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Review a brief history of coronaviruses in Thailand

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1. Introduction

The world is currently undergoing a pandemic of historic proportions. The pandemic is driven by the spread of a novel virus, the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), which results in a range of symptoms and a disease termed Covid-19. The virus is a member of the species Severe acute respiratory syndrome-related coronavirus, which is a member of the genus Betacoronavirus of the family Coronaviridae (Coronaviridae Study Group of the International Committee on Taxonomy, 2020). At the time of finalizing this article (1st August 2020), more than 17 million people have been reported to have been infected worldwide, resulting in more than 660,000 deaths (WHO, 2020a). The first cases of human transmission of this virus are believed to have occurred in Wuhan, China with the first cases being reported in December 2019 (Huang et al., 2020). Thailand was the first country outside of China to report a case (imported) of SARS-CoV-2 infection of a visiting tourist which occurred in January 2020 (WHO, 2020c). Since then some 3312 cases of locally acquired and imported infection have been reported in Thailand (WHO, 2020a). SARS-CoV-2 is the third highly pathogenic respiratory coronavirus to have been imported by travelers to Thailand, with the prior importation of cases of the severe acute respiratory syndrome coronavirus (SARS) and the Middle East respiratory syndrome coronavirus (MERS). Unlike SARS and MERS, SARS-CoV-2 was able to establish local transmission in Thailand. In addition to the imported coronaviruses, Thailand has a number of endemic coronaviruses that can affect livestock and pet species, as well as four human coronaviruses that are mostly associated with the common cold. This article seeks to review what is known on both the endemic and imported coronaviruses in Thailand.

2. The coronaviridae

The family Coronaviridae contains 2 subfamilies, 5 genera and 46 species of virus (Walker et al., 2019). The first subfamily, Letovirinae, contains only one genus (Alphacoronavirus) which has only a single virus species (Microhyla letovirus 1) which infects amphibians (Bukhari et al., 2018). In contrast, the second subfamily, Orthocoronavirinae, contains the remaining 45 viral species in this family distributed in four genera (Alphacoronavirus, Betacoronavirus, Deltacoronavirus and Gammacoronavirus). The viruses in this family have a positive sense, single stranded RNA genome that can vary from 26.4-31.7 kb, making them amongst the largest RNA genomes (Payne, 2017). The genome is capped and polyadenylated, and possesses 5′- and 3′- untranslated regions as well as multiple open reading frames (Payne, 2017). Viruses in the subfamily Orthocoronavirinae can infect a range of birds and mammals and proposed infection routes include formites, aerosols and oral-fecal
transmission, depending upon the specific virus. While the primary reservoirs for coronaviruses are animals, some coronaviruses are zoonotic, able to establish infection in humans, resulting in human-to-human transmission, and to date seven human coronaviruses have been identified (Chen et al., 2020). Across the subfamily Orthocoronavirinae, the viruses primarily target respiratory and enteric epithelial cells (Holmes, 1999), consistent with their modes of transmission, and infection generally result in broadly gastrointestinal or respiratory manifestations, albeit that these manifestations may be associated with a range of other symptoms.

3. Endemic animal coronaviruses in Thailand

A number of both animal and human coronaviruses have been shown to circulate in Thailand. Animal coronaviruses include those of domesticated animals including livestock (cattle, pigs and chickens) and pets (cats and dogs). In addition, bats in Thailand have been shown to harbor a number of different coronaviruses. Human coronaviruses (HCoV) endemic in Thailand include HCoV-229E, HCoV-OC43, HCoV-NL63 and HCoV-HKU1.

Two coronaviruses that affect pigs in Thailand have been identified, namely Porcine epidemic diarrhea virus (PEDV; Subfamily Orthocoronavirinae, genus Alphacoronavirus, species Porcine epidemic diarrhea virus) and Porcine deltacoronavirus (PDCoV; Subfamily Orthocoronavirinae, genus Alphacoronavirus, species Coronavirus HKU1(15)). PEDV was first discovered in 1977 after an outbreak of diarrhea affecting pigs in pig farms in Belgium, and while the virus affects pigs of all ages, mortality is higher in younger pigs and piglets (Pensaert and de Bourc, 1978). PEDV was first detected in Thailand in 1995, although the outbreak was relatively confined (Srinuntapunt et al., 1995). PEDV was first detected in 1995, although the outbreak was relatively confined (Srinuntapunt et al., 1995). PEDV was subsequently emerged in 2007 in pig farms in Nakhon Pathom province, outbreak was relatively confined (Srinuntapunt et al., 1995). PEDV was first detected in Thailand in 1995, although the outbreak was relatively confined (Srinuntapunt et al., 1995). PEDV was subsequently emerged in 2007 in pig farms in Nakhon Pathom province, a high density pig farming area in Thailand (Puranaveja et al., 2009). Since then continued circulation of PEDV has been confirmed in studies looking at samples from 2008 to 2012 (Temevesyen et al., 2014), 2008–2015 (Stott et al., 2017) and 2011–2016 (Tuanthap et al., 2019). PDCoV was originally identified in pigs in Hong Kong in 2012 (Woo et al., 2012), and subsequently in Ohio, USA (Wang et al., 2014), South Korea (Lee and Lee, 2014) and China (Dong et al., 2015; Song et al., 2015). PDCoV was first detected in pig farms in an eastern province of Thailand in 2015 (Janetanakit et al., 2016; Lorsirigool et al., 2017), however interestingly, subsequent evolutionary analysis suggested that Thai strains, as well as those from neighboring countries were somewhat evolutionarily distinct from both the USA and China strains (Saeng-Chuto et al., 2017a, b).

