Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

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Emerging infectious diseases (EID) have been defined as diseases whose incidence increased over the past decades or are predicted to increase in the foreseeable future (“see Relevant Websites section”). This definition includes known infections with new properties, or known infections in new geographic regions, infections that were not previously recognized, and new infections resulting from spillover of pathogens from an animal reservoir to humans. Although difficult to state with certainty, current consensus is that EID outbreaks have increased significantly in the past decades, both in terms of size and number of causative pathogens (Smith et al., 2014; Allen et al., 2017). The majority of EIDs are thought to originate from animals, of which wildlife is the most important source of human outbreaks (Allen et al., 2017; Jones et al., 2008). Such spillovers can occur directly, or through vectors such as mosquitos, ticks and sandflies. Examples of past outbreaks are SARS (Peiris et al., 2004), MERS (Zaki et al., 2012), Avian Influenza (Lai et al., 2016), Ebola (Dudas et al., 2017) and Zika virus (Gubler et al., 2017). Compared to common endemic diseases, the burden of disease may be relatively limited, but the unexpected nature, high case fatality rate, the uncertainty of sources and modes of transmission, and the paucity of medical and non-medical countermeasures make EIDs a threat to global human and animal health. Fear of spread, travel restrictions, and unpredictable self-imposed avoidance of a region can cause serious socio-economic disruptions on local and global level (McCloskey et al., 2014).

Drivers of (Emerging) Zoonotic Diseases

Infectious disease emergence has proven extremely challenging to predict, and human cases of a wide range of emerging or re-emerging pathogens have been reported all over the world and throughout the year. However, when outbreak data of emerging disease outbreaks in the last decades are combined, some specific conditions or risk factors seem to drive disease emergence (Woolhouse, 2011). The main general drivers that have been described can be summarized as changes in (1) human demographics with the consequential growing demand for food production (Jones et al., 2008), (2) land use, including agricultural changes (Jones et al., 2013; Gortazar et al., 2014) (3) international travel and trade (Gortazar et al., 2014; Randolph and Rogers, 2010), (4) climate change and weather (Allen et al., 2017; Gortazar et al., 2014) (Fig. 1).

Fig. 1   Global changes acting as drivers of infectious disease emergence and spread in the One Health domains.
In the case of zoonotic EIDs, the first step towards an outbreak of human disease or mortality is the occurrence of spill-over of a pathogen from an animal reservoir host to humans (Plowright et al., 2017; Karesh et al., 2012; Petersen et al., 2018). The majority of human EIDs originate from wildlife (Jones et al., 2008; Allen et al., 2017). However, humans are usually not in close contact with wildlife. Therefore, occasionally there is an additional intermediate host species involved where a pathogen is amplified and that is in closer contact with humans (Karesh et al., 2012; Plowright et al., 2015). Well known examples are Nipah virus, Hendra virus or SARS-CoV, that originate from bats and amplify in pigs, horses and civet cats used as food source, respectively (Plowright et al., 2015). The risk of animal to human spill-over depends on a plethora of factors. The aforementioned drivers of disease emergence create circumstances that facilitate such spill-over. Additionally, the risk of spillover is influenced by the pathogen itself. In general, RNA viruses are zoonotic more often than DNA viruses (Olival et al., 2017). A possible explanation for this is their genetic plasticity, caused by the replication mechanism: most RNA viruses replicate with the use of virus-encoded RNA polymerases which - in contrast to the host cell DNA polymerase- do not have so-called proof-reading capacity. Proofreading is a mechanism to reduce the amount of errors in the nascent strands of newly produced copies of (pathogen) genomes, and the lack of proofreading leads to copies that contain a higher number of mutations when comparing the progeny genomes with those of the parent sequences. As a consequence, hosts infected with such RNA viruses shed a mutant swarm of viruses. When they then encounter a bottleneck, for instance an exposure of a new host, chances are that within the swarm variants exist that are better adapted (by chance) to infect a new host (Domingo and Perales, 2019).

