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The Importance of Two Epidemiological Tasks in General Medicine that are not Usually Performed in an Infectious Outbreak: Monitoring Negative Cases and Tracing Back Positive Cases: The Example of Covid-19

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In recent years, there has been growing interest in infectious disease outbreaks. The pandemics of SARS, influenza A, MERS, Ebola, and, especially, covid-19 that occurred in the 21st century have demonstrated the difficulty of controlling high-incidence epidemics without collaboration and coordination between public health services and general medicine. In fact, despite the fact that, due to epidemiological transition processes, the main health burden has shifted from infectious diseases to chronic diseases, the number and variety of epidemic outbreaks has increased in recent decades, as has the vulnerability of our societies and healthcare systems to these phenomena [1,2].

There is an area where epidemiology and General/Family Medicine (GM) merge. GM offers a unique opportunity to detect new cases of diseases and study their natural evolution, as it continuously examines the human life cycle. No one is better qualified to observe everything from family history to the ultimate consequences of any health problem than the general practitioner (GP). A good starting point for epidemiological research is the critical analysis of each patient: a man and his little world [3-5].

Public health practices, and especially epidemiology, in the management of outbreaks and epidemics range from case detection to contact tracing, explaining transmission routes, and establishing essential measures to curb infections [6].

With SARS-CoV-2, the causative agent of covid-19, the effectiveness of control measures depends on several key epidemiological parameters, including the serial interval (the duration between the onset of symptoms in successive cases in a chain of transmission) and the incubation period (the time between infection and the onset of symptoms). There are two important epidemiological tasks applicable to primary care/GM that are not routinely performed during an infectious outbreak, such as that of covid-19: monitoring negative cases and tracing positive cases.

From a Clinical Epidemiological Perspective, Monitoring Should be as Strict with Negative Cases as with Positive Cases

Regarding testing accuracy, the main problem in an outbreak is false negatives [7]. All tests generate some false positives and false negatives. The consequences of high false negative rates are more severe in symptomatic people who can transmit disease. For example, in some phases of the covid-19 pandemic, it was reported that up to 30% of people with SARS-CoV-2 infection were missed by swab-based PCR tests [8,9]. The sensitivity of molecular detection depends on the severity of the disease, the type of sample, and the timing of sampling during the course of the infection [10,11].

Sometimes, the sample is not collected correctly. Sometimes there is a problem with the device, and someone may test positive but have not yet shed the virus. After the virus that causes covid-19 enters the body, it has to penetrate our cells and corrupt their operating instructions so that it can produce more copies of itself to infect more cells and make more copies. It takes a few days for this copy to become large enough to be detected by a test. In the case of covid-19, it takes 3 to 5 days after infection for someone to make enough copies to be picked up by a test. There appears to be a small window, perhaps as short as hours, when a person is shedding the virus and is infectious, but does not yet have enough virus in their body to be detected by a less sensitive rapid test. If a person is tested while in this window, their case will be missed [12].

Reacción en cadena de la polimerasa diagnostic tests (PCR), which involve a nasopharyngeal swab, can be inaccurate in two ways. A false-positive result mislabels an infected person, with consequences including unnecessary quarantine. False-negative results are more problematic because infected people, who may be asymptomatic, may not be isolated and can infect others. If SARS-CoV-2 diagnostic tests were perfect, a positive test would mean someone is carrying the virus, and a negative test would mean they are not. With imperfect testing, a negative result simply means a person is less likely to be infected. The pre-test probability may depend on local covid-19 prevalence, SARS-CoV-2 exposure history, and symptoms [13].

The probability of obtaining a false-negative result is 100% on the day of exposure, decreasing to 38% when symptoms begin approximately 4 days later, and to 20% 3 days after symptom onset. It subsequently increases again. Therefore, caution should be exercised when interpreting PCR tests for SARS-CoV-2 infection performed in the early stages of infection. If clinical suspicion is high, infection should not be ruled out based on PCR alone; rather, the clinical and epidemiological situation should be carefully considered [14,15].

If the pre-test probability is too high (e.g., greater than 50%), the test loses its value, as negative results cannot reduce the probability of infection sufficiently to reach the threshold. Negative results, even with a highly sensitive test, cannot rule out infection if the pre-test probability is high, so clinicians should not rely on unexpected negative results. It is possible that performing multiple simultaneous or repeated tests could overcome the limited sensitivity of a single test [16-21]. Furthermore, false-positive results in covid-19 swab tests are increasingly likely in a context of low virus prevalence in the population. When the pre-test probability is low, positive results should be interpreted with caution, and a second sample should be tested for confirmation.

Consequently, from a clinical-epidemiological perspective, it is probably advisable to monitor negative cases (already routine for asymptomatic contacts, but should also be performed for symptomatic patients with a negative PCR, including repeat testing) as closely as positive cases. This monitoring is part of the routine continuity of care for GP [22].

Backtracking the Contacts of Positive Cases (Searching for the Source of a New Case)

Contact tracers have been urged to spend more time searching for the source of a new case, along with that person's contacts, than the contacts of the new case; after all, the patient may not infect anyone else, but they likely contracted the virus as part of a cluster [23].

Looking back can actually give you a disproportionate benefit in terms of identifying infections. It has been estimated that "backward contact tracing" could prevent twice as many infections as forward contact tracing alone. Contact tracers could spend more time understanding where someone was infected and finding other people in the same cluster. This is called backward contact tracing. It can help find further chains of transmission. Backward contact tracing also helps scientists better understand where superspreading events occur. This could help prevent more such events in the future [24].

In the case of covid-19 and many infectious diseases, most people do not infect anyone else. A small percentage of people cause most of the transmission. The intensity of this pattern depends on the disease, but superspreading appears to be particularly important in covid-19. Putting more effort into finding clusters of cases should also help epidemiologists understand where and how they arise: changes in the social structure and interactions of populations, cases in certain communities, bars and barbecues, gyms and factories, schools and churches, ships, workplaces, etc. [25,26]. An useful strategy is to trace the contacts of a new case back to fifteen days before they contracted the virus, rather than the usual 48 hours, to identify who infected them. This "backward contact tracing" is extremely effective for the coronavirus because of its propensity to transmit in super-spreader events. A study in Hong Kong found that 19% of covid-19 cases were responsible for 80% of transmission, and 69% of cases did not transmit the virus to anyone else. (The SARS outbreak in 2003 had similar transmission dynamics). Any new case is more likely to have arisen from a cluster of infections than from an individual, so there is value in working backward to figure out who else was linked to that cluster [27].

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