Bovine coronavirus (BCoV; Subfamily Orthocoronavirinae, genus Betacoronavirus, species Betacoronavirus 1) was originally identified by Mebus and colleagues during trials of a vaccine for bovine rotavirus (Mebus et al., 1973a, b; Mebus et al., 1972; Stair et al., 1972). Infection of BCoV in cattle is associated with enteric diarrhea in calves, and winter dysentery in adult cattle (Hodnik et al., 2020), and the virus can infect both wild and domesticated ruminants (Salem et al., 2020). While a role for BCoV in enteric disease is well established, the virus may also play a role in the disease bovine respiratory disease complex (Ellis, 2019). There is little data on the prevalence of this virus in Thailand. However, an early study (Atumlama et al., 1992) suggested the presence of antibodies to BCoV in a high proportion of bulk milk samples collected in Muaklek (Saraburi province, Thailand), while molecular confirmation of circulation of BCoV was shown with the detection of the virus by PCR in three of 25 diarrheic fecal samples collected from cattle in the central region of Thailand (Singua et al., 2017). Given the economic importance of this virus (Hodnik et al., 2020), further surveillance is warranted.

Infectious bronchitis virus (IBV; Subfamily Orthocoronavirinae, genus Gamma coronavirinae, species Avian coronavirus) causes the severe poultry disease infectious bronchitis (Bande et al., 2016). The disease was first observed in North Dakota USA in 1930 (Schalk and Hawn, 1931), and the virus was first propagated in embryonating eggs in 1937 (Beaumette and Hudson, 1937), making it the first coronavirus to be cultured. Unlike porcine and bovine coronaviruses where the symptoms are predominantly enteric, IBV infection primarily manifests as a respiratory disease, although involvement of the kidneys and reproductive track can also occur (Bande et al., 2016). The virus is present worldwide and causes significant economic losses (Cavanagh, 2007). In addition, some studies have suggested that pheasants may also be susceptible to this virus (Liebing et al., 2020). In Thailand infectious bronchitis in chickens was first reported in 1962 (Chindavang, 1962), and outbreaks have occurred continuously since that time (Antarasena et al., 1990; Munyahongase et al., 2020; Pohuang et al., 2009, 2011; Promkuntod et al., 2015; Upatoom et al., 1983) despite the use of vaccination, possibly due to strain specific vaccine breakthrough (Jordan, 2017).

Coronaviruses in Thailand can affect both cats and dogs. Dogs can harbor two unrelated coronaviruses. The first, canine coronavirus (CCoV; Subfamily Orthocoronavirinae, genus Alphacoronavirus, species Alphacoronavirus 1) was originally identified in 1971 during an outbreak of diarrhea in military dogs in Germany (Bian et al., 1974). Since then the distribution has been established to be worldwide (Decaro and Buccinauglia, 2008). The second canine coronavirus, canine respiratory coronavirus (CRCoV; Subfamily Orthocoronavirinae, genus Betacoronavirus, species Betacoronavirus 1) associated with the respiratory disease kennel cough was first identified in the United Kingdom in 2003 (Erles et al., 2003), and is also found widely distributed (Priestnall et al., 2006). Studies have shown that both CCoV (Sakulwira et al., 2003; Tingpalapong et al., 1982) and CRCoV (Plewang et al., 2017; Pohuang et al., 2009) are circulating in Thailand. Feline infectious peritonitis (FIP) is a common disease in cats that can be fatal in kittens (Tekes and Thiel, 2016). While FIP was first described in 1963 (Holzworth, 1963), it was not until 1979 that the causative agent was determined to be a coronavirus (O’Reilly et al., 1979) originally termed feline infectious peritonitis virus, but now known as feline coronavirus (FCoV; Subfamily Orthocoronavirinae, genus Alphacoronavirus, species Alphacoronavirus 1), a virus belonging to the same viral species as CCoV. Infection with FCoV is believed to be generally asymptomatic or to cause only mild enteric symptoms, but in a proportion of cases of infection the virus can undergo changes to cause the more severe FIP causing bovte (Licitra et al., 2013). The first molecular evidence of the circulation of FCoV in cats in Thailand was in 2009 (Manasateinkij et al., 2009), and other studies have confirmed this observation (Techarangsuan et al., 2012, 2013).