One possible consequence of this flexibility is described as “phylogenetic host breadth” and “host plasticity”, which reflect the diversity of known hosts, and therefore are significant predicting factors for zoonotic potential of viruses (Olival et al., 2017; Kreuder Johnson et al., 2015). Additionally, the dynamics of a pathogen in a reservoir host population is a very important factor for human health risk, and is governed by population structure, host density, host behavior and contact patterns, shedding patterns, stability of pathogens outside a host, levels of immunity, events that stress the population, and more. As a consequence, the resulting risk of infection for humans may vary depending on season, location, weather and host distribution for example (Plowright et al., 2017; Karesh et al., 2012).

The second step towards outbreaks of emerging diseases is the ability of a pathogen to transmit between humans. In general, it is thought to be less likely that enveloped viruses and segmented viruses are associated with human-to-human transmission, similar to viruses with acute durations of infection but the evidence for that is largely observational and certainly not black and white (Geoghegan et al., 2016; Walker et al., 2018). For instance, the majority of top ranking epidemic and pandemic threats listed by the world health organization (WHO) are enveloped viruses (“see Relevant Websites section”). Viral host plasticity is not only associated with spill-over but also increases the risk of human-to-human transmission and international spread (Kreuder Johnson et al., 2015). Moreover, the increased interconnectivity and the overall increase of the human population facilitate rapid spread of novel pathogens.

### Disease X

A recent report by the Global Preparedness Monitoring Board warned that a global Influenza pandemic, similar to the 1918 Spanish flu, could spread around the world within 36–50 h, and would take the lives of 50–80 million people. Such an epidemic could destroy nearly 5% of the global economy (“see Relevant Websites section”). The examples of Ebola, SARS, and avian influenza have shown that zoonotic disease outbreaks can be very disruptive because of fear for spread and uncertainty of how to contain them even when there is limited onward transmission (Bartsch et al., 2015; Qiu et al., 2018). (“see Relevant Websites section”). The devastating Ebola outbreak in West Africa in 2014–1015 led to a specific call for action by the members of the World Health Assembly, charging the WHO to come up with a new vision to be better prepared for the future, given the increasing likelihood of such outbreaks. A list of priority diseases was developed, for which an urgent need for accelerated research and development of countermeasures was identified, due to their potential to cause a public health emergency. (“see Relevant Websites section”). In an update in 2018, the term disease X was used to describe a serious international epidemic caused by a pathogen currently unknown to cause human disease. The rationale behind the inclusion of disease X is that a completely unknown disease etiology limits the ability for development of fast track diagnostics, vaccines and therapeutics. Therefore, preparedness and response in case of disease X requires a significantly different approach compared to the other diseases on the list.

According to the International Health Regulations, WHO Member States are obliged to maintain effective disease surveillance and laboratory systems and to report newly emerging diseases that could spread internationally (“see Relevant Websites section”). However, setting up surveillance for diseases that are still unknown is complicated, and extensive surveillance can be costly, especially in the case of diseases that emerge at the human-animal interface. The disease X track therefore is thought to stimulate thinking in terms of generic solutions that increase EID preparedness.

### Emerging Disease Detection and the One Health Concept

A key component of early control of emerging diseases is their early detection (Bonacic Marinovic et al., 2014; Chan et al., 2010). As part of the WHO Blueprint initiative, the need for diagnostics for the priority diseases has been stressed. The West African Ebola virus outbreak in 2014 had already disseminated widely into three countries by the time it was confirmed by an international
laboratory, almost 4 months after the index case succumbed to the disease (Baize et al., 2014; Coltart et al., 2017). Similarly, phylogenetic reconstruction of Zika in the Americas predated the time of introduction to almost two years before it was recognized as a health emergency (Thézé et al., 2018). Although easily criticized, the delays in disease detection are not surprising as symptoms of most EID are not specific, and overlap with major “common” diseases that clinicians are familiar with (Sigfrid et al., 2018). Similarly, clinical diagnostic laboratories focus on these common conditions, and may not have the expertise to detect rare and novel causes of disease (Sigfrid et al., 2018). Efforts to increase preparedness for EID are increasingly moving towards risk-based early detection. As most EID come from animal reservoirs, the need for this has reinvigorated the One Health approach.

