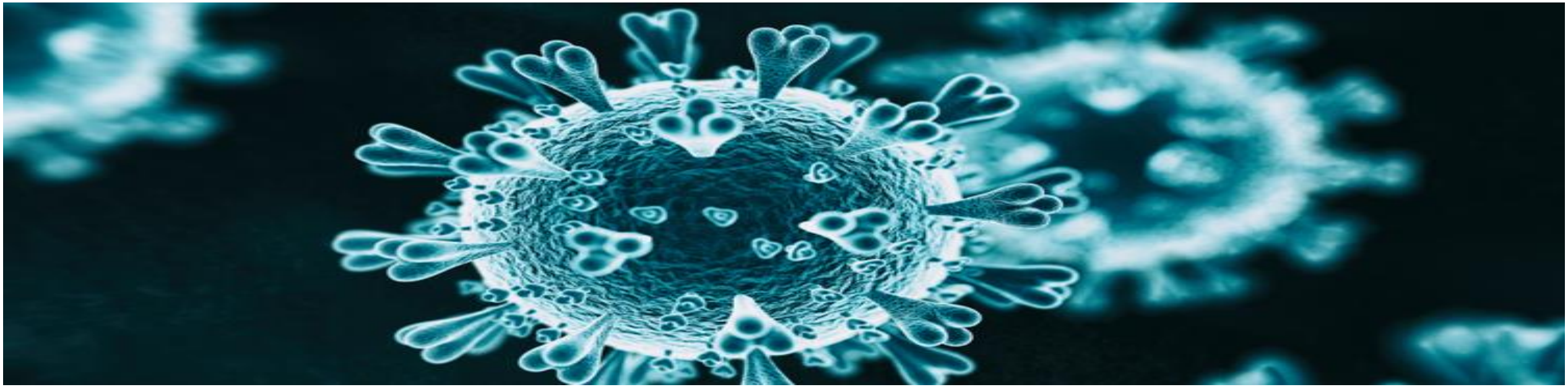


La gestione clinica dei pazienti Covid-19: la ventilazione

Venerdi' 10 Aprile 2020, ore 17:00 **https://who-euro.webex.com/join/Venice**

SIMIT Società Italiana di Malattie Infettive e Tropicali

World Health Organization

SIAARTI PRO VITA CONTRA DOLOREM SEMPER

Obiettivo del webinar

- Condividere aggiornamenti OMS sulla gestione clinica dei pazienti

- Mantenere una piattaforma che faciliti lo scambio di esperienza clinica tra i clinici che gestiscono i pazienti COVID in Italia

World Health Organization

Agenda

- Introduzione (5 min)
- Aggiornamenti OMS (15 min)
  - Systematic reviews : Clorochina/HC
  - COVID e HIV
  - IPC
  - Test diagnostici
- Condivisione esperienza per centro/regione (60 min)
- Aggiornamento studi in corso (AIFA) (5 min)

