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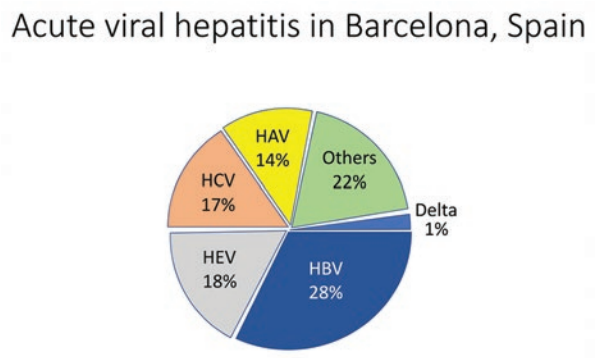
Hot News

Acute Viral Hepatitis in Men Having Sex with Men

For the past 5 years, all adults presenting with > 10-fold liver enzyme elevations at the emergency department of the largest hospital in Barcelona were tested for markers of acute viral hepatitis. Out of all positive tests, hepatitis B was detected in 28%, followed by hepatitis E (18%), hepatitis C (17%), and hepatitis A (14%), and only 1% had hepatitis D. The remaining 22% were associated with herpesvirus infections, mostly Epstein–Barr virus (14%) and cytomegalovirus *(Llaneras et al. Clin Gastroenterol Hepatol. 2020).*



Interestingly, there has been a shift in the route of transmission of hepatitis A, B, and C, where sexual transmission among men having sex with men (MSM) is becoming more frequent, particularly when compared with previous similar studies that showed that fecal-oral route was the most frequent mechanism of contagion for hepatitis A, whereas injection drug use was the most common risk behavior for hepatitis C.

Nearly 30% of cases of acute hepatitis A or B occurred in migrants from endemic areas and poor vaccination coverage, mostly in Latin America and Northern Africa. Overall, jaundice was present in more than 60% of patients presenting with acute viral hepatitis. Three out of 100 patients died, two of them due to liver failure. One of them was the single individual presenting with acute hepatitis delta superinfection.

The results from this study reflect an increase on high-risk sexual practices, particularly among MSM, as well as a decrease in injection drug use along with improvements in vaccination coverage and health-care safety procedures, including blood transfusions.

Multiple outbreaks of sexually transmitted hepatitis A and/or C among MSM have been reported during the last decade in Europe *(Minosse et al. PLoS One. 2020; 15:e0234010; Sanchez et al. Liver Int. 2013;33:1357-62).* Several factors might explain this phenomenon, such as multiple sex partners, oral-anal sexual practices, and bleeding during anal sex. HIV coinfection in a subset of that population may also increase susceptibility to infection with viral hepatitis due to impaired immunity.

Altogether, these data reinforce the need for testing hepatitis viral markers when screening for sexually transmitted infections *(Soriano and del Romero. AIDS Rev. 2018;20:187-204).* This information would provide a unique opportunity to benefit from vaccination and/or antiviral treatment. Ultimately, these interventions will stop further viral hepatitis spread among risk populations.

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Rapid antigen Testing and Mask Wearing While Waiting for COVID-19 Vaccines

After the rapid surge of COVID-19 in Europe during the spring of 2020, implementation of lockdowns succeeded in drastically reduce the number of cases and deaths within 2-3 months. However, it came at a heavy socioeconomic cost, representing the deepest recession since World War II. Now, easing COVID-19 restrictions during the summer has being followed by a new surge of cases that, again, are challenging all governments.

Although reimposing a lockdown is strongly being considered in some places, lessons learned from the first COVID-19 wave should prompt to take initiatives that allow to keep alive schools and enterprises while confronting again this unprecedented health threat.