The concept of One Health is described by the US Center of Disease Control (CDC) as follows: “One Health recognizes that the health of people is connected to the health of the animals and the environment. It is a collaborative, multisectoral, and transdisciplinary approach—working at the local, regional, national, and global levels—with the goal of achieving optimal health outcomes recognizing the interconnection between people, animals, plants, and their shared environment.” Although the concept has already been known since Hippocrates launched his theories on human health around 400 BCE (“On Airs, Waters, and Places”; Aristotle “Historia Animalium”) The specific term “One Health” however only came up in the 21st century (Evans and Leighton, 2014; Sikkema and Koopmans, 2016). Since then, the One Health concept is increasingly being endorsed and implemented in national and international policy and research. An important milestone was the publication of the FAO-OIE-WHO tripartite concept note, on “Collaboration, sharing responsibilities and coordinating global activities to address health risks at the animal-human-ecosystems interfaces” (“see Relevant Websites section”) Also, the number of scientific publications that mention the term “One Health” showed a major increase in the recent decade (Sikkema and Koopmans, 2016). Although in practice true integration of information and collaboration between different sectors still proves to be challenging (Sikkema and Koopmans, 2016; Farag et al., 2019; Dos et al., 2019; Manlove et al., 2016), the implementation of the One Health concept has great potential for EID preparedness and response.

Moreover, there has been a vast increase of (digital) data in the past decade that has great potential to be used for zoonotic disease prediction, early detection and control (Becker et al., 2019; Masri et al., 2019). This is not only caused by the shift of traditional diagnostics to multi-analyte technologies such as next generation sequencing, but also by the large increase of for example environmental, financial and social media information collection (Simonsen et al., 2016; Shi and Wang, 2019). However, the use of this “Big Data” with different data types of multiple origins also makes the analysis much more challenging (Khoury and Ioannidis, 2014). The use of big data has been advocated and explored in some aspects of public health and infectious disease prediction, but this is also mostly restricted to only one of the required domains (clinical, public health, academia) or sectors (human health, animal health, environmental health, informatics, artificial intelligence) instead of a true crosscutting One Health analysis. Moreover, this, again, calls for multidisciplinary collaborations, since the traditional expertise involved in One Health or Public Health, such as veterinary or medical specialists or epidemiologists, generally do not have sufficient experience in working with such large and diverse data sets.

Developing Targeted, Risk Based Sampling

To identify risk areas, or so-called hotspots of disease emergence or spread, both knowledge of possible drivers or risk factors for emergence can be used, as well as detailed spatial and quantitative information on these drivers, for example locations where ecosystem disruptions took place or where farming systems or livestock population sizes have gone through significant changes. Other information, that could be mapped to identify risk areas for known and unknown diseases are vectors, animal reservoirs, human population, habitat and climate. (“see Relevant Websites section”). There are currently many open-access databases available online, that contain information that has great potential to be used for zoonotic disease prediction, early detection and control. Examples of currently available information are: animal tracking data (Tian et al., 2015) (“see Relevant Websites section”; “see Relevant Websites section” United States Geological Survey), animal and human outbreak information (Cauchemez et al., 2014) (WAHID; ADNS; WHO), animal populations and trade (Simons et al., 2016) (FAOSTAT), weather and climate (Ryan et al., 2015) (NASA; ECA&D; USGS FEWS NET), country economic data (Farag et al., 2018) (World Bank) and many others.