World Health Organization

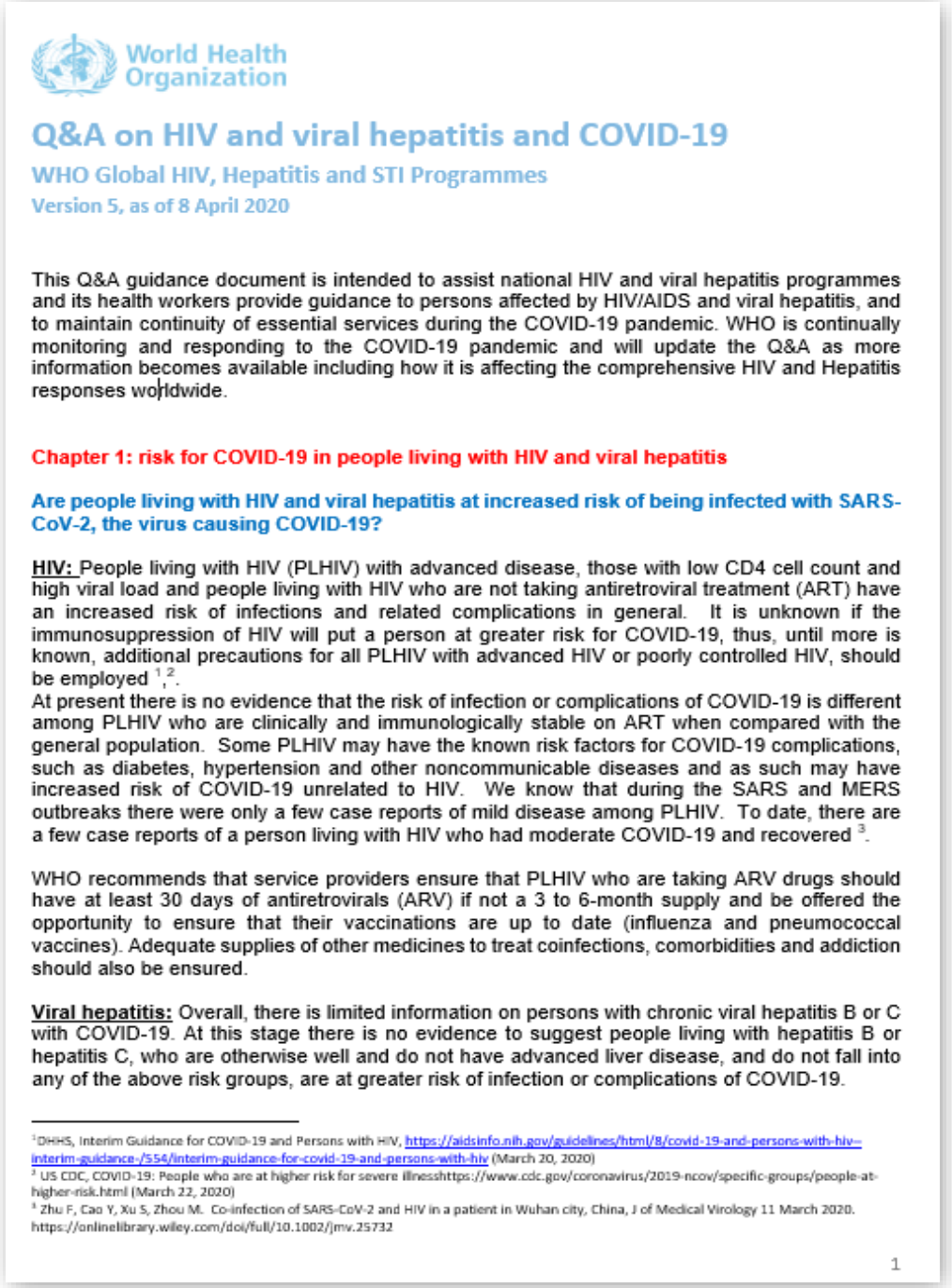
Per facilitare la comunicazione durante il webinar per cortesia

- Disattivate il microfono appena collegati
- Cliccate sull'icona ✋ per intervenire
- Per fare domande utilizzate la chat box

World Health Organization

COVID-19 in People with HIV and viral hepatitis

- At present there is **no evidence that the risk of infection or complications of COVID-19 is different among PLHIV** who are clinically and immunologically stable on ART when compared with the general population.
- Some PLHIV may have the known **risk factors for COVID-19** complications, such as diabetes, hypertension and other noncommunicable diseases and as such may have increased risk of COVID-19 unrelated to HIV.
- PLHIV who are taking ARV drugs should have at least 30 days of antiretrovirals (ARV) if not a **3 to 6-month supply** and be offered the opportunity to ensure that their **vaccinations** are up to date (influenza and pneumococcal vaccines).
- At this stage there is **no evidence to suggest people living with hepatitis B or hepatitis C, who are otherwise well and do not have advanced liver disease, and do not fall into any of the above risk groups, are at greater risk** of infection or complications of COVID-19.



World Health Organization

Q&A on HIV and viral hepatitis and COVID-19

WHO Global HIV, Hepatitis and STI Programmes

Version 5, as of 8 April 2020

This Q&A guidance document is intended to assist national HIV and viral hepatitis programmes and its health workers provide guidance to persons affected by HIV/AIDS and viral hepatitis, and to maintain continuity of essential services during the COVID-19 pandemic. WHO is continually monitoring and responding to the COVID-19 pandemic and will update the Q&A as more information becomes available including how it is affecting the comprehensive HIV and Hepatitis responses worldwide.

Chapter 1: risk for COVID-19 in people living with HIV and viral hepatitis

Are people living with HIV and viral hepatitis at increased risk of being infected with SARS-CoV-2, the virus causing COVID-19?