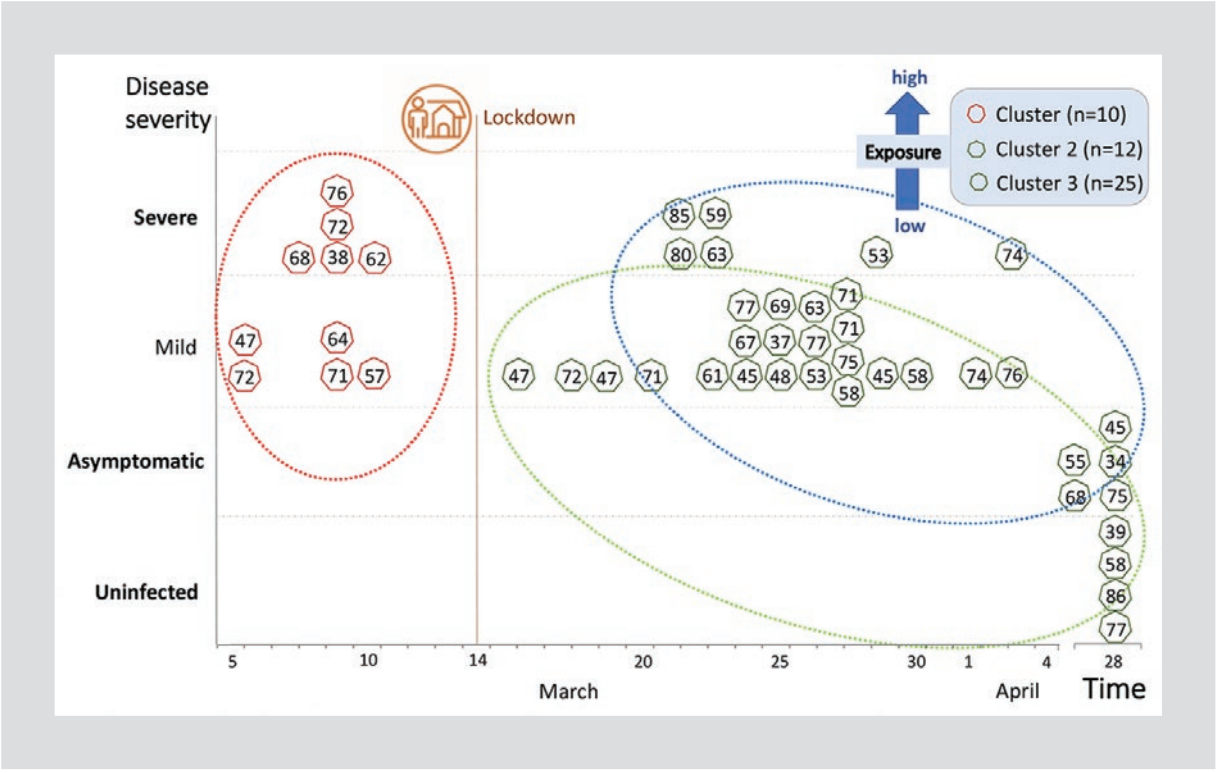

Figure 1. *Impact of SARS-CoV-2 inoculum on COVID-19 disease severity in three clusters (Adapted from Guallar et al. 2020).*

During this second hit, instead of medical questions, organization and logistics seem to be the Achilles hell. Hence, there is a need to leader actions tended to avoid that COVID-19 imbibes everything and paralyzes again the whole society. COVID-19 needs to be split out from the rest of activities whose resumption is critical for persons and societies.

Easing COVID-19 restrictions safely

Theoretically, lockdowns should not be left if there is "community transmission," defined as more than 50 new daily cases per 100,000 residents for 7 consecutive days. If so, mitigation measures should replace contention strategies, meaning contact tracing, isolation, and quarantines.

A group of international experts has identified five prerequisites before easing COVID-19 restrictions: (i) good knowledge of the country infection status; (ii) community engagement with social distancing measures; (iii) adequate public health capacity, including testing, tracing, and isolating; (iv) adequate health system capacity, represented by health care workers, hospitals, protective equipment, and drug supply; and (v) border controls, with inbound travel restrictions *(Han et al. Lancet 2020).*

First, to have reliable data on the extent of the pandemic, the mechanisms of diagnosis and reporting should be centralized at national level. Uniform criteria and updated information should be established. Countries should then report to supranational level contributing to build global strategies.

