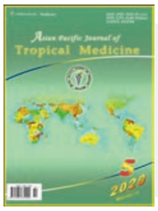

Perspective

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COVID–19 epidemic control approach in Italy

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1. Diffusion of pathogens and globalization

The diffusion of health risks in a globalized world is characterized by an exponential increase of transmission opportunities requiring more important and extensive control and prevention measures against possible impact on public health and agro-zootechnics production. Various keywords in this global situation are: diffusion of vectors, alien and invasive species, mutations, international trade, migrations, emerging diseases, climate changes and global warming. As a result, for example, we can observe the geographic extension of arboviruses and subsequent diffusion of different pathogens as the West Nile, Chikungunya or Zika viruses. All of them are previously negligible African diseases: West Nile (Uganda, 1937), until the beginning of 90s, was sporadic and considered as minor risks for men, and is now the most common cause of mosquito-borne disease in the USA and is included in the list of climatic change indicators. Chikungunya (Tanzania, 1952) previously a self-limiting nonfatal disease was responsible for a serious outbreak at La Réunion in 2005 and could also cause meningo-encephalitis. Zika (Uganda, 1947), previously a banal infection with flu-like symptoms, then caused high numbers of serious fetal brain defects, especially in Brazil during 2015.

The 2019 coronavirus disease (COVID-19) is a new emerging zoonosis. This is not a surprising event, according to the World Health Organization (WHO), more than 60% of newly identified infectious agents that have affected people over the past few decades have been caused by pathogens originating from animals or animal products. Of these zoonotic infections, 70% originate from wildlife, and chiropters have been indicated as important reservoirs of new dangerous and deadly zoonoses such as Ebola, Marburg, Lyssavirus (rabies), Melaka or Henipavirus (Nipah virus). Attention to coronaviruses (CoVs) (hosted worldwide in several bat species, their main reservoir) has also increased during the last decade due to the high number of human infections caused by the zoonotic beta-CoVs, severe acute respiratory syndrome coronavirus (SARSCoV) or Middle East respiratory syndrome coronavirus (MERS-CoV), that cause several respiratory diseases. The genome of CoVs is characterized by a high frequency of mutations and recombination events, increasing their ability to switch hosts and their zoonotic potential. Among coronaviruses, human alpha-CoV, which may cause mild respiratory disease that can change to severe disease in children, elderly and individuals affected by illnesses, revealed their evolutive correlation with genomes of bats origin. Such emergence of a similar risk could not be excluded even in Italy, as suggested by a study, on alpha-CoV genera detected in Italian bats (*Pipistrellus kuhlii*) and present also in other European countries[1].

2. The COVID–19 epidemic in Europe

In 2019, Europe focused on various social, economical and political issues, as welcoming or not migrants, or fighting against unemployment, or contesting legal reforms as on retirement in France. In December, China reported the emergence of a new zoonosis, a novel coronavirus[2] of animal origin[3] (named SARS-CoV-2), affecting people in an epidemic center in Wuhan, a city with the eleven million inhabitants in the province of Hubei (a name unknown to most Europeans until that time). At the beginning, the news attracted public opinion in the same manner

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of various ones reported by the media in the recent previous years as the SARS in Asia, respiratory syndrome in the Middle East or Ebola in Africa, which was considered frightening, but always and luckily far from the developed and hyper medicalized countries. Gradually, the perception changed due to the increasing number of cases and fatalities reported from China, and the growing interest of sanitary authorities. The World Health Organization (WHO) communicated the possibility to declare the pandemic status for the coronavirus infection, a rare event since its establishment in 1948. Even if pandemic was initially not confirmed, European institutions reacted rapidly through the application of a number of preventive measures. Flights from and to China have been suppressed. Health border controls have been strengthened. Guidelines to prevent pathogen diffusion have been prepared and circulated at the different institutional levels, including police forces or educational institutes. Aircrafts equipped with high risk containment facilities have been employed to repatriate citizens from China. Upon arrivals, affected patients have been hospitalized in dedicated health settings. All this demonstrated preparedness and high sanitary technological efficiency against a potential pandemic.

A pandemic, a word that in the memory of Europeans may mean the Spanish flu, which occurred in 1918-1919, just after the first world war. Spanish flu, caused by a H1N1 virus of avian origin, was characterized, as typically actual influenza strains, by high spreading among humans, but in addition high pathogenicity, causing high mortality rate, and killing at least fifty million people.

While in China drastic containment efforts (including millions of people quarantined) allowed the mitigation of the epidemic, which nevertheless accounted for more than 80 000 cases and about 4 600 deaths, some cases were reported in other countries. COVID-19 also reached Europe, and the virus is now in 210 countries and territories on nearly all continents[4]. Despite applied preventive measures, Italy faced an unexpected diffusion of the virus, the highest in Europe. On the 8th of March 2020, the number of cases exceeded 7 000, with a death toll of 366, and only ten days later, on the 17th, cases were about 28 000 with 2 158 deaths[5], and is currently reaching nearly 181 000 cases, with about 2 500 in critical conditions, and 24 114 deaths (20th of April).

