The only solution is large-scale testing: GAUTAM MENON

Gautam I. Menon is a professor of physics and computational biology at Ashoka University, Sonepat, and the Institute of Mathematical Sciences, Chennai. In the interview with Ananya Dasgupta he answers our questions about the global pandemic COVID-19, especially in the Indian context.

Q: ***What can be done to prevent a similar pandemic in the near future given that the present one had its origin in a wet market in Wuhan, dealing with consumption of wild animals?***

GAUTAM MENON: There are many reasons to shut down those parts of wet markets that deal with exotic and endangered species, the possibility that novel viruses could jump from animals to humans under such conditions being only one of them. Better surveillance for potential emerging diseases, strong basic research funding for laboratories to study them in the intervals between outbreaks, more attention to ecological issues connected to the destruction of habitats and implications for the animal-human interface, and far more attention to the determinants of a high quality public health system that can be used by rich and poor alike would all help us deal better with a pandemic in the future. The One Health initiative of the WHO is particularly important in this regard, since it recognizes that an integrated multi-sector approach, combining public health, animal health, plant health and the environment is the best way to deal with emerging public health challenges.

Q: ***We hear that the regular flu virus mutates so rapidly that a vaccine made for one year's flu season has very limited use the next year. Do we know yet how fast the coronavirus mutates? Are there already many distinguishably different strains of the virus? If so, do some strains have a higher mortality rate than others? How is India placed in this regard?***

GM: SARS-CoV-2 (which is the virus that causes COVID-19 and the virus we mean when we say 'coronavirus') is an RNA virus, so it mutates at a faster rate than DNA viruses. The coronavirus doesn't seem to be mutating very fast, perhaps about 4 times slower than for influenza, but the influenza virus does have a more complex (segmented) genome with many more options for re-assortment. There are already multiple distinguishable strains of SARS-CoV-2 and these have been used to identify when the virus was introduced into different countries. We have no information about whether the different strains are noticeably different in terms of their virulence. We don't have data for India yet because of a lack of sequences (only 4 so far) and no ability to correlate the strains to patient records to determine changes in virulence.

Q: ***Is there an Indian effort to make a vaccine against the coronavirus? If so, which labs are leading this effort?***

GM: I'm not knowledgeable about the ongoing vaccine efforts in India, although I am sure the NIV in Pune and the NII in Delhi, to name just two organizations that will be able to, are both working on vaccines. The large-scale efforts are from outside India. The multi-national coalition for epidemic preparedness (CEPI) is funding eight vaccine technology efforts, from Curevac, Inovio, Moderna, Novavax, the University of Queensland, the University of Hong Kong, Oxford University and an Institut Pasteur-led consortium. There are a large number of initiatives going on apart from these.

Q: ***What is a realistic timescale for the development and testing of a vaccine? Once a vaccine has been developed and validated, how long would it take to produce billions of shots of the vaccine?***
GM: The development of a vaccine, pre-clinical testing and the sequence of phased trials to assess safety and efficacy should take between a year to 18 months in the best case scenario. My guess is that ramping up production should not be a rate-limiting factor, given the high levels of public and private support to make an inexpensive vaccine available to the world.

Q: ***Given the fact that most slum dwellers in - e.g. Mumbai - live in very cramped apartments and also share water and toilet facilities, is there any chance that a lockdown can be successfully implemented in urban Indian slums?***
GM: The challenges posed by very dense urban agglomerations is a huge challenge for epidemic control at all times. The current strategy of a large-scale lockdown will be hard to implement there for any length of time. The only - and best - solution is large-scale testing to identify those infected, as well as those immune because of having caught the disease earlier.

Q: ***Do any of the epidemiological models of the spread of the virus make a serious effort to incorporate Indian realities - e.g. the near impossibility of social distancing in urban Indian slums - into their equations?***
GM: No, none of them do, currently. Some work that we are doing currently using agent-based models with very detailed information about a specific urban slum region for which we have data should help us understand this question better. This model can be extended to other regions if we have information about them.