Second, information given to the general public has to be simple and uniform, avoiding discordances, contradictions, and complexities. For instance, use a clear working definition for "suspicion case" based on three assumptions: close exposure (< 1.5 m), for longer than 15', and without wearing a facial mask. This subset of individuals needs to be tested within 24-72 h using either PCR or antigen. High viral exposure seems to be associated with an increased risk of both infection and severity. The importance of the inoculum has been highlighted in several studies. Figure 1 records three clusters identified in Madrid in which the inoculum size was strongly linked to disease severity *(Guallar et al. Int J Infect Dis 2020).* In that report, ensuring activities outdoors seemed to be critical.

Third, widespread coronavirus testing is important. All people complaining cold symptoms (dry cough, fever, tiredness, headache, etc.) should have access to testing as soon as possible. Rapid antigen tests

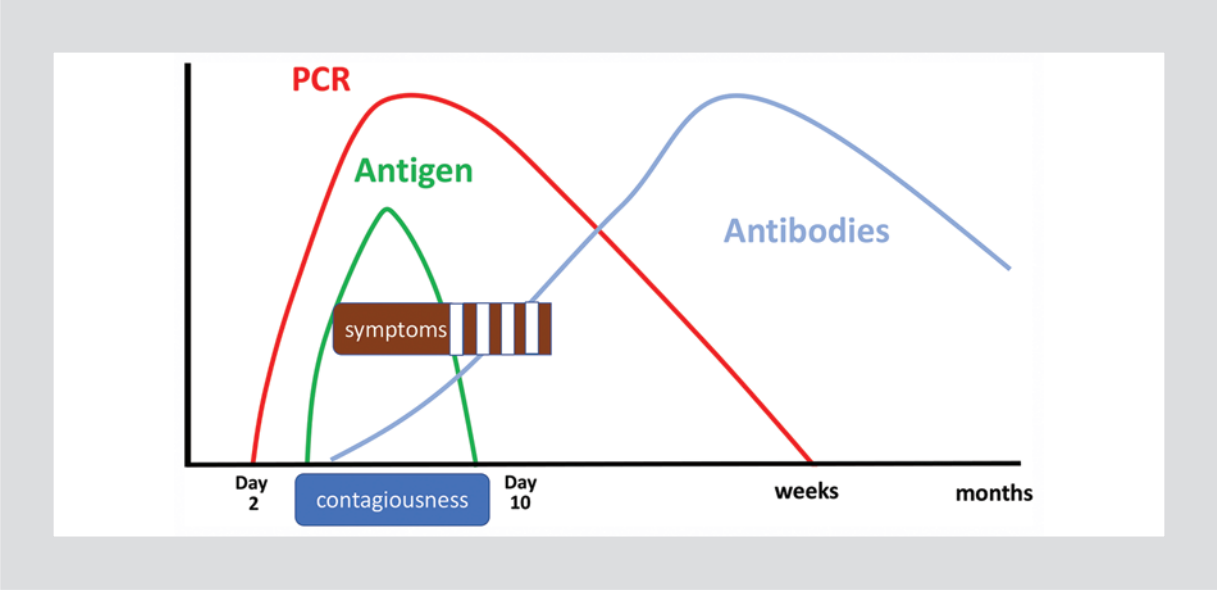

Figure 2. *Diagnostic tests for SARS-CoV-2 infection.*

depict several advantages over PCR for screening, given that they are cheaper (< 5€), faster (< 30'), easy to perform, and interpret (no need for laboratory equipment), and more importantly, and seem to reflect more accurately the infectious period when contagion is more likely (PCR can still give positive results several weeks on resolution) (Fig. 2).

To accomplish its largest benefit, several improvements are needed for SARS-CoV-2 rapid antigen tests. They should be test saliva instead of nasopharyngeal fluids and sell in pharmacies (packs of 25-100) to be used as pregnancy tests and repeated as much as considered necessary. In this way, the efficiency of self-testing and home testing in coronavirus detection would be maximized providing the opportunity for earlier identification and isolation. Think on screening before traveling (airports, train stations, etc.) or entering schools, universities, workplaces, etc., or attending familiar gatherings (weddings, etc.).