3. Eradication or cohabitation with pathogens?

In veterinary medicine, rinderpest has represented one of the most important diseases affecting zootechnics. The virus was widely distributed throughout Europe, Africa, Asia and West Asia. The epidemic in the 1890s wiped out 80%-90% of all cattle in sub-Saharan Africa. An outbreak of rinderpest in imported animals in Belgium in 1920 was the impetus for international cooperation in controlling animal diseases, and a key factor leading to the establishment of the World Organization for Animal Health (Office International des Épizooties: OIE) in 1924. Specific characteristics such as no carrier state, no vertical transmission, no arthropod vector, and availability of vaccines were fundamental elements that suggested the possibility to eradicate rinderpest. Surveillance and control measures were widely applied. Eradication campaigns were launched. The most important programme, the Global Rinderpest Eradication Programme (GREP), was supported by the Food and Agriculture Organization (FAO) of the United Nations and OIE. In 2007, the Somali ecosystem was the only region with rinderpest left. In 2010, FAO announced that it was dropping its field surveillance efforts because it felt that eradication had been achieved. Rinderpest was officially declared worldwide eradicated on 25 May 2011 by the World Organization for Animal Health (OIE). The world's first veterinary school was set up in Lyon, France, in 1761 for the control of rinderpest, which means that it took mankind 250 years to eradicate this disease.

To date, only one infectious disease that affects humans has been eradicated. In 1980, after decades of efforts by the WHO, the World Health Assembly endorsed a statement declaring smallpox eradicated. Coordinated efforts rid the world of a disease that had once killed up to 35% of its victims and left others scarred or blind. Measles is a highly contagious viral illness. The aetiological agent belongs to the genus Morbillivirus, closely related to the Rinderpest virus. Evolutionary history investigations suggest a common virus ancestor evolved in an environment where cattle and humans lived in close proximity, and genetic divergence occurred around the 11th to 12th centuries[6]. Worldwide, measles is a significant cause of morbidity and mortality. In 2000, measles was estimated to cause approximately 31 to 39.9 million illnesses worldwide with an estimated 733 000 to 777 000 deaths, making it the fifth most common cause of death in children under 5 years of age[7]. Control efforts have substantially altered the global distribution. Measles incidence has decreased substantially in regions where vaccination has been instituted, and measles in the developing world has been attributed to low vaccination rates[8]. The World Health Assembly adopted the WHO/UNICEF Global Immunization Vision and Strategy, which included a goal of 90 percent reduction in global measles mortality[9]. A further collaborative effort of the WHO, UNICEF, the American Red Cross, the United States Centers for Disease Control and Prevention, and the United Nations Foundation launched a new Global Measles and Rubella Strategic Plan which covers the period 2012-2020. The Plan includes new global goals for 2015 and 2020: to reduce global measles deaths by at least 95% compared with 2000 levels, and to achieve measles and rubella elimination in at least five WHO regions. Taking into account that, apart New World and Old World monkeys that may become secondarily infected, humans are the primary reservoir, and there are no other known measles virus reservoirs outside of humans[10], there are no asymptomatic infectious carriers, and safe and efficient vaccines are available, thus supporting the potential for successful eradication strategies, measles might be candidate as the next eradicated infectious disease.

4. Choice taken: How to operate?

As above discussed, since eradication is so complex, other options have to be considered. Separation of human beings from the pathogens or a compromised contact with such health risks? Separation is not simple and requires important resources and is often simply unachievable. Probably, a resonated contact with the pathogens is a practicable way to ensure acceptable levels of public health. Also vaccination is in reality a way to ensure contact with the pathogen. However, when a risk is perceived too high, confinement is retained as the unique option. In Italy, the growing numbers of confirmed cases and deaths induced the Government to adopt strict confinement approach. Urgent measures for the contagion containment as per presidential decrees or ordonnances of the Ministries of Health and Interior of the Republic of Italy, dated 23rd of February and 9th and 22nd of March 2020, referred on stringent movement limitation of persons, initially in restricted zone of northern Italy, extended to the entire national territory.

The Italian government introduced wide and drastic measures, including the isolation of entire urban centers, imposing movement restrictions and domestic confinement of their populations. Such measures, initially perceived possibly excessive by neighboring countries, have been further followed as adequate approach. Among consequences, national economy was affected due for example to the drastic drop of tourism. Preventive and control measures required consistent human and economic resources, under the supervision of *ad hoc* national and regional crisis units. Health and logistic assistance to confined populations was a major task, in addition to monitoring activities, flanked with awareness campaigns at national level, since the infection was reported in all the administrative regions. Such activities, at a so wide scale, represented an unprecedent effort supported by the National sanitary system and all public/governmental bodies as the Civil Protection or local and national police; in summary, an activity largely surpassing any crisis management or exercise that Italy had never before faced in the last decades.

