human populations) to address a newly emerging disease in an integrated manner. Such teams require the necessary infrastructures (BSL-3 laboratories and animal facilities, etc.) to conduct targeted and integrated work
- rotating, short-term fellowships must be provided for veterinary scientists to undertake co-operative projects with their medical counterparts at medical schools and public health laboratories, the USA CDC, WHO, etc., and for medical scientists to rotate through the counterpart organisations such as Colleges of Veterinary Medicine, veterinary diagnostic laboratories, the United States Department of Agriculture, the OIE, the Food and Agriculture Organization, etc. This will foster closer ties between the various organisations and favour the networking required in emergencies to address the multifaceted aspects of emerging zoonotic disease outbreaks in a more integrated manner
- international exchange and training programmes and co-operative grants must also be provided for scientists from developing countries to enhance disease monitoring and control efforts and to foster mutual trust and international co-operation.

e) Better containment and universal and rapid disinfection/detection procedures (airports, passengers, baggage, hospitals, etc.) are required for application to the 21st Century environment. Moreover, highly effective control measures for more rapidly spreading aerosol respiratory pathogens need to be developed.

f) Government co-operation at all levels and transparency in reporting animal and human disease outbreaks are required to contain regional outbreaks and prevent pandemics.

Les coronavirus animaux et leur enseignement pour le syndrome respiratoire aigu sévère

L.J. Saif

Résumé

En 2002, un nouveau coronavirus responsable d’un syndrome respiratoire aigu sévère (SRAS) et mortel pour l’homme fait son apparition en République populaire de Chine. L’épidémie se propage rapidement dans le monde avant d’être endiguée en 2003, même si quelques cas sporadiques continuent à se manifester en Asie après cette date. Le virus serait d’origine zoototique et issu d’un réservoir animal sauvage (civettes [Paguma larvata]), mais l’identité de son hôte n’a toutefois pas été établie. L’éventualité d’une transmission du coronavirus du SRAS aux rongeurs ou aux chats domestiques (prouvée par voie expérimentale) et d’une perpétuation de la maladie chez ces espèces suscite l’inquiétude. Les coronavirus sont reconnus responsables de plusieurs infections entériques et respiratoires du bétafet et de la volaille dont l’issue s’avère souvent fatale pour les jeunes animaux. L’émergence du SRAS a surpris la communauté médicale, même si des spécialistes vétérinaires des coronavirus en avaient déjà isolé chez des animaux sauvages et fait état dans leurs publications d’une transmission interspécifique aux bovins. De surcroît, les scientifiques détenaient les preuves incontestables de l’émergence de nouvelles souches de coronavirus et de la mutation des souches existantes, conduisant à l’apparition de nouveaux syndromes de maladie chez les animaux, mais la juste mesure de l’évolution et de l’impact pathologique des coronavirus n’avait pas été
prise avant l’épidémie de SRAS. Cette étude porte notamment sur la pathogénèse comparée des infections à coronavirus et sur les facteurs aggravants de l’affection respiratoire dans le contexte particulier de l’élevage bovin et de l’aviculture. Elle vise à améliorer notre connaissance de la transmission des coronavirus et des mécanismes pathologiques susceptibles d’intervenir dans le SRAS. Par ailleurs, elle met en évidence la contribution des chercheurs vétérinaires à cet effort. Ces exemples témoignent de la nécessité, pour les communautés vétérinaires et médicales de communiquer entre elles et de collaborer à la compréhension et à la lutte contre les maladies zoonotiques émergentes du xxᵉ siècle.

Mots-clés
Coronavirus animal – Coronavirus entérique et respiratoire – Syndrome respiratoire aigu sévère – Zoonose.

¿Qué pueden enseñarnos los coronavirus animales sobre el síndrome respiratorio agudo severo?

L.J. Saif

Resumen
En 2002, un nuevo coronavirus asociado al síndrome respiratorio agudo severo (SRAS) y mortalidad en el hombre, emergió en la República Popular China. La epidemia se extendió con celeridad por el mundo antes de quedar bajo control en 2003, aunque posteriormente siguieran registrándose casos esporádicos en Asia. Se presume que el virus es de origen zoonótico y cuenta con un reservorio entre la fauna salvaje (la civeta [Paguma larvata]), pero se ignora cuál es su huésped definitivo. La posibilidad de que el coronavirus asociado al SRAS se transmita a roedores o gatos domésticos (fenómeno ya descrito en condiciones experimentales) y perpetúe la enfermedad en esas especies es preocupante. Se sabe que los coronavirus provocan infecciones intestinales y respiratorias en ganado y aves de corral, que a menudo resultan mortales en animales jóvenes. Aunque la aparición del SRAS sorprendió a la comunidad médica, el aislamiento de coronavirus en animales salvajes y su transmisión al ganado han sido descritos con anterioridad por coronavirólogos veterinarios. Además, los científicos disponían de una serie de sólidos indicios que apuntaban a la aparición de cepas, nuevas o mutantes, capaces de provocar nuevos síndromes en animales. Sin embargo, antes del SRAS no había consciencia general de los cambios que estaban experimentando los coronavirus y del peligro sanitario que ello encerraba. El autor describe un estudio comparativo de la patogénesis de las infecciones por coronavirus (incluyendo los factores agravantes de la enfermedad respiratoria que provocan), centrándose especialmente en el ganado y las aves de corral. Con ello pretende ofrecer elementos que aclaren la transmisión y patogenia de estos virus y que posiblemente puedan aplicarse al caso del SRAS, subrayando al mismo tiempo la contribución de la comunidad científica veterinaria en este terreno. Estos ejemplos ponen de relieve el hecho de que para entender y controlar las enfermedades zoonóticas emergentes del siglo XXI es absolutamente necesario que la profesión médica y la veterinaria se comuniquen y trabajen concertadamente.

Palabras clave
Coronavirus animal – Coronavirus intestinal y respiratorio – Síndrome respiratorio agudo severo – Zoonosis.
References