HIV: People living with HIV (PLHIV) with advanced disease, those with low CD4 cell count and high viral load and people living with HIV who are not taking antiretroviral treatment (ART) have an increased risk of infections and related complications in general. It is unknown if the immunosuppression of HIV will put a person at greater risk for COVID-19, thus, until more is known, additional precautions for all PLHIV with advanced HIV or poorly controlled HIV, should be employed [1,2].
At present there is no evidence that the risk of infection or complications of COVID-19 is different among PLHIV who are clinically and immunologically stable on ART when compared with the general population. Some PLHIV may have the known risk factors for COVID-19 complications, such as diabetes, hypertension and other noncommunicable diseases and as such may have increased risk of COVID-19 unrelated to HIV. We know that during the SARS and MERS outbreaks there were only a few case reports of mild disease among PLHIV. To date, there are a few case reports of a person living with HIV who had moderate COVID-19 and recovered [3].

WHO recommends that service providers ensure that PLHIV who are taking ARV drugs should have at least 30 days of antiretrovirals (ARV) if not a 3 to 6-month supply and be offered the opportunity to ensure that their vaccinations are up to date (influenza and pneumococcal vaccines). Adequate supplies of other medicines to treat coinfections, comorbidities and addiction should also be ensured.

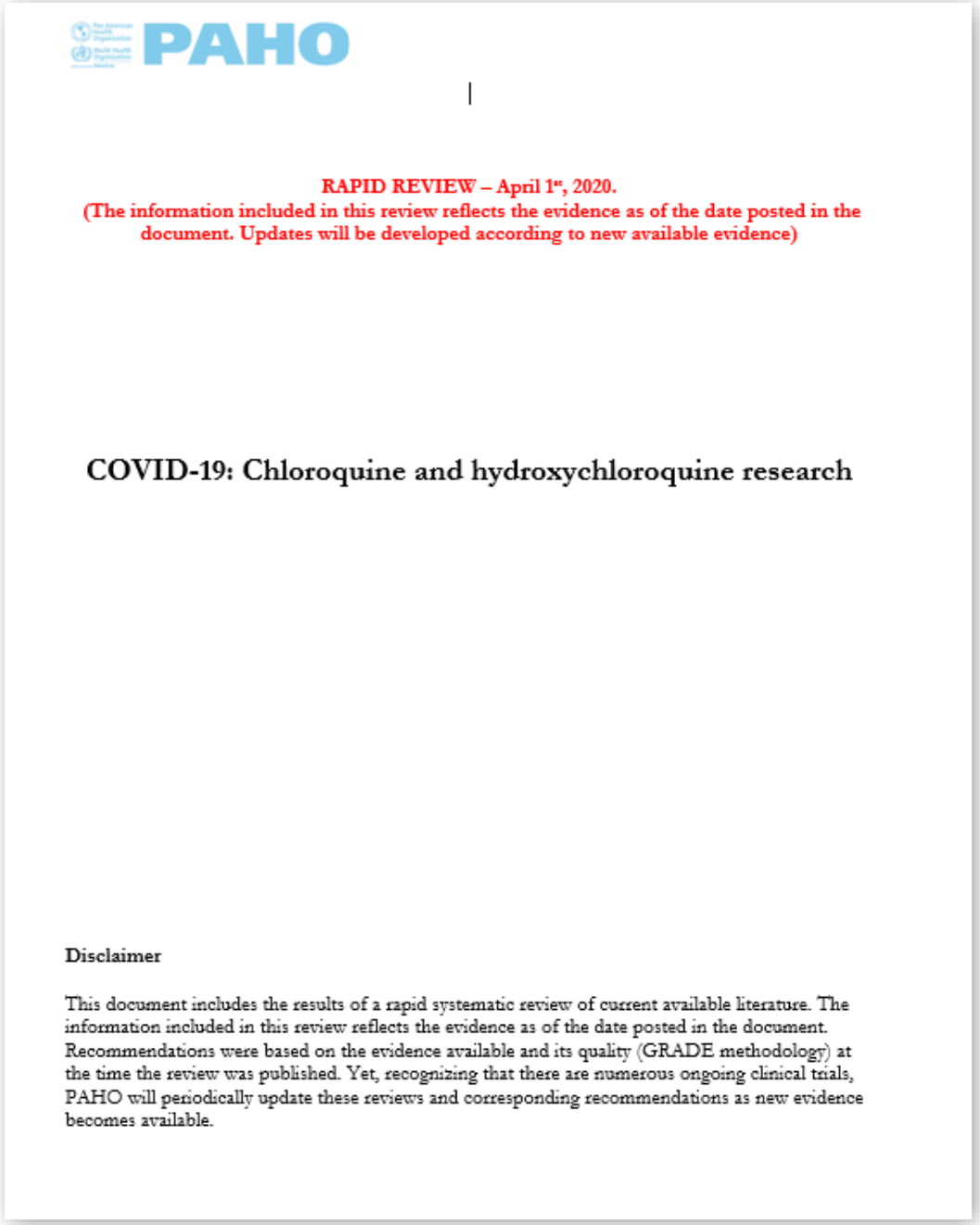
Viral hepatitis: Overall, there is limited information on persons with chronic viral hepatitis B or C with COVID-19. At this stage there is no evidence to suggest people living with hepatitis B or hepatitis C, who are otherwise well and do not have advanced liver disease, and do not fall into any of the above risk groups, are at greater risk of infection or complications of COVID-19.