The base of the chosen containment approach is the confinement of the human population. Despite super-spreading events are unlikely and restricted in nosocomial environment, occurrence of high viral loads in the upper respiratory tract and the potential for persons infected with SARS-CoV-2 to shed and transmit the infectious virus by aerosol (*e.g.* micro droplets) and fomite while asymptomatic is possible. In addition, it is assumed that infectiousness occurs from 12 hours prior to the onset of symptoms. In confinement circumstance, it is important that operativity will ensure the highest level of efficacy, and asymptomatic contacts are traced as much as possible. However, movement is allowed in specific cases as for health reasons or food supply. Transmission risk associated with such movements should be prevented. Meanwhile, it may be assumed that high level of hygiene is applied in health settings, as an infected shopkeeper might come in contact with a large number of people and goods each day.

From another side, all the movements are monitored by documentary controls performed by public officials on dedicated road checks. Consequently, high numbers of people, moving from their confinement, enter in contact with control operators, who may become key elements among hazard critical points in an epidemiologically sensitive environment. Therefore, accurate information for diffusion mitigation efforts should be considered for controls operated by public officials. With reference to controls on movements of persons operated by public officials, some considerations are necessary, taking into account risk of direct and indirect virus transmission. Aerosol and fomite transmission of SARS-CoV-2 is plausible, since the virus can remain viable and infectious in aerosols for hours and on surfaces up to days, as demonstrated by data provided by a virus stability study performed by the National Institute of Allergy and Infectious Diseases, Hamilton, USA[11]. According to the data, SARS-CoV-2's resistance can be resumed as follows: a) in aerosols virus may remain viable for 3 hours (median estimates of approximately 1.1 to 1.2 hours); on plastic viable virus may be detected up to 72 hours (highest virus load estimated median of approximately 6.8 hours); on cardboard viability do not exceed 24 hours. SARS-CoV-2 strains circulating in Italy are likely to be similar to Asian strains indicating common biological characteristics, including resistance features.

Police (and other public forces) controls should be adapted to minimize contact with self-certification or identity documents which may be owned by a potential asymptomatic SARS-CoV-2 infected subject, to avoid further dissemination of virus contamination to other subjects during control procedures. Taking into account available SARS-CoV-2 resistance data, with reference to self-certification or identity documents, cardboard and plastic may be considered as approximative similar surface reference for paper and plastic/latex gloves, respectively.

Therefore, it might be worthwhile to consider some precautions during control operations. It should be better that each passenger will maintain closed vehicle windows and upon request he may show documents (*e.g.* certificate and identification card) clearly visible behind the window glass. Only in case of doubts, the passenger documentation will undergo more accurate examination, implying physical contact. In this case, adequate distance should be taken from the passenger, to avoid aerosol transmission by ocular mucosa (unless wear protective glasses – avoid contact lenses as per American Academy of Ophthalmology recommendations)[12]. The conjunctive is a potential entry for SARS-CoV-2 propagation. It is important to limit as much as possible the use of contact lenses, taking into account that the virus persists active on hydrogel and silicone even up to 5 days. Furthermore, masks and gloves should be considered risk material to be disposed adequately after use, to avoid environmental contamination. To be noted that during 2003 SARS epidemic in China, Coronavirus was also detected in rodent droppings and the bodies of cockroaches. As the rodents showed no signs of infection or disease, ways of environmental contamination should not be neglected.

5. Conclusions

Effective health and welfare strategies require the support of interdisciplinary interventions, in accordance with the "One health" principle. In particular, harmonious and coordinated efforts between the human healthcare sector and veterinary medicine are required to fight zoonotic diseases. Despite the "One health" principle is indicated as a basis for sustainable health strategies by various international organizations as the WHO, FAO and OIE, further work has to be done in this direction.

Various means of prevention and control are available. Epidemiology, diagnostic, risk analysis, communication, law, cooperation, sanitary capacity and One Health against zoonoses among them. A complex thematic which needs a multidisciplinary approach and an harmonized network of international surveillance to face adequately to such new challenges. Emergency preparedness is the base for adequate and successful fighting against sanitary risks. Nevertheless, when a risk reaches a national level, difficulties become rapidly evident, and human resources become scarce, health settings with not sufficient operational capacity, especially for high numbers of patients in critical conditions, up to minor aspects as dedicated information phone lines often unreachable.

Health institutions and public administrations are currently highly engaged to control and prevent further diffusion of the coronavirus in the country, and certainly the national standards will allow in short/mid term to regain normality. The media are currently carefully following the ongoing epidemic and public is now aware and well informed on the risk, the measures taken and the way to protect himself. There is no doubt that the epidemic will end. However, probably, people will not easily forget this experience. Similarly, health professionals and all stakeholders of risk management will gain precious experience. A lesson learned, possibly useful against an hypothetical occurrence of a novel Spanish flu?

Declare of interest statement

We declare that we have no conflict of interest.

Authors' contributions

MG and PT contributed equally in the present study.

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