After defining geographical hotspot areas, risk of EID outbreaks also requires a detailed understanding of human and animal populations at risk. For example, past research indicates that humans in contact with animals, especially in the case of wildlife or animal populations that experienced changes in husbandry, population size or other characteristics are at a higher risk of infection with an (emerging) zoonotic pathogen (Jones et al., 2008; Jones et al., 2013; Allen et al., 2017). However, the intensity and nature of the human-animal interface differs greatly, depending on animal species, animal husbandry systems, eating habits, traditions, etc. Additionally, with human demography, migration and travel, current populations and communities are no longer homogeneous or isolated. Selecting a human population at-risk therefore is complex and people-at-risk move in an increasingly large geographical area. (“see Relevant Websites section”).

Therefore, there is an increasing need and necessity to tailor surveillance and risk predictions to local circumstances. This calls for the inclusion of social sciences in disease surveillance and infectious disease preparedness (Bedford et al., 2019). (“see Relevant Websites section”).

Animal trading patterns and common practices surrounding animal trading have been shown to be particularly important factors in the spread of zoonotic infectious diseases. Livestock farming has undergone massive changes and expansion in the past decades, with increasing international trade (“see Relevant Websites section”). Increasing size and connectivity of the trading networks, including human contacts such as farmers, traders and consumers, result in increased risks of disease transmission and
Infrared cameras captured fruit bats feeding on palm sap collection devices, and urinating when the sap collection pots during the night, contaminating the sap with their infectious saliva. (Luby with disease. Several interviews pointed towards fruit bats (Pteropus giganteus) as probable source of infection as they drink from knowledge on possible exposures and risk behaviors. It became clear that drinking raw date palm sap was signi

valuable in outbreak investigations of emerging diseases. Case investigations of a Nipah outbreak in humans in Bangladesh in and on-site slaughtering (Zhou

of mixing of birds of different origins and species but also because of particular preferences in some regions for fresh poultry meat

disease introduction and spread (Zhou

on drinking palm sap was accepted by the local population as intervention (Nahar

contaminating the sap with viruses (Halpin

such as vaccination history was only reported in 0.4%, and travel destination was completed in only 42% of patient dossiers

diagnosis. In practice, complete and timely collection of metadata proves to be challenging. When routine diagnostic data in the

and subject selection (especially in an outbreak situation), appropriate sample type and suf

is important to decide on the optimal sampling protocol, the use of detection methods and the interpretation of results. Moreover,

ty of surveillance and research.

Not only diagnostic testing methods and quality are carefully assessed and compared (Reusken et al., 2015; Charrel et al., 2017; Pas et al., 2015) (“see Relevant Websites section”) but also the standardized collection of metadata is increasingly important in the era of big data and NGS, for correct interpretation and analysis of the large amount of data that is generated. Therefore, standardized epidemiological questionnaires are being developed and published alongside of the guidelines for infectious disease diagnosis. In practice, complete and timely collection of metadata proves to be challenging. When routine diagnostic data in the Netherlands was assessed for its use for surveillance of arboviral infection in travelers, researchers found that essential information such as vaccination history was only reported in 0.4%, and travel destination was completed in only 42% of patient dossiers
Especially during outbreaks, medical records and associated epidemiological information is often incomplete or absent. This has been illustrated for example in Sierra Leone during the Ebola outbreak (Owada et al., 2016). Examples of efforts to standardize infectious disease surveillance and clinical research are the global Consortium for the Standardization of Influenza Seroepidemiology (CONISIE) that is aiming to standardize influenza sero-epidemiology and develop investigation protocols (“see Relevant Websites section”) and the International Severe Acute Respiratory and Emerging Infection Consortium (ISARIC), a federation of clinical research networks, providing tools and protocols for research response to outbreak-prone infectious disease (“see Relevant Websites section”). Moreover, the WHO, FAO and OIE publish extensive laboratory diagnosis guidelines and are involved in training and capacity building activities.