[1] DHHS, Interim Guidance for COVID-19 and Persons with HIV, https://aidsinfo.nih.gov/guidelines/html/8/covid-19-and-persons-with-hiv--interim-guidance-/554/interim-guidance-for-covid-19-and-persons-with-hiv (March 20, 2020)
[2] US CDC, COVID-19: People who are at higher risk for severe illnesshttps://www.cdc.gov/coronavirus/2019-ncov/specific-groups/people-at-higher-risk.html (March 22, 2020)
[3] Zhu F, Cao Y, Xu S, Zhou M. Co-infection of SARS-CoV-2 and HIV in a patient in Wuhan city, China, J of Medical Virology 11 March 2020. https://onlinelibrary.wiley.com/doi/full/10.1002/jmv.25732

1

Systematic Reviews

- There is **no high-quality evidence** on benefits and harms
- Two small studies (one RCT) with many **methodological concerns** and are at best, low quality evidence.
  - France: 80pt receive 600 mg of hydroxychloroquine daily and their viral load in nasopharyngeal swabs was tested daily in a hospital setting; depending on their clinical presentation, azithromycin was added. HCQ significantly associated with viral load reduction/disappearance in COVID-19 patients and its effect is reinforced by azithromycin
  - China: RCT, enrolled 30 treatment-naive patients with confirmed COVID-19. Patients in HCQ group were given HCQ 400 mg per day for 5 days plus conventional treatments. On day 7, COVID-19 nucleic acid of throat swabs was negative in 13 (86.7%) HCQ cases and 14 (93.3%) cases in the control group (P>0.05).
- Care must be exercised in extrapolating in vitro results to in vivo, and potential **side effects, toxicities and interactions** with other drugs must remain a key consideration.
- Multiple **clinical trials are underway** to strengthen the data and better characterize effectiveness
- If this drug is effective in COVID-19, this may drive **unavailability** for malarial patients and other chronic diseases as a treatment and as a prophylaxis.



PAHO

RAPID REVIEW – April 1st, 2020.
(The information included in this review reflects the evidence as of the date posted in the document. Updates will be developed according to new available evidence)

COVID-19: Chloroquine and hydroxychloroquine research

Disclaimer

This document includes the results of a rapid systematic review of current available literature. The information included in this review reflects the evidence as of the date posted in the document. Recommendations were based on the evidence available and its quality (GRADE methodology) at the time the review was published. Yet, recognizing that there are numerous ongoing clinical trials, PAHO will periodically update these reviews and corresponding recommendations as new evidence becomes available.

Infection Prevention and Control

https://www.who.int/publications-detail/advice-on-the-use-of-masks-in-the-community-during-home-care-and-in-healthcare-settings-in-the-context-of-the-novel-coronavirus-(2019-ncov)-outbreak

Advice on the use of masks in the context of COVID-19

Interim guidance

6 April 2020

World Health Organization

Background

This document provides advice on the use of masks in communities, during home care, and in health care settings in areas that have reported cases of COVID-19. It is intended for individuals in the community, public health and infection prevention and control (IPC) professionals, health care managers, health care workers (HCWs), and community health workers. It will be revised as more data become available.

