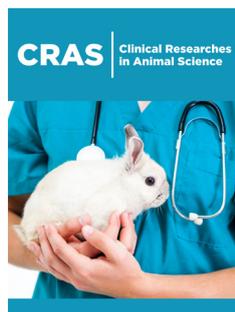


# The Reemergency of Swine Coronaviruses in the Framework of the SARS-CoV-2 Pandemic

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## Opinion

The emergence of SARS-CoV-2 on the human health with more than two thirds of the world population in quarantine, six million of dead as well as the unpredictable economy impact have popularized the morphology of the SARS-CoV 2 virus, the clinical and epidemiological characteristics of the COVID 19 as well as the popularity of human physicians, virologists and epidemiologists with limited experience in the surveillance and control of the CoVs. “Never in the history of humanity have such drastic interventions into the lives of populations occurred in the name of health on such a scale and in a short period of time” [1]. Conversely, veterinarians, particularly, swine practitioners, since 1946, the first description of porcine transmissible gastroenteritis (TGE) have acquired extensive field experience on epidemiology, clinical manifestations, pathology, biosecurity and control of porcine CoVs diseases that can be useful to predict what will be like the post CoVs stage. However, his/her opinion and expertise has not been consulted leaving the publicized concept One Health in a fallacy. The SARS-CoV-2 emergency has been linked with the reemerging of African swine fever virus infection (ASF) in China in 2018, which reduced more than 50% of pig’s stock and favored the illegal trafficking of wild live animals for their commercialization and consumption, such as that occurred in the “Wet Wulhan Market” [2] as well as the creation of wild animal breeding farms. An analogy related with this new pandemic could be postulated with what happened with the development of the pig production. In a few years, it moved from extensive small outdoor farms with a broad spectrum of diseases entities to large indoors “High health” farms with homogeneous genetics, age, immune status and strict biosecurity measures. Otherwise, cities from Europe countries (Spain, Italy, France, Germany, UK) with millions of inhabitants receives in summer season without previous quarantine (external biosecurity), millions of tourists with different “immune status” which could act as subclinical carriers that break the concept of “herd immunity”. In several cities (Barcelona, Paris) SARS-CoV2 has been circulated in the population several months before the pandemic declaration as it was detected in archived sewage. The question arise, how in this new emerging virus appeared without a previously warning such as occur in influenza A virus. The answer was that it did happen. Human SARS-CoV in 2002/3 was reported in 29 countries and MERS in 2011/12 limited to Arabian Peninsula [3]. However, its limited regional diffusion as well as the rapid regression avoid further studies in particular epidemiological surveillance as well as the development of vaccines or antivirals drugs. Why weren’t vaccines developed against these emerging human CoVs?. The answers can be simplified in concept of cost-benefit. The development of a vaccine by private laboratories requires a large investment in R&D and financial support for not

less than 2-5 years for their license with the doubt that after that period no demand for potential application could occur. Besides, in the field of animal health, there is an international policy with certain reportable diseases that a region/country must be free to be able to get access to international market. Coronavirus, an RNA virus, and single-strand DNA viruses both have a wide range of hosts are more likely to generate emerging viruses due to the several properties [4,5]. They multiply in the cell cytoplasm with a high point mutation rate (10<sup>-4</sup>-10<sup>-5</sup> nucleotides per replication cycle) resulting from polymerase errors (infidelity) during transcription (genetic drift) due to poor synthesis by RNA viruses transcriptase enzymes that self-correct errors that occur during viral RNA synthesis. A pig or human being with a viremia by RNA virus will give rise in each multiplication cycle to a spectrum of "mutants" that have variations of genome sequences closely related to the parent virus called "*quasispecies*" or "*cloud*". *Quasispecies* is defined as the total number of variations originating from a related but genetically distinct viral genome continually subject to competition, selection, genetic variation and host pressure and which contribute to characterizing a viral population [5]. Many of these variants with changes in critical areas are not viable (defective viral particles) and are dangerous for the survival of the virus, however in certain cases those changes are beneficial for viral replication and dissemination in a particular environment or "*fitness*" (environment, immunity, genetics, age, nutrition, vaccines, stress, other pathogens). As a consequence, a "*cloud*" of variants will originate through a series of multiplication cycles. The new generation of viruses produced at each multiplication cycle at the cellular level or at each interspecies jump might had antigenic and immunogenic modifications, deletions or insertions. The "*quasispecies*" concept was a mathematical development to explain the evolution of life in the "pre-cellular RNA" stage and today to explain the evolution dynamics of RNA viruses [2,5-7]. Viruses' fitness is more adaptable when the susceptible animal-human population is large, so the global trend towards mega-productions of pigs is a practice that favor of appearance of emerging viruses [6]. Likewise, farms with highest health status are most likely to detect new CoV as happened in Argentina in swine with hemagglutinating encephalomyelitis (PHE), influenza H3N2 human-like, reassortants H1N1pdm09 and TGE [4,8-11]. In analogy, cities with high health standards population are more like to exhibit clinical signs. Porcine CoV antigenic *drift* does not seem to occur as fast as was in SARS-CoV2 ( $\delta$  and omicron strains). Change of TGE, with enteric tropism, to porcine respiratory coronavirus (PRCoV) with respiratory tropism took 38 years and porcine epidemic diarrhea (PED) of low pathogenicity to PED of high pathogenicity, 34 years. Recombination seems to be the most effective mechanism in the evolution of CoVs and occurs between different genomes within strain the same subgroup such happened between two porcine

$\alpha$ -CoVs reported in Italy, Germany and Slovakia that have the property of sharing the TGE spinal column and PED S spicule and called swine enteric coronavirus (SeCoV) [7,12]. The mechanism is due to a discontinuous strategy used by polymerases and the presence in the genome of regulatory sequences in transcription that originate phenotypes with a wide range of virulence and tropism [13]. How it happened with emerging pigs CoV (HP-PED, delta CoV, SeCoV) SARS-CoV2 is here to stay [14,15]. Now on, will pig and human CoV behave like the influenza virus with emerging strains of periodic presentations? We still don't have the answer.

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