The Value of Non-Invasive and Bulk Samples

Although smart, risk-based strategies can be developed to optimize sampling efficiency, reliable disease monitoring, especially in the case of emerging diseases, requires a huge sample size to reach sufficient population and/or geographical representation. Traditional surveillance of humans and animals make use of invasive sampling, to screen blood samples or swabs for pathogens. However, the use of such samples needs medical-ethical approval that is increasingly difficult to obtain, as well as approval for animal population studies and experiments. Additionally, invasive sampling can cause significant discomfort, can pose an additional risk for infection of healthcare workers or animal care-takers and can only be executed by specialists in the human or veterinary field. Therefore, setting up and validating surveillance using non-invasive sampling can potentially be easier to execute and to scale up as well as better for human and animal welfare.

Feces or urine collection and testing can be a practical and animal friendly surveillance method. Especially in the case of wildlife, where catching and sampling animals can be particularly stressful for an animal, fecal or urine surveillance is very suitable. Feces, or even urine, can be collected without handling the animal or even be in the vicinity at the time of sample collection. This has been described for multiple pathogens, such as Lyssaviruses and Paramyxovirus in bats (Begeman et al., 2020; Peel et al., 2019) and tapeworms in foxes (Umhang et al., 2016). In humans, there may also be a large number of pathogens that can be detected via saliva, urine or feces, although it is generally not included in standard diagnostic algorithms (Niedrig et al., 2018).

Although alternative, non-invasive sample types increase the ease of sample collection and welfare of the sampled subject, the number of samples will not decrease. Therefore, validation of pooled samples or novel sample types that can be used to monitor groups or populations of humans, animals or a certain geographical area. In Asia, environmental surveillance of live animal markets is routinely implemented as main means of monitoring of Avian Influenza viruses (Bai et al., 2019; Henning et al., 2019; Khan et al., 2018). Various surfaces, such as poultry cages, chopping boards and defeathering machines, are sampled and tested on a regular basis as an indirect measure of poultry infections and public health risk. Similarly, environmental sampling are also being used for the detection of pathogens in healthcare settings (Kim et al., 2016; Kapetshi et al., 2018). Additionally, air sampling may be promising, both in hospital settings, farms and even markets and airports (Scoizec et al., 2018; Zhou et al., 2016; Bailey et al., 2018).

Sewage or wastewater monitoring is another example of such a sample type, that can be used to monitor infectious diseases of large numbers of humans. Sewage monitoring has already been used for many years to monitor polio (Asghar et al., 2014) as well as the monitoring and detection of emerging Norovirus and Enterovirus strains (Mabasa et al., 2018; Majumdar and Martin, 2018). However, sewage could have great potential to be used for virus discovery and emerging disease detection (Fernandez-Cassi et al., 2018; Nordahl Petersen et al., 2015). Other sample types, representing large numbers of animals, that can be can be used to monitor circulating of pathogens are: manure composting plants, bulk milk and ponds (Himsworth et al., 2019; Garcia et al., 2014; Balmer et al., 2014).

However, the use of non-invasive sampling or pooled sample types may impact the sensitivity of pathogen detection. In the case of non-invasive sampling, each pathogen may have different shedding characteristics, making it impossible to know the optimal sample type to detect emerging diseases. This also impacts the use of sewage for emerging disease surveillance, for example, because not all pathogens are excreted via feces or urine, making it difficult to detect via sewage sampling.

Catch-All Detection Methods

A challenge for risk-based surveillance is the huge potential diversity of pathogens that could cause human disease when spilling over from an animal reservoir. Therefore, even if targeting detection efforts through the approaches described above would succeed, the choice of diagnostic method is a critical one. Depending on how the risk-based surveillance was organized, the choice of potential pathogens to target may be limited or more extensive. An interesting development is the use of unbiased third-generation metagenomic sequencing to characterize all genomic material (DNA and RNA) in a sample, without prior knowledge of possible etiologies. Clinical and environmental samples can be processed with procedures that either enrich for bacteria, parasites or viruses, and subsequently be subjected to sequencing (Wilson et al., 2019; Takhampunya et al., 2019; Zolfo et al., 2018; Nieuwenhuijse and Koopmans, 2017; Hendriksen et al., 2019).