Q: ***The lockdown in Italy seems to have been pretty successful - the daily growth of infected people is now below 3 per cent, significantly lower than a couple of weeks ago. If the lockdown were to be eased tomorrow, however, wouldn't the rate of infections pick up again?***
GM: That, in general, will be the case — in that case numbers will rise post-lockdown. The idea of the lockdown is to be able to isolate individual cases and quarantine them while imposing a high level of social distancing by fiat to halt the epidemic. If all cases can be identified and quarantined so as to prevent further spread, that would severely slow or even halt the epidemic in its tracks. However, this is typically infeasible and there will be some stealthy growth in the number of cases, typically asymptomatics that our current policies of identifying potential people infected will not access. Thus, numbers should be expected to grow again once the lockdown is withdrawn. Virtually all models I know of predict this.

Q: ***We are now over 3 weeks into the Indian lockdown. Is there any evidence from the figures that the lockdown is beginning to work? Can this be quantified in any way?***
GM: There seems to be a slight leveling off of the number of cases per day but I would certainly not risk saying this definitively. We have too little data to tell. Also, we have no idea of the spread of the disease among patients who remain asymptomatic.

Q: ***What effect do you think the large scale movement of migrant workers had on the spread of the disease? Has this reality been incorporated into any of the epidemiological models that try to predict the progress of the disease in India?***
GM: We don't know what the background levels of infection are, given that asymptomatic individuals may form 75 per cent or more of cases, and we certainly don't know the extent to which these migrant workers might have been infected. Absent this information, it is impossible to model this effect at any convincing level. Models we are currently working on look at flows of people between states and how the migration of infected people might promote the epidemic in places where it has not reached yet. But these models must make certain assumptions and it isn't clear which input numbers might represent reality.

Q: ***Are antibody tests (as opposed to antigen tests) being used in India?***
GM: The ICMR page lists 7 antibody-based rapid tests that have been validated by the NIV. To my understanding, these have not been used at scale yet but imagine they will be very soon; there's nothing to prevent this. The bulk of current testing is being done using the real-time-RT-PCR method.

Q: ***We hear that the rate of testing of the infection in India is one of the lowest in the world per capita? Why is the case? Presumably the low rate of testing means that the official figures underestimate the extent of the spread of the disease in India. Would you be willing to venture a guess for the extent of the underestimation? Is the true number of infected people likely to be twice, or ten times or a hundred times the official figures?***
GM: My own guess is that it is significantly higher. Somewhere between a factor of 10 and 100 would be my own guess.

Q: ***Is the official count of the number of deaths due to COVID in India likely to be more reliable than the count of the total number of patients? Or is it plausible that several deaths take place outside hospitals and so are not recorded?***
GM: We don't know this and there are many problems. One is the fear of stigmatization, so patients would avoid going to a doctor in the first place until it might be too late. The other is the fact that most patients who die have comorbidities, such as cardio-vascular conditions or diabetes or some respiratory

condition, so it's not necessary that the death will be recorded as having been due to COVID-19. So I'd think it's plausible that the count of COVID-19 associated deaths is underestimated, perhaps severely, although we don't know.

Q: ***Do you know whether hospitals in parts of India are beginning to report a noticeable rise in the number of severe cases of pneumonia in India?***
GM: As far as I know, based on anecdotal evidence, there have been no reports of an unusually large number of cases that are straining ICUs, say of patients with COVID-like symptoms or general symptoms of respiratory infections, such as generic severe acute respiratory illness (SARI) or influenza-like illness (ILI). This is heartening if it's really the case, since it would suggest a milder trajectory for the epidemic in India. Whether this is still early days for the epidemic and whether rising numbers of serious cases might be seen only later, is a topic of discussion at the moment.

Q: ***Fatality rates from the disease have varied greatly from place to place. For instance, fatality rates in Italy are on the higher side, while those in Germany are on the lower side. What is the reason for this difference? Where does India stand on this scale?***
GM: Italy is a somewhat different case because of its relatively larger fraction of elderly people who are at an increased risk, compared to, say, India. The countries that do better have universal public health, high-quality nursing care, very good follow up in contact tracing, a general faith in the public health system and good communication between the government and the citizenry. In India, I think we're doing a good job on some fronts, such as the way state machinery was mobilized for the lock-down. Communications from the Prime Minister convey the seriousness with which the government is taking the epidemic. We're not doing well on other aspects of communication and transparency and especially in making data available for scientists outside the government system to access. There is an epidemic of misinformation about the disease in India as well which many of us are making an effort to tackle, but this is not unique to India. □

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