Bats have long been known to be a natural reservoir for many viruses. One study in the Indian Flying Fox (Pteropus giganteus) found evidence for 55 viruses from nine viral families (Anthony et al., 2013), and viruses known to have a natural reservoir in bats include rabies virus (family Rhabdoviridae, genus Lyssavirus, species Rabies lyssavirus (Pawan, 1948)), Nipah virus (family Paramyxoviridae, genus Henipavirus, species Nipah henipavirus (Yob et al., 2001)) and Ebola virus (family Filoviridae, genus Ebolavirus, species Zaire ebolavirus (Leroy et al., 2005)). The tolerance of bats to viruses possibly results from a robust interferon response, coupled with a reduced inflammatory response (Gorbunova et al., 2020). Somewhat surprisingly, the presence of coronaviruses in bats was not established until 2005 (Lau et al., 2005; Li et al., 2005) in surveys of wildlife undertaken in response to the 2003 SARS epidemic. Currently (23/7/2020), some 4460 bat coronavirus sequences from around the world have been deposited in the database of bat-associated viruses (Chen et al., 2014) with sequences originating from a number of different bat species, and at least 90 bat-associated viruses have been fully sequenced (Wong et al., 2019). Importantly, bats are believed to be the original source for many coronaviruses that affect both animals and humans (Gorman et al., 2018). In Thailand the first report of bat-associated coronaviruses was in a study on bat guano (Wacharapluesadee et al., 2013) which detected group C coronaviruses (currently Orthocoronavirinae, genus Betacoronavirus, subgenus Merbecovirus). Subsequent studies by the same group identified a number of alpha- and betacoronaviruses in as many as 14 different bat species.
which would later become the species type virus (Tyrrell and Bynoe, 1965). At about the same time a study undertaken in medical students at the University of Chicago identified five novel agents, of which four were isolated from students with mild upper respiratory disease (Hamre and Procknow, 1966). The agents isolated in this study included one designated 229E, but had a “one-way serologic relationship” with strains of mouse hepatitis virus (Subfamily Orthocoronavirinae, genus Betacoronavirus, species Murine coronavirus), that had been identified in by Cheever and Daniels in 1949 (Cheever and Daniels, 1949), and independently by Gledhill and Andrews in 1951 (Gledhill and Andrews, 1951).

A virus belonging to a second species of human coronavirus, HCoV-OC43 (Subfamily Orthocoronavirinae, genus Betacoronavirus, species Betacoronavirus 1) was isolated from respiratory specimens that had originally failed to show evidence of any virus, by using a tracheal organ culture system (McIntosh et al., 1967b). The virus was subsequently adapted to growth in sucking mouse brain (McIntosh et al., 1967a), and it was shown that this virus was serologically distinct from HCoV-229E, but that was identical.

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A number of studies have shown evidence of circulation of human coronaviruses in Thailand, and all four endemic HCoVs have been shown to be present. Two studies have detected all four endemic HCoVs in patients with pneumonia (Dare et al., 2007) and in patients with respiratory infection in southern Thailand (Suwannakarn et al., 2014). Three human coronaviruses (HCoVs) were identified in patients with pneumonia in Thailand in 2003 (Taylor et al., 2007). Most recently, a HCoV-HKU1 virus was detected in a non-ill bat guano miner (Joyjinda et al., 2019). All of these studies support the ongoing circulation of these HCoVs, and their association with respiratory illness.

5. Coronaviruses imported to Thailand

In addition to the four human endemic coronaviruses, three human coronaviruses, SARS, MERS and SARS-CoV-2 have been imported into Thailand. However, only one of these viruses, SARS-CoV-2, has established local transmission. SARS cases are believed to have first occurred in the city of Foshan, Guangdong Province, Southern China in November 2002 (Xu et al., 2004). A physician from southern China who attended a conference in Hong Kong is believed to be the index patient (Hui and Chan, 2010) for the outbreak of SARS that occurred in Hong Kong (Lee et al., 2003), as well as in other countries including Canada (Booth et al., 2003), Singapore (Hsu et al., 2003) and Vietnam (Nishiyama et al., 2003). In total, some 8896 cases and 774 deaths occurred around the world (as cited in (Shaw, 2006)). Ancestor viruses of SARS were subsequently identified in bats (Lau et al., 2005; Li et al., 2005), although it is probable that the bat SARS virus had first jumped species to palm civets before transmission to humans (Wang and Eaton, 2007). SARS was first introduced into Thailand by a World Health Organization physician (who subsequently died of his disease) who had treated a SARS patient in Vietnam, (Chaovavanich et al., 2004). By the end of the outbreak, a further 8 cases had been identified, all of which were imported, and of the nine infected people, two died (ProMed-Mail, 2003) and there were no reports of local transmission.