Fourth, the health-care system must be reconverted to the new circumstances. General practitioners should receive education on how to best manage "suspicious cases" or mild and asymptomatic patients, including management of contacts. At this timeframe in the pandemic, primary care practices should consider separating a COVID-19 area from the rest of services, which need to keep running as normal as possible. Forgotten attention to other medical conditions has been unacceptable and a pay tall too painful during the COVID-19 first wave. In hospitals, ensuring enough protective equipment for health care workers, separating COVID-19 areas from the rest, and reinforcing staff should allow to maintain medical assistance even with high COVID-19 admissions. The benefit of corticoids, remdesivir, anti-inflammatory agents, and other drugs for COVID-19 along with improvements in managing severe illness will reduce hospital stay and mortality. A last consideration for patient's management in hospitals and skill nursing facilities for the elderly is the need to balance the risk of propagation with the need to comfort sick patients and attend solitude (Abbott et al. JAMA 2020). This is an essential aspect of the medical profession that needs to be resuscitated. Dying alone and forgotten cannot be permitted by doctors *(Del Rio et al. AIDS Rev. 2020).*

Fifth, large flows of travelers and exchanges of population should be restricted as much as possible to preserve that local measures work and there is no refilling with external cases. Otherwise, the potential target population for any new founder effect would produce new surges. In countries where illegal immigration is an issue, rapid tests should be allocated at immigration centers along proper management of new positives with isolation and quarantine.

SARS-CoV-2 reinfections

All these measures should be implemented and maintained for a while in the hope that a vaccine is on the horizon. We cannot live like this forever. Enthusiasm