Analysis generally takes place by assembly of sequence reads and annotating the resulting reads using reference databases of (publicly) known sequences. The metagenomics research field, studying and profiling genetic material abundance in diverse matrices and environments is rapidly growing, as well as the number of novel viruses that are being discovered and described (Simmonds and Aiewsakun, 2018). Often the aim of metagenomics studies of the environment is to map all micro-organisms in...
potential reservoirs in order to identify potential human health threats (Carroll et al., 2018). However, all viruses that have been characterized to date likely only make up a minor fraction (estimated to be around 0.005%) of the estimated total number of viruses on earth (Geoghegan and Holmes, 2017). This means that the number of new viruses and virus families will increase immensely in the coming years. Moreover, the lack of closely related reference virus genomes makes public health risk assessment of novel viruses very complicated (Geoghegan and Holmes, 2017). Moreover, even if viruses belong to a known virus family with known human viruses, this does not necessarily mean that there is a risk of spill-over.

**From Genotype to Phenotype: Deriving Meaningful Information From Genomic Data**

The pathogen genomic sequence alone will often give insufficient information on possible human health risks. Therefore, ideally, metagenomics or NGS approaches are supplemented with phenotypic data such as antigenic characteristics, pathogenicity, virulence, host-specificity and transmission characteristics. For novel variants of known viruses, some indications of phenotype or zoonotic risks can be derived from the sequence, based on experimental study outcomes. The impact of inferring phenotype traits from genotype data can be exemplified by the “H5N1 inventory” compiled by the United States Centers for Disease Control (“see Relevant Websites section”). This inventory summarizes all mutations that have been shown to affect virus replication, virulence, tissue or cellular tropism, host-range, transmission, antigenic properties, immune escape, and antiviral drug resistance.

However, in the case of an emerging virus that was previously unknown, novel phenotypic data needs to be generated. This data is important for risk assessment, but information on potentially relevant sequences or epitopes can also be used for development of diagnostics and preventive antiviral strategies. For example, one of the key components influencing ability to spread for an emerging pathogen from a spill-over event is the level of measured or predicted immunity in the population, as this impacts on the likelihood of infection of individuals (humans, livestock, wildlife) and their ability to shed and spread the infection.

*In silico* epitope prediction can predict B-cell epitopes based on sequence data (Potocnakova et al., 2016). The predicted immunogenic virus proteins can then be used to set up serological assays to determine the prevalence and host range of the virus. For this, multiplex antigen arrays can be used to not only measure antibodies to the newly identified antigen, but also to (distantly) related variants of the same virus family, thus providing information on potential cross-protection or disease enhancing antibodies (Mina et al., 2019; Cleton et al., 2017; Freidl et al., 2015). Possible resistance markers can be predicted when analyzing the sequences, for instance for drugs targeting the polymerase or protease genes. Host binding motifs can be predicted from their location on predicted protein structures. However, all such inferences need to be validated as the choice of in vitro systems and animal models can have a significant impact on their validity (Rothenburg and Brennan, 2020; Setoh et al., 2019; Reyes-Ruiz et al., 2019).

**Conclusion**

The risk of emergence of novel human pathogens has increased in the past decades. Early detection is becoming even more important due to the potential rapid spread and impact considering the ever increasing size of human and animal populations and their movements all over the globe. The unpredictable nature of emergence of diseases makes surveillance and preparedness a huge challenge. However, recent history has shown that outbreaks of emerging diseases will happen again, and all sectors involved in infectious disease surveillance and response need to be ready to detect and handle the next disease X. It has been argued that the design of infectious disease surveillance and response should therefore move from crisis response to true integration and evaluation of a strategy to detect and control emerging diseases (Bedford et al., 2019). This involves a One Health approach, integrating not only the humans, animal and environmental health sectors, but also social sciences, bioinformatics and more. Technical developments in recent years, such as the use of Big Data and metagenomic sequencing will aid the rapid detection of novel pathogens on the human-animal interface.