The first known case of MERS occurred in an elderly man who was admitted to a hospital in Jeddah, Saudi Arabia in 2012 (Zaki et al., 2012). The virus (MERS-CoV) was isolated from sputum samples of the patient, and subjected to sequencing analysis which identified the agent as a Betacoronavirus (Zaki et al., 2012). Some three months later, a novel coronavirus, that was subsequently shown to have high homology to the Saudi Arabian isolate, was identified in a Qatari national with a history of travel to Saudi Arabia upon his hospitalization in UK (Bermingham et al., 2012). By the end of January 2020 some 2519 laboratory-confirmed cases of MERS, including 866 associated deaths have been reported worldwide, albeit that the majority of cases (2121 cases) have occurred in Saudi Arabia (WHO, 2020b). Dromedary camels have been implicated as the main zoonotic reservoir (Elfadil et al., 2018), with African bats as the likely ancestral reservoir host for MERS-CoV (Goldstein and Weiss, 2017). MERS has been imported to Thailand three times, and again, in no case has local transmission occurred. The first case occurred in a 75-year-old Omani man who had travelled to Thailand to seek medical attention for a heart condition in June 2015 (Pilip et al., 2017; Suttha et al., 2018). Upon initial screening at a private hospital in Bangkok, the patient was diagnosed with suspected pneumonia, and given his history of recent travel from the Middle East, MERS was suspected. However, it was only in the third day of hospitalization that MERS infection was confirmed, and the patient was transferred to the Thai Ministry of Public Health designated priority hospital (Bamrasnaradura Infectious Diseases Institute, Bangkok) for MERS patients and those suspected to be infected with MERS (Pilip et al., 2017; Suttha et al., 2018). The second importation of MERS to Thailand also occurred in an elderly Omani man visiting Thailand for medical reasons in June 2016, while the third case was an 18-year old Kuwaiti man visiting Thailand for a vacation in July 2016 (Suttha et al., 2018). All three cases were treated at the Bamrasnaradura Infectious Diseases Institute, and all three survived their infection. Markedly, the case fatality rate for MERS infection is believed to be around 35% (Guerner, 2020). As with the cases of SARS imported to Thailand, no case of local transmission of
MERS has been reported.

As noted earlier, the first case of SARS-CoV-2 infection reported outside of China occurred in January 2020 in Thailand (WHO, 2020c), and since then some 3312 cases of locally acquired and imported SARS-CoV-2 infection and 58 deaths have been reported (as of 1st August 2020; (WHO, 2020a)). Unlike both SARS and MERS, there have been a number of cases of community acquired infection. However, the fact that in 7 months only slightly over 3000 cases have been detected is quite remarkable. In dramatic contrast, the first cases of SARS-CoV-2 infection in the United Kingdom (a country of an approximately similar population size to Thailand) were detected in late January 2020 (Lillie et al., 2020), and as of 1st August 2020 the United Kingdom has reported some 303,185 infections and 46,119 deaths (as of 1st August 2020; (WHO, 2020a)). The reasons for the great discrepancy in infection rates remains unknown. However, Thailand has a long history of dealing with infectious diseases (Aungkulanon et al., 2012) and part of the reasons for the great discrepancy in infection rates remains unknown. However, Thailand has a long history of dealing with infectious diseases (Aungkulanon et al., 2012) and part of the

6. Conclusions

Thailand has a number of endemic coronaviruses, and has seen the repeated importation of severe respiratory disease associated coronaviruses. For the endemic coronaviruses, the coronaviruses found in bats represent a particular concern as all three severe respiratory disease associated viruses (SARS, MERS and SARS-CoV-2) are believed to have an ancestor in bats, albeit with possible transmission to other species before emerging in humans (Boni et al., 2020; Corman et al., 2018). Thus there is the potential for an endemic, severe respiratory disease associated virus to arise in Thailand. Given the large population flux in Thailand, there is always the risk of importation of viruses that have a significant risk to the Thai population. These include not only coronaviruses, but other viruses such as highly pathogenic avian influenza viruses and Ebola. On the positive side, Thailand has shown a remarkable track record in controlling disease spread when importation of a highly transmissible virus has occurred. In particular, with both SARS and MERS there was no reported transmission to healthcare workers, unlike the situation in some other countries (Suwantranit and Apisarnthanarak, 2015). While the situation in Thailand currently looks positive with no community transmission for around nine weeks (as of 1st August 2020), the easing of restrictions on businesses, travel and education will need to be carefully monitored.

Author statement

Duncan R. Smith is the sole author, and no other person contributed to the review. The author has no conflict of interest.

Declaration of Competing Interest

None.

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