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Editorial

Epidemics will always come (and go): The need to prepare for the next one, research on COVID-19, and the role of molecular and cellular endocrinology



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It was almost 3000 thousand years ago and the Greeks were at war (Rees, 1991). Agamemnon and Achilles were fighting for supremacy, and the former refused to return the daughter of Chryses, Apollo's priest. Apollo, the God, got mad and what did he punish the Greeks with? an epidemic, which killed many men. A savant told the Greeks that the only way the epidemic would end, would be if Agamemnon gave up the girl, which he did only after he took away Achilles's girl, the beautiful Trojan Briseïs. Of course, the story went on but not before the Greeks and other allied nations were affected by the epidemic. Both Agamemnon and Achilles, the two competing leaders had to sacrifice, to end the epidemic.

This is probably the first historical documentation of a massive, communicative illness. The notion of a sacrifice to end it was explicit in the Homeric description, and it rings so true today: you can't end an epidemic without some sort of sacrifice!

Epidemics arise because humans live in close proximity, in urban environments and can travel to suburban and rural landscapes spreading disease; epidemics started as soon as urban settings and organized societies were established (McNeill, 1976). The Greeks, among the first people on earth to live in cities, run organized communities and have large armies and navies, knew early on that proximity to each other could lead to communicative diseases. Hippocrates talked about lepra, its transmission and how, like COVID-19 today, "these diseases are easier to heal when they appear in the youngest patients and are of the most recent origin" (Prorrhetic, 1995).

As Jared Diamond called it in his best seller "Guns, germs, and steel" in 1997, the lethal gift of domesticated and other livestock to the first human settlements (Diamond, 1999) was (infectious) disease: from measles, tuberculosis and small pox (all from cattle) to typhus, the plague (Black Death), and cholera of the middle ages, to the flu, pertussis, malaria, AIDS, SARS, Zika and now COVID-19, our urban life is susceptible to unexpected entry, easy transmission, and massive casualties. For as long as humans live next to and/or depend on livestock, animal pathogens, from viruses to bacteria and parasites will get transmitted directly to people and cause epidemics.

So, none of this is new: from the epidemic of the Greek troops in Troy, to the typhus of Athens (430-426 BCE) which killed a quarter of

its population, including its leader Pericles and helped Sparta to eventually win the Peloponnesian war, to the smallpox of Rome which killed thousands of Romans between 165 and 180 CE, to Constantinople's so-called Justinian plague (541–542 CE), and the European Black death (1347–1351 CE) which led to millions of people (one third to one half of the population at the respective time and places) dying from the plague (transmitted from rats and their fleas), to the modern era, the cholera epidemics of New York city in 1832, 1849, and 1866, the 1918 Spanish and 1957 Asian flu pandemics, and the AIDS, SARS and Zika epidemics of the 1980s and 2010s, respectively, transmissions of infectious agents to humans from wildlife or domestic species and from human-to-human contact has caused havoc to societies from death, to economic and cultural deprivation, and at times seismic changes and historical shifts. As climate changes and population movements continue unabated, the chances for epidemics (and consequently pandemics) increase.

What are the lessons for us in 2020? Like any other adversity, an epidemic can teach us some important things. First, epidemics are a fact of life: all we can do is learn the lessons from this one and be better prepared for the next one; because the next one will be here, in our lifetime, almost certainly. Second, we are so interconnected that what millennia ago took decades and/or centuries to spread, now takes mere weeks, or even days. It is unacceptable to demonize a "foreigner's virus"; it is essential to accept that pathogens do not recognize borders, social classes, or other human-made distinctions and it is critical to study other determinants of pathogenicity (biological factors such as age and sex, or environmental factors, such as climate and location). The connectivity of our times has an inescapable consequence for our societies: the health of anyone is concerning all of us and we can't afford to allow certain regions or populations to be affected by an infectious disease that may spread. Third, health systems are necessary to fight epidemics, safeguard the population, and prevent the next widespread disease. A centralized care system is needed regardless of whether there is single or multiple payers and private or public funding for its function. In fact, flexibility in any centralized system is a must, as recent experience with the best performing systems in response to COVID-19 demonstrates, too. Last, but not least, a research infrastructure needs to

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be built to exploit the amazing new tools of modern biology, computational A.I., and other disciplines that will be able to respond to new challenges quicker and more effectively than what happened with COVID-19.

Which brings us to the current situation and the role of each of us, as cellular and molecular endocrinologists and researchers. We know that patients with diabetes mellitus (DM), hypertension (HTN), obesity, and cardiovascular morbidities, (but interestingly not lung diseases, as frequently) are at higher risk for COVID-19-related complications (Zhou et al., 2020). Furthermore, DM appears to be the most common comorbidity among COVID-19 deaths (Zhou et al., 2020; Drucker, 2020). Molecular and cellular work was essential in understanding how COVID-19 interacts with angiotensin-converting enzyme 2 (ACE2) receptors (Hirano and Murakami, 2020). Higher expression of ACE2 protein in the pancreatic islets has been associated with damage by corona viruses and resultant DM (Liu et al., 2020). Interaction with ACE2 may prove to be the Achilles' heel for the novel virus as it has already been exploited to stop its propagation in vitro (Monteil et al., 2020). In addition, there is a biased sex ratio among COVID-19 patients (more males being affected than females); it is important to study the possible effects of lifestyle and/or potential link to sex hormones or genetic sex, with regards to this significant observation (Cai, 2020; Gausman and Langer).

At Molecular & Cellular Endocrinology (MCE) we join the call from many to increase research infrastructure to fight the current and the inevitable next epidemic.

And we remain committed to publishing the best science towards this goal. We invite you to submit your research on the interplay between COVID-19 (SARS-Cov-2) and cellular and molecular endocrinology to MCE.

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