**Note Added in Proof: December 2020**

**SARS-CoV-2**

In December 2019 several cases of pneumonia of unexplained etiology in patients in Wuhan city (China) linked to a seafood wholesale market were reported to the WHO (“see Relevant Websites section”). In the beginning of 2020 it became clear that this Disease X that had emerged was also a betacoronavirus, most closely related to SARS, that was already on the WHO Blueprint priority list in public health emergency contexts (“see Relevant Websites section”). In the following months the outbreak developed into a pandemic, with over 68 million human cases and 1,55 million deaths, as of 8 December 2020 (Dong et al., 2020).

**One Health and Animal Reservoirs**

Bats are known to harbor a range of different coronaviruses (Cui et al., 2019). Indeed, closely related SARS-like viruses have previously been detected in horse shoe bats, in China (Zhou et al., 2020; Hu et al., 2018). However, although the SARS-CoV-2 genome is 96% identical to the closest bat sequence, the genetic distance between the closest horseshoe bat SARS-like coronavirus
and SARS-COV-2 likely reflects several years and even decades of virus evolution (Boni et al., 2020). SARS-related coronaviruses are also found in pangolins, where specifically the RBD domain is closely related to SARS-CoV-2 (Boni et al., 2020). Therefore, the role of bats as SARS-CoV-2 reservoir remains to be proven and other mammalian species are considered as possible intermediate hosts, as was previously the case for SARS, MERS and Nipah (Epstein et al., 2006; Wang et al., 2005; Reusken et al., 2013). To date, an animal intermediate host of SARS-CoV-2 has not been found yet (“see Relevant Websites section”).

However, multiple animal species are found to be susceptible for SARS-CoV-2. Ferrets, raccoon dogs, cats and hamsters show infection and virus replication after experimental infection as well as the ability to transmit the virus (Shi et al., 2020; Richard et al., 2020; Sia et al., 2020; Freuling et al., 2020). Other animals that showed infection after experimental inoculation include rabbits, dogs and tree shrews (Shi et al., 2020; Mykytyn et al., 2020; Bosco-Lauth et al., 2020). Additionally, animal infections have been detected in the field, mainly in dogs, cats and mink (Sit et al., 2020; Barrs et al., 2020). Although there is evidence for efficient transmission between cats, infection in these animals is not considered a major concern given the small numbers of animals in households. This is different for the recent outbreaks in mink farms in Europe and the US (Cahan, 2020), with the first described SARS-CoV-2 animal-to-human transmissions (Oude Munnink et al., 2020b). These outbreaks were the first large scale outbreaks in animal populations, and large scale mink passages have specifically sparked concern on the risk of specific mutations, affecting virus properties and possibly resulting in immune escape (Koopmans, 2020).

The multiple susceptible animal species and the search for the original animal reservoir, that was at the origin of the SARS-CoV-2 pandemic, clearly shows the need for a One Health approach. Introductions of SARS-CoV-2 into susceptible animal populations can continue to occur, possible resulting in (additional) animal reservoirs and virus evolution and the risk of continuing evolution and spill backs into the human population (Koopmans, 2020; Olival et al., 2020). Therefore, collaboration between different disciplines remains crucial in monitoring, understanding and containing the SARS-CoV-2 pandemic as well as many other (emerging) pathogens.

Emerging Disease Detection, Full Genome Sequencing and Rapid Data Sharing

The Chinese authorities officially announced the isolation of a novel coronavirus (2019-nCoV) as the causative agent on 7 January 2020 (“see Relevant Websites section”) and the full sequence was released in a publicly accessible discussion forum (“see Relevant Websites section”). Four other sequences were shared on 12 January in the Global Initiative on Sharing All Influenza Data (GISAID) database. A validated real-time RT-PCR assay was developed, validated and published online only 5 days later, on 17 January 2020, and published for PCR validation in a peer-reviewed journal on the 23rd of January (“see Relevant Websites section”) (Corman et al., 2020). Validation panels were available on the European Virus Archive (“see Relevant Websites section”) shortly after. The first validated serological assay followed early April (Okba et al., 2020). This clearly illustrates the technical progress that has been made in the last 17 years, as well as the value of virus sequencing and rapid data and sample sharing.