Current information suggests that the two main routes of transmission of the COVID-19 virus are respiratory droplets and contact. Respiratory droplets are generated when an infected person coughs or sneezes. Any person who is in close contact (within 1 m) with someone who has respiratory symptoms (coughing, sneezing) is at risk of being exposed to potentially infective respiratory droplets. Droplets may also land on surfaces where the virus could remain viable; thus, the immediate environment of an infected individual can serve as a source of transmission (contact transmission).[1]

WHO has recently summarized reports of transmission of the COVID-19 virus and provided a brief overview of current evidence on transmission from symptomatic, pre-symptomatic, and asymptomatic * people infected with COVID-19 (full details are provided in WHO COVID-19 Situation report 73).[2]

Current evidence suggests that most disease is transmitted by symptomatic laboratory confirmed cases. The incubation period for COVID-19, which is the time between exposure to the virus and symptom onset, is on average 5-6 days, but can be as long as 14 days. During this period, also known as the "pre-symptomatic" period, some infected persons can be contagious and therefore transmit the virus to others.[3-8] In a small number of reports, pre-symptomatic transmission has been documented through contact tracing efforts and enhanced investigation of clusters of confirmed cases.[3-8] This is supported by data suggesting that some people can test positive for COVID-19 from 1-3 days before they develop symptoms.[9,10]

Thus, it is possible that people infected with COVID-19 could transmit the virus before symptoms develop. It is important to recognize that pre-symptomatic transmission still requires the virus to be spread via infectious droplets or through touching contaminated surfaces. WHO regularly monitors all emerging evidence about this critical topic and will provide updates as more information becomes available.

In this document medical masks are defined as surgical or procedure masks that are flat or pleated (some are shaped like cups); they are affixed to the head with straps. They are tested according to a set of standardized test methods (ASTM F2100, EN 14683, or equivalent) that aim to balance high filtration, adequate breathability and optionally, fluid penetration resistance. This document does not focus on respirators; for guidance on use of respirators see IPC guidance during health care when COVID-19 infection is suspected.[11]

Wearing a medical mask is one of the prevention measures that can limit the spread of certain respiratory viral diseases, including COVID-19. **However, the use of a mask alone is insufficient to provide an adequate level of protection, and other measures should also be adopted.** Whether or not masks are used, maximum compliance with hand hygiene and other IPC measures is critical to prevent human-to-human transmission of COVID-19. WHO has developed guidance on IPC strategies for home care[12] and health care settings[11] for use when COVID-19 is suspected.

Community settings

Studies of influenza, influenza-like illness, and human coronaviruses provide evidence that the use of a medical mask can prevent the spread of infectious droplets from an infected person to someone else and potential contamination of the environment by these droplets.[13] There is limited evidence that wearing a medical mask by healthy individuals in the households or among contacts of a sick patient, or among attendees of mass gatherings may be beneficial as a preventive measure.[14-23] However, there is currently no evidence that wearing a mask (whether medical or other types) by healthy persons in the wider community setting, including universal community masking, can prevent them from infection with respiratory viruses, including COVID-19.

Medical masks should be reserved for health care workers. The use of medical masks in the community may create a false sense of security, with neglect of other essential measures, such as hand hygiene practices and physical distancing, and may lead to touching the face under the masks and under the eyes, result in unnecessary costs, and take

* An asymptomatic laboratory-confirmed case is a person infected with COVID-19 who does not develop symptoms. Asymptomatic transmission refers to transmission of the virus from a person, who does not develop symptoms. The true extent of asymptomatic infections will be determined from serologic studies.

Testing strategies (COVID19)

Purpose of testing

- Detect acute infection → molecular test (maybe antigen test*)
- Contact tracing → Molecular test (maybe antigen test*)
- Serosurveillance → antibodies
- Immunity? → antibodies?

Advice on the use of point-of-care immunodiagnostic tests for COVID-19

Scientific brief

8 April 2020

World Health Organization

In response to the growing COVID-19 pandemic and shortages of laboratory-based molecular testing capacity and reagents, multiple diagnostic test manufacturers have developed and begun selling rapid and easy-to-use devices to facilitate testing outside of laboratory settings. These simple test kits are based either on detection of proteins from the COVID-19 virus in respiratory samples (e.g. sputum, throat swab) or detection, in blood or serum, of human antibodies generated in response to infection.

WHO applauds the efforts of test developers to innovate and respond to the needs of the population.

However, before these tests can be recommended, they must be validated in the appropriate populations and settings. Inadequate tests may miss patients with active infection or falsely categorize patients as having the disease when they do not, further hampering disease control efforts. **At present, based on current evidence, WHO recommends the use of these new point-of-care immunodiagnostic tests only in research settings. They should not be used in any other setting, including for clinical decision-making, until evidence supporting use for specific indications is available.**

WHO continues to evaluate available immunodiagnostics tests for COVID-19 and will update this scientific brief when necessary.

