COVID-19 Commentary – February 28, 2020

"He was born with a gift of laughter and a sense that the world was mad."

Scaramouche (Rafael Sabitini)

I began to write this commentary last weekend but the rapid evolution of events and reactions each day since has delayed its completion. Now looking back over the past few days I feel today as if Scaramouche has been cloned and is alive and well but has lost his gift of laughter.

Over the past week, there has, indeed, been a significant spike in the number of COVID-19 cases reported outside of China and some 50 countries are now involved. Paralleling this, there has been a concomitant and crescentic rise in global anti-Chinese sentiment which continues to cause significant socio-economic harm to China and its citizens, as well as people of Chinese extraction residing in countries around the world. By extension, others of Asian heritage are similarly affected and are likewise too often shunned and avoided.

And now, in light of recent outbreaks the global economy is being threatened with a 3000 point loss in the US Dow Jones Average alone, losses characteristic of those suffered across the Globe. Unfortunately, alarmist headlines and newscasts continue to cultivate the fears and paranoia underlying these reactions which, once instilled are difficult, if not impossible, to reverse. Just as difficult to reverse are the national policy decisions that lead to closed borders, disrupted transportation systems and official exclusionary actions.

The question for medical and public health leaders to address is whether or not these responses are justified by an analysis of our data to date on the COVID-19 epidemic and our knowledge of the epidemiology of SARS and MERS.

In describing what we can expect as to the public health implications of COVID-19, we should accept two facts:

(1) there is a lot more we do not know about this agent as opposed to what we do know, and
(2) the data and numbers, and their implications, change over time and guidance on treatment protocols, risks , and control measures should be adjusted as our knowledge base improves. At this point in time, as the epidemic in China abates, I believe there is more to be accomplished by focusing on the epidemiological characteristics of the cases

OUTSIDE of China, where new cases now outnumber new cases reported from within China. The spread outside of China is also reflected in the number of countries reporting at least one case.

While this spread is certainly a cause for concern and vigilance, we must remember that, in all likelihood, there has been continued global exposure to COVID-19 for at least two months now and probably longer, and we might reasonably expect to see a significantly greater number of cases in more countries at this juncture. Further, given the experiences in China, we would expect to see more explosive outbreaks than the limited number reported this week. The specific reasons for these results are difficult to define specifically they are probably due to the containment measures taken in China coupled with the increased awareness, early case identification and effective public health contact tracing taking place outside of China, and given the clustering of these outbreaks, some degree of super-spreader effect.

Another interesting aspect of the extra-China cases (excluding the Diamond Princess) is that the majority have occurred within other Asian countries and are associated with cluster outbreaks. This of course, can be explained, in whole or in part, by proximity to China with increased person to person contact and the effect of increased spreading by some individuals. Another possible contributor to this pattern that I have not seen addressed is the possible increased susceptibility to COVID-19 in Chinese and other Asians. Much has been written about the S protein viral mutation spike that characterizes COVID-19 and accounts for the increased infectiousness at the cellular level within the respiratory system and other tissues as well. Further, it is not unreasonable, given current data, to postulate that there is likewise an increased affinity to infection in Chinese and other Asians based on undefined inheritable factors at the cellular, receptor level. This would help explain the apparent differences in COVID-19 epidemiology within and outside China, and would certainly be worth examining in the development of vaccines and pharmacological countermeasures going forward.

Before going on to discuss COVID-19 relative risks outside of China, there are some considerations we should take into account regarding the virus itself. COVID-19 is defined by a single mutation in a complex RNA virus; it is still a corona virus and can be expected to behave as other members of this family, a family that has been part of our microbial ecology for thousands of years. As an infectious agent, corona viruses generally cause a relatively mild upper respiratory infection and are responsible for 20-25 percent of the "colds" we have each year. They are seasonal, generally active in winter, do not confer lasting immunity, and have a very low mortality rate; further, up to 50 percent of cases may be sub-clinical. With COVID-19, as with SARS and MERS before it, the mutation in the outer envelope enhances invasion of cells in the lower

respiratory system and leads to significant pneumonic complications, with significantly higher mortality, especially among the elderly with co-morbidities such as cardiovascular disease and diabetes. One other characteristic of the virus we need to consider when looking at risks and proposed interventions is its relative viability in the environment. As a large enveloped virus that can be spread by the respiratory and other possible routes such as the GI tract, it has shown a relative hardiness and survivability in the environment.

Turning now to the risk of cases and outbreaks outside of China. We are witnessing them in several countries and must be concerned with addressing these and controlling further spread to the degree possible. What we need to understand is that these sporadic cases and outbreaks will continue to occur; what we need to further understand is that with case identification, proper clinical intervention and effective contract tracing, the overall attack rates and mortality from COVID-19 can be mitigated as per our experience with SARS and MERS. However, the real issue here is better quantifying and explaining what the risk is in terms of what we know, not what we fear. Unfortunately, we tend to dichotomize the risk to a great extent as all or none and react accordingly. Based on the fear generated, we take the conservative position and assume great risk, when often in fact the science supports the opposite. And as we increase the risk side of the equation, we do the same on the response side and turn to quarantines, exclusion policies, and stigmatizing whole classes of people. In the final analysis, as with SARS and Ebola, the negative consequences outweigh the benefits.

In the case of COVID-19, the public health irony is that the group we are stigmatizing as dangerous may well, in the end analysis, deserve increased protective measures. So what do we do? The only effective antidote, in my view, short of an available vaccine or treatment, is striving to educate our citizens as to what we currently know of corona viruses in general and COVID-19 in particular with emphasis on the relative risks to individuals and communities. Further, these messages need to be consistent, current, and delivered through the media outlets from which most of us gain our information and not buried in relatively obscure sites frequented by scientists and health professionals.

And that brings me to another concern that needs to be addressed before we replay this scenario with the appearance of the next novel bio-agent and that is the definition of what we mean by a pandemic and its declaration. WHO is poised to declare COVID-19 a pandemic if they have not done so already. What do we mean by a pandemic? Historically, it defined an-out break caused by an agent both highly infectious and pathogenic. If we look at the COVID-19 attack rate (in terms of identified cases), it is less than one percent for Hubei province and infinitesimal from a world perspective. This is

not to downplay the seriousness of COVID-19 or its potential for further spread; rather it is to use caution in using such a highly charged term which will only exacerbate the fear and the resulting socio-economic harms from ill-advised policies based on emotion not science. We should not use such a term in the sense of yes it is or no it is not a pandemic - we are again guilty of dichotomizing a continuous variable. We have a Richter scale for earthquakes and a Saffir-Simpson hurricane scale; we need to build a corresponding scale for pandemics: one that quantifies risk and doesn't needlessly fuel fear with its destructive consequences.

In summary, the current risk to individuals in the US on the whole is minimal. The risk to individuals with known contact to a case is of course real and appropriate actions need to be taken which include medical and public health interventions. For the rest of the population following the common sense recommendations for minimizing exposure to seasonal influenza should be followed. More stringent measures should only be applied when and if risk measurably increases. From a national perspective airport screening is certainly a reasonable measure but understanding it is a porous measure at best. Far more important is the investment in public health infrastructure and the necessary enterprise for accelerated vaccine and countermeasure development.

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