

Historical and methodological highlights of quarantine measures: from ancient plague epidemics to current coronavirus disease (COVID-19) pandemic

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Sir,

The ongoing 2020 coronavirus disease (COVID-19) pandemic is an enormous challenge for the health systems and the entire societies of the countries involved. Since at present the outbreak continues to evolve (April 2020), the World Health Organization (WHO) has declared it a public health emergency of international concern, specifying that public health interventions aimed at the prevention of the further spread of this disease include quarantine (1). Quarantine, that may be defined as a restraint on the activities of people or on the traffic of goods, targeted to the prevention of the diffusion of communicable pathologies, is a concept profoundly rooted in the history of mankind (2-6).

From an epidemiological point of view, quarantine has been implemented from many centuries in Europe and the health concept underlying quarantine is embedded in the health history of Western civilization. Even if in the twentieth century quarantine has been, at least to a certain extent, underestimated in the Western world, mainly because of the large availability of powerful vaccines and effective antimicrobial drugs, its actuality is evident (7-9). Infectious diseases have not been defeated, not even in the Western world; the pandemic of COVID-19 clearly indicates this, and quarantine as an effective measure for the containing of contagion still proves to be fundamental even in the present global emergency. The current COVID-19 pandemic scenario is characterized by the complete absence so far of vaccines targeted to coronavirus and by the presence of few pharmacological agents. In such an epidemiological context, not only does the intro-

duction of quarantine interventions have the potential of delaying the penetration of infectious disease into a geographical zone or a country, but it also has the potential of delaying the peak of the epidemic in an area in which the transmission of the virus is already ongoing (10-13).

From a linguistic point of view, the word quarantine derives from the Italian term “quaranta”, meaning forty. Forty days was in effect the time period, already identified by the Hippocratic School in the fifth century B.C., within which “acute” transmissible diseases, such as plague, manifested themselves. In the Hippocratic conceptual framework, pathologies becoming clinically evident after forty days could not be acute, and therefore plague could be indirectly ruled out. Consequently, the pathological paradigm of plague set a standard of forty days for the fixed length of preventive measures, and its reference standard was quarantine (14, 15).

Forty days was also the length of the Medieval quarantine established for plague in the Republic of Venice (Italy) in the course of the fourteenth century A.D.. After the so-called “plague of Justinian” (541-543 A.D.), an outbreak that afflicted the Eastern Roman Empire, plague virtually disappeared from Europe; nevertheless, its later resurgence in the XIV century was devastating. During the famous 1347-1349 Black Death, a great epidemic of plague that led to the death of about 30% of the European population of the time, a council of sages had the task of detaining both single persons and entire ships in the Venetian lagoon for forty days (16).

From the coining of the term “quarantine” onwards, Italy has always played a major role in defining

and developing preventive health measures in the history of Western world. Not by chance, the word "lazzaretto" too, the place where quarantine was materially performed, comes from Italy; in the fourteenth century the Republic of Venice again disposed that the quarantine of clearly infected or just suspected persons with plague should be performed on the island of the Venetian lagoon where the monastery of Santa Maria of Nazareth was, and whose health personnel came from the hospital of Saint Lazzaro (1423). It was in 1486, in another Venetian island, that the so-called "lazzaretto novo" for the quarantine of persons and goods was established. In the late Middle-Ages the foundation of lazarettos was crucial; since the physicians of the time, due to the absence of effective therapeutic agents, were not able to cure individual patients, health authorities intervened with regard to the care, in a preventive perspective, of the health of entire communities, thus giving rise in Italy to public health interventions and initial sanitary administration (17, 18). Quarantine was the cornerstone of preventive measures for Medieval times, and its linguistic Italian origin is worth remembering; for example, the word quarantine made its appearance in the English language only centuries later, in the sixteen hundreds.