Rapid diagnostic tests based on antigen detection

One type of rapid diagnostic test (RDT) detects the presence of viral proteins (antigens) expressed by the COVID-19 virus in a sample from the respiratory tract of a person. If the target antigen is present in sufficient concentrations in the sample, it will bind to specific antibodies fixed to a paper strip enclosed in a plastic casing and generate a visually detectable signal, typically within 30 minutes. The antigen(s) detected are expressed only when the virus is actively replicating; therefore, such tests are best used to identify acute or early infection.

How well the tests work depends on several factors, including the time from onset of illness, the concentration of virus in the specimen, the quality of the specimen collected from a person and how it is processed, and the precise formulation of the reagents in the test kits. Based on experience with antigen-based RDTs for other respiratory diseases such as influenza, in which affected patients have comparable concentrations of influenza virus in respiratory samples as seen in COVID-19, the sensitivity of these tests might be expected to vary from 34% to 80%.[1]

Based on this information, half or more of COVID-19 infected patients might be missed by such tests, depending on the group of patients tested. These assumptions urgently require further study to understand whether they are accurate. Additionally, false-positive results – that is, a test showing that a person is infected when they are not – could occur if the antibodies on the test strip also recognize antigens of viruses other than COVID-19, such as from human coronaviruses that cause the common cold. If any of the antigen detection tests that are under development or commercialized demonstrate adequate performance, they could potentially be used as triage tests to rapidly identify patients who are very likely to have COVID-19, reducing or eliminating the need for expensive molecular confirmatory testing.

With the limited data now available, WHO does not currently recommend the use of antigen-detecting rapid diagnostic tests for patient care, although research into their performance and potential diagnostic utility is highly encouraged.

Rapid diagnostic tests based on host antibody detection

There is another, more common type of rapid diagnostic test marketed for COVID-19; a test that detects the presence of antibodies in the blood of people believed to have been infected with COVID-19.[2,3] Antibodies are produced over days to weeks after infection with the virus. The strength of antibody response depends on several factors, including age, nutritional status, severity of disease, and certain medications or infections like HIV that suppress the immune system.[4,5] In some people with COVID-19, disease confirmed by molecular testing (e.g. reverse transcription polymerase chain reaction: RT-PCR), weak, late or absent antibody responses have been reported.[6,7,8] Studies suggest that the majority of patients develop antibody response only in the second week after onset of symptoms.[5,6,7,10-14] This means that a diagnosis of COVID-19 infection based on antibody response will often only be possible in the recovery phase, when many of the opportunities for clinical intervention or interruption of disease transmission have already passed. Antibody detection tests targeting COVID-19 may also cross-react with other pathogens, including other human

Advice on the use of point-of-care immunodiagnostic tests for COVID-19

Scientific brief

8 April 2020

World Health Organization

Rapid diagnostic tests based on antigen (Ag) detection: Ag are expressed only when a virus is **replicating**, thus such test can be used to identify **acute or early infection**.

- **Sensitivity (FN): 38-80%.**
- FP also possible due to **cross reaction** with other coronavirus.
- If available tests demonstrate adequate performance, can be used as **triage** test to identify people v likely to have COVID19, reducing the need for molecular confirmatory tests needed.

With the **limited data** now available, **WHO does not currently recommend the use of antigen-detecting rapid diagnostic tests for patient care**, *although research into their performance and potential diagnostic utility is highly encouraged*.

Serology COVID19

Advice on the use of point-of-care immunodiagnostic tests for COVID-19

Scientific brief

8 April 2020

World Health Organization

- Majority of pts develop Ab response only in the **2nd week after onset** of symptoms.
- In some pts with COVID-19 + confirmed by molecular testing (e.g. RT-PCR), **weak, late or absent antibody responses** have been reported (**false negative results**) (1,2,3)
- Ab detection tests targeting COVID-19 may also **cross-react with other pathogens**, including other human coronavirus and **give false-positive results.**
- No evidence to date to support that immune response protect from reinfection with the COVID-19 virus.