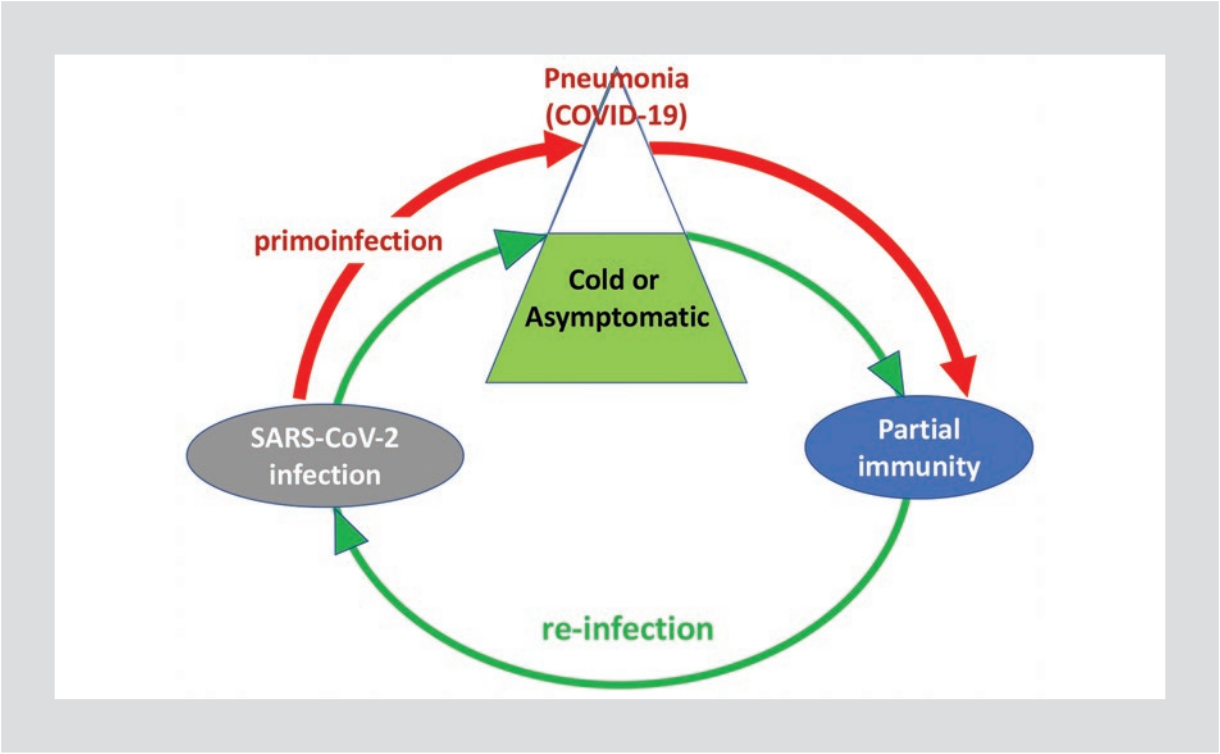

Figure 3. *Impact of SARS-CoV-2 reinfections on expected COVID-19 disease severity.*

unabated with news claiming that encouraging results from Phase III vaccine trials will be available before Christmas, the recent report of SARS-CoV-2 reinfections has fallen like a jug of cold water.

Until recently, the persistence of a positive PCR in individuals already recovered from COVID-19 was thought to reflect either a laboratory error or residual "trash" viremia, meaning that was no longer infectious. Anecdotal cases of positive PCR persisting for 3-4 weeks or 1-2 months already had been reported. However, during the last weeks, several well-documented reports of reinfections have been published. In all instances, viral sequences collected during the first and second episodes, spared between 3 and 5 months, and were genetically different. Distinct viruses were responsible for each episode rather than evolving of the original virus overtime.

The first reinfection was reported in a 33-year-old male from Hong Kong that had been on holidays in Spain. At the airport on arrival, he was tested for SARS-CoV-2 and found PCR positive, despite being asymptomatic *(To et al. Clin Infect Dis. 2020).* The patient reported that he had been hospitalized in Hong Kong with COVID-19 on March and had completely recovered within 2 weeks.

The mutation rate of SARS-CoV-2 is low in comparison to other RNA viruses since it has a unique correction proof enzyme that reduces misplacements of nucleotides during viral replication. In the Hong Kong patient, the genetic variability between the first and second viral strain was high, supporting that a reinfection with a new virus instead of reactivation of the former took place. Of note, the second infection was asymptomatic and self-limited within a couple of days, suggesting that prior immunity might not have prevented infection but favored a milder clinical course.

Several additional cases of well-documented SARS-CoV-2 reinfection have been reported during the last weeks in Belgium, The Netherlands, and the United States. It should be highlighted that in all of them prior immunity did not prevent contagion 3-4 months later and that occasionally the second episode was more severe than the first one.

SARS-CoV-2 from pandemic to endemic?

In a recent study of infection by the four human coronaviruses that cause winter respiratory tract infections, Dutch researchers examined the rate of reinfections and the duration of protective immunity *(Edridge*

et al. Nat Med. 2020). They had access to samples from 10 adult males followed every 3-6 months since the eighties belonging to the Amsterdam HIV cohort. All subjects had antibodies against each of the four coronaviruses. Neutralizing antibodies declined within the first 2 months after infection. Reinfections with the same coronavirus were common and occurred on average 12 months after prior infection, indicating that protective immunity was only short-lived. The authors concluded that caution should be taken when relying on policies that require long-term immunity, such as vaccination or natural infection to reach "herd immunity."

Swedish authors have examined carefully the immune response to SARS-CoV-2, acknowledging that cellular responses can be found in more than 2-fold of the people with antibodies *(Sekine et al. Cell. 2020).* These T-cell responses are protective and sustained for years, in contrast with B-cell responses and antibodies, which may vanish within a couple of months, especially in individuals that experienced mild or asymptomatic infections. The authors suggest that the presence of this immunity in a growing proportion of the population will steadily reduce the pathogenicity and severity of SARS-CoV-2 (Fig. 3), adding it to the list of recurrent seasonal coronaviruses.

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