Samples of the first patients in Wuhan city were sequenced using an unbiased deep meta-transcriptomic sequencing method (Wu et al., 2020). When the sequence was known, amplicon-based methods were developed to sequence the new virus in a timely and sensitive manner (Oude Munnink et al., 2020a) (“see Relevant Websites section”). Whole genome sequencing was performed at unprecedented scale, with almost 250,000 SARS-CoV-2 whole genome sequences that had been shared on the GISAID platform as of 8 December 2020. The timely release of unpublished genomic information through GISAID was essential for fast track development of diagnostics, vaccines and therapeutics as well as the application of WGS in outbreak investigation and public health control measures (Oude Munnink et al., 2020a; Voeten et al., 2020).

With the ever-increasing numbers of sequences that are being generated, the need for rapid characterization of viruses with specific mutations remains high. A high number of papers are published describing the evolution and mutations in the SARS-CoV-2 genome, but assessing the relevance and effect on virus properties, and, consequently, public health, is still challenging (Grubaugh et al., 2020).

Population Surveys and Sero-epidemiological Studies

Serologic studies can provide important information for understanding the extent of past transmission, the current state of the epidemic, and future transmission in an affected population. Moreover, serology is a very useful tool on the human-animal interface (Wernike et al., 2020). It can be used to screen potential animal reservoirs, as has been used to determine the likely reservoir species for MERS-CoV, (Reusken et al., 2013; Deng et al., 2020). Serological surveys in several animal species did not point towards the SARS-CoV-2 animal reservoir species, but did show significant exposure of dogs and cats in Wuhan and Italy, which were severely affected by SARS-CoV-2 (Zhang et al., 2020; Patterson et al., 2020). Also, serological assays can be an additional tool to gain insight in the potential and scale of animal-to-human transmission, when combined with epidemiological information on exposure, as was done for mink farm employees on SARS-CoV-2 on infected mink farms (Oude Munnink et al., 2020b; Sikkema et al., 2016). However, it is important to realize that coronaviruses including betacoronaviruses are common in many animal species, and can result in cross reactivity and false positives (Franzo et al., 2020; Nemoto et al., 2019; Erles and Brownlie, 2008).

In addition to patient diagnostics and surveillance efforts in symptomatic and asymptomatic individuals, wastewater sampling can be used to monitor the circulation of SARS-CoV-2 in the population (Medema et al., 2020; Hart and Halden, 2020). This approach is currently integrated in the national COVID-19 surveillance in multiple counties (“see Relevant Websites section”).
Concluding Remarks

With the emergence and worldwide spread of a novel coronavirus, the disease X scenario that many scientists had warned about came true. The SARS-CoV-2 pandemic lead to drastic government measures worldwide, with massive economic and social consequences. The spread of the virus has proven to be difficult to contain, despite extensive lockdowns, information campaigns, travel bans and compulsory mouth masks. However, previous investments in surveillance, diagnostics, novel laboratory techniques, open data sharing and vaccine platforms did pay off. A cluster of pneumonia of unknown origin was detected in December 2019 in Wuhan, and at the end of January 2020, a set of whole genomes are publicly shared and a validated PCR assay has been set up which was implemented in 24 of 30 EU/EEA countries and many more worldwide (Reusken et al., 2020). Moreover, in December 2020, the first COVID-19 vaccine was licensed ("see Relevant Websites section"). The speed of these key developments in the surveillance and control of the new virus is unprecedented. How the SARS-CoV-2 pandemic will evolve remains to be seen, but recent developments reinforce the call for preparedness research and a One Health approach, as highlighted in the current article.

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