From a historical point of view, it was during the Renaissance period that, on the one hand, the first thorough notion of contagion appeared in Europe thanks to the Italian physician Girolamo Fracastoro (1476/78-1553) and, on the other, bills of health were introduced to expand and potentiate the quarantine health system. Fracastoro hypothesized that small particles could transmit diseases, paving the way to the idea of the structured air transmission of infectious pathologies (3). Bills of health were certificates declaring that the last port frequented by a ship was clear from diseases, and that as a consequence persons and goods in that ship were (according to the medical knowledge of the time) healthy. Health regulations became diffused in the Renaissance centuries, as documented by an official paper of the Health Authority of Milan (Italy), dating back to 1577. In this text the opportunities for people meeting were limited by law in the course of epidemics, and it furthermore ordained the suspension of public markets and religious ceremonies, also forbidding children to leave their homes (19). Recent Italian government legal

dispositions during the current COVID-19 pandemic have therefore clearly documentable historical roots dating back to approximately five centuries ago, and repropose them almost exactly. Moreover, the Italian writer Alessandro Manzoni (1785-1873) in his masterpiece "I Promessi Sposi" ("The Betrothed"), while describing the 1630 plague epidemic in Milan, remembered that even more drastic measures were taken in that occasion, including domestic isolation (19, 20).

In more recent times (2003) the violent onset of a "new" epidemic, the severe acute respiratory syndrome (SARS), boosted the return of the ever-lasting measure of quarantine (21). On that occasion the US Centers for Disease Control and Prevention explicitly stated that quarantine measures were very effective in protecting people from severe acute respiratory syndrome (3); in the highly technological therapeutic medicine of the third millennium, historical preventive measures proved, once again, to be of paramount importance. For SARS the appropriate length of quarantine was 10 days, while today (April 2020), in accordance with the incubation period of each specific infectious disease, as illustrated in the next section of this paper, that of the COVID-19 is 14 days (22, 23).

From a methodological point of view, the term "quarantine" has a remarkable wealth of meanings, and different parameters are traceable in the original use of the term itself, including "pathology", "setting", "time", "separation" and "restraint" (24). Pathology refers to the variety of diseases which, in the course of Western history, have been subjected to quarantine, ranging from cholera to yellow fever, from plague to coronavirus disease. Setting refers to the context in which quarantine has been applied, ranging from specific geographical areas to whole nations. Time refers to the temporal period of implementation of this preventive measure, classically of forty days for plague, but with changing lengths according to the (known or presumed) incubation period of different infectious diseases. Separation and restraint are relative on the one hand to the variety of subjects involved in quarantine (classically people and means of transportation, but also animals and goods) and on the other to the degree of the necessary limitation of individual autonomy weighed against the public health risk. These parameters have undergone profound changes through time, but all retain their

intrinsic value and relevance. Not by chance, for the current COVID-19 pandemic, has the World Health Organization issued overall indications relative to the global containment strategy, that can be comprised under the preceding parameters. In fact, the current approach for coronavirus disease includes the timely identification of laboratory-confirmed cases and their consequent isolation and management at home or in a medical facility. It should also be remembered that quarantine is formally included in the legal framework of the 2005 International Health Regulations, and exactly in articles 30, 31 and 32 (1).

The lessons of the past are always pertinent for the present and for the future, in particular from a public health standpoint (25). One of the most relevant of them is connected with previous influenza pandemics, similar to the current COVID-19 2019/2020 pandemic, and it indicates that it is practically impossible, even in recent times, to contain the infection in the geographic area where it has risen and to prevent its trans-national disseminated spread. With specific reference to the COVID-19 pandemic, therefore, health authorities still adopt “classical” preventive interventions, namely workplace social distancing measures and quarantine, to reduce the transmission of the disease. In the course of the present world diffusion of coronavirus, such measures aim at achieving different effects, including that of delaying the epidemic peak so as to gain time for the appropriate preparation of national health systems, that of decreasing the magnitude of epidemic peaks so as to reduce the number of deaths and that of diluting the spread of infections so as to support in-hospital and out-patient health care (22).

Only the future will testify the precise overall effectiveness of preventive public health interventions in containing the impact of the present coronavirus pandemic. However, what in this epidemiological scenario is already known, is that the multi-century international health value of quarantine remains essential and unavoidable.

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