

Silent disease-spreading

How important is “silent spreading” in the covid-19 epidemic?

Possibly, very

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FEW STORIES are as prominent in the study of infectious diseases as that of Mary Mallon, a cook to wealthy families, and also to a maternity hospital, in New York in the early 1900s. As she went from one employer to another, typhoid fever, then deadly in one case in ten, followed in her wake. Public-health officials eventually joined the dots and identified her as a carrier of *Salmonella typhi*, the bacterium that causes the disease. What was striking about Typhoid Mary, as the newspapers nicknamed her, was that she herself was healthy—proof that people could harbour and transmit *S. typhi* without showing symptoms of the illness it causes.

Such silent transmission, as epidemiologists call the phenomenon, has since been observed in many diseases—among them measles, influenza and HIV/AIDS. A fresh addition to the list is SARS-CoV-2, the coronavirus behind the covid-19 pandemic now raging. Accumulating evidence suggests a substantial chunk of the infections it causes are transmitted by people whose symptoms have not yet appeared—or even, like Mallon, who never develop symptoms at all. That has implications for the methods countries are employing to curb the pandemic (see article).

Currently, none of the evidence on asymptomatic transmission is watertight. According to Gerardo Chowell of Georgia State University, in Atlanta, the best way to determine the share of SARS-CoV-2 infections that happen in this way is to follow up a large number of households in which someone is already infected and then track who subsequently infects whom. For this to work, everyone involved would have to be tested daily. If this were done, comparing subtle variations from person to person in the virus's genetic material would show who caught it from whom.

Definitive studies of this nature are not yet available, though some are probably in the works, Dr Chowell reckons. In the meantime, a growing collection of other research is shedding light on the matter. This work comes in three strands.

The first is a set of studies of people in groups for which unusual circumstances have made possible tallying each and every infection. These studies permit a fairly precise estimate of the share of those infected who have no symptoms. One such group are the passengers and crew of the *Diamond Princess*, a cruise ship on-board which the infection rate exploded because of a

bungled quarantine. Of 634 people thus infected, 52% had no symptoms at the time of testing, including 18% who never developed symptoms. The residents of Vo, an Italian town in which all 3,300 people were tested twice, is another much-cited example. Of those in Vo found to be infected, 50-75% had no symptoms at the time of the test. A smaller but similarly useful cohort was several planeloads of Japanese evacuated from Wuhan, the Chinese city where the epidemic began. Among the 12 people in this group found to be infected, five have never developed symptoms.

The rest is silence

All this suggests that the number of infected people unwittingly infecting others could be quite large. What is unclear is how infectious these people actually are. That is what the second strand of research on the asymptomatic and presymptomatic transmission of SARS-CoV-2 deals with. It draws on various laboratory studies. In several of these the amount of the virus in nasal and throat swabs taken from infected people who were presenting no symptoms at the time was similar to the amount found in those who had symptoms. Indeed, for those who do go on to develop symptoms, the amount of virus they have in them peaks close to the onset of those symptoms, which suggests that it may be easily transmissible at an early stage of infection.

As a persistent cough is a common symptom, it might be expected that those who are symptomatic are more effective in spreading the virus than those who are not. Contrariwise, however, those with symptoms often feel unwell and take to their beds. They are, therefore, coughing mainly onto their sheets and blankets rather than onto strangers in the street.

The third strand of research into the question of silent spreading is mathematical modelling. One such study was published in *Science* on March 31st by Luca Ferretti of Oxford University and his colleagues. It used data on 40 infected people for whom the source of their infection was known with high probability, and the timing of their symptoms and those of the people who infected them was well documented. The researchers estimate that between a third and a half of transmission occurs from people who are without symptoms at that point—a result which broadly agrees with estimates from similar studies by others.

Collectively, all this research may help explain why SARS-CoV-2 has spread with such ferocity. But the study, in particular, of those who are infected but never present symptoms is also crucial to understanding how that spread may ebb—for the pool of those who have been infected and are, therefore, immune to reinfection at least in the short term also includes these people. Pandemics end when the pathogen causing them runs out of individuals to infect. Some of those susceptible will have died. Enough of the rest would then be immune for the population to have developed “herd immunity”. In the case of the current pandemic of SARS-CoV-2, the more silent infections there have been, the faster this herd immunity will arrive. ■