- SEROLOGY: Support **vaccines** development, and improve understanding of **the extent of infection among people who are not identified through active case finding and surveillance** efforts, the attack rate in the population, and the **infection fatality rate**.
- **Limited utility for clinical diagnosis,** although some clinicians has used for **presumptive diagnosis** of recent COVID-19 **in cases where molecular testing was NEG** but where there was a strong epidemiological link to COVID-19 infection and paired blood samples (acute and convalescent) showing rising antibody levels.

Based on current data, WHO does not recommend the use of Ab-detecting rapid diagnostic tests for patient care but encourages the continuation of work to establish their usefulness in disease surveillance and epidemiologic research

1. Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, et al. Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. medxriv [Internet]. 2020; Available from: https://www.medrxiv.org/content/10.1101/2020.03.02.20030189v1.full.pdf
2. Okba N.M.A, Muller M.A., Li W, Wang C, et al. SARS-COV-2 specific antibody responses in COVID-19 patients. medxriv [Internet]. 2020; Available from: https://www.medrxiv.org/content/10.1101/2020.03.18.20038059v1
3. Lin D, Liu L, Zhang M, Hu Y, et al. Evaluation of serological tests in the diagnosis of 2019 novel coronavirus (SARS-CoV-2) infections during the COVID-19 outbreak. medxriv [Internet]. 2020; Available from: https://doi.org/10.1101/2020.03.27.20045153

Condivisione esperienza clinica

ANTIVIRALI

1. Importanza della precocita' di utilizzo antivirali (primi 7-10 gg dall'insorgenza dei sintomi). Avrebbe un senso a domicilio?

2. Sembra essere meno utile nel paziente avanzato in TI tranne che nel caso di utilizzo di Remdesivir, che puo' aggiugere chances al paz grave ed accelerare la negativizzazione virale

STEROIDI

1. In mancanza di antivirali rischio di negativizzazione piu lenta
2. Steroidi a pz con insuff respiratoria da piu' giorni (7 giorni)
4. Buona risposta con riduzione della necessita' di intubazione ma finestra ristretta

OSSIGENOTERAPIA:

cardine del trattamento

<u>IMPORTANZA USO di farmaci in studi controllati per generare evidenza!</u>

MONOCLONALI

1. Discreta utilizzazione di Tocilizumab con esperienza positiva specialmente nei pz ancora non in ICU, miglioramente anche di pz in CPAP, anche se in alcuni pz si e' osservato un peggioramento a 24 hrs dalla somministrazione.
2. Buona correlazione tra marcatori (Ddimero, PCR, ferritina) e IL6: con almeno 2 o 3 marcatori elevati inizio monoclonali
3. Uso di immunomodulanti ha una finestra ristretta

ANTICOAGULANTI

1. Tromboembolia polmonare frequente
2. Profilassi con eparina bpm per tutti i pz (4000 unita/g)
3. Profilassi a domicilio. Azzardo? Morti improvvise documentate e emorragie ge.
4. Se d-dimero aumenta (4-5 vv): eparina a dosaggi terapeutici
5. In acuto, utilizzo di anticoagulanti orali e' complicato

Condivisione esperienza clinica

La VENTILAZIONE nel PAZIENTE COVID-19

Aggiornamento studi in corso

AIFA

Aggiornamento AIFA

Clinical Trials:

- Remdesivir: 2 Gilead RCT, hospitalized
- Tocilizumab: 3 trial (1 CT; 2 RCT), hospitalized
- Anakira vs Emapalumab vs SOC: RCT SOBI, hospitalized
- Sarilumab RCT Sanofi, hospitalized
- WHO Solidarity trial, hospitalized
- Hydro Stop Trial (HCQ): RCT, non profit, outpatients

Compassionate use programmes

- Remdesivir
- Ruxolitinib
- Canakinumab

Conclusione

Domande e suggerimenti per i prossimi webinar?

LINK: https://who-euro.webex.com/join/Venice

- bertagnolios@who.int
- penazzatom@who.int
- zambonf@who.int

Mercoledi 15 Aprile ore 17:00
WEBINAR con direzioni sanitarie

Giovedi 16 Aprile
ore 18:00
INFETTIVOLOGI

Venerdi 17 Aprile
ore 17:00
INTENSIVISTI

Sostegno psicologico

- Per un sostegno psicologico gratuito gli operatori possono contattare l'associazione https://emdr.it/ , gli operatori sono disponibili anche telefonicamente o con un colloquio online.
- Altre associazioni che si stanno attivando per un sostegno nel territorio sono :

http://www.psicologiperipopoli.it/,

https://www.sipemsos.org/

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