Since the start of the COVID-19 pandemic, the World Gastroenterology Organisation (WGO) has developed a great effort to keep its members updated with the best evidence available. Our website was updated several times due to the great load of information that became available through time. Even now we are still getting new results from different studies that are letting us understand better the pandemic and how it is affecting our members and specifically our patients.

In this first issue of 2021, a special edition devoted to COVID-19, you will find a summary of all the work performed as highlighted in the message of the Editors. This is just the beginning of what you will continue to find on our website and social media platforms as we update.

A final word on our own changes: we have just updated our logo as you will find out in this issue. This change comes at a most interesting time when everything is changing and will continue to adapt to the new normality after the pandemic. A worldwide vaccination program is starting and after a while we will know how life is going to be to adapt to this pandemic and how to prepare for the new challenges ahead.

You will see WGO’s change in the next weeks in our publications like e-WGN and our webpage and different social media. We expect you will find our changes appealing and are looking forward to your reactions and comments.
**WORLD GASTROENTEROLOGY NEWS MARCH 2021**

**Contents**

©2021 World Gastroenterology Organisation. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form without the prior permission of the copyright owner.

---

**VOL. 25, ISSUE 2**

**Editors**

Anita Afzali, MD, MPH, FACG
Abercrombie and Fitch Endowed Chair in Inflammatory Bowel Disease
Wexner Medical Center
The Ohio State University
Columbus, Ohio, USA

Mário Reis Álvares-da-Silva, MD, PhD
Professor of Hepatology
Hospital de Clínicas de Porto Alegre
Universidade Federal do Rio Grande do Sul
Porto Alegre, Brazil

---

**e-WGN Editorial Board**

- Dan Dumitrascu, Romania
- Sara Elfadil, Sudan
- Ernst Fredericks, South Africa
- Waseem Hamoudi, Jordan
- Nassir Alhaboob Arabi Mohammad, Sudan
- VG Naibo, South Africa
- Alejandro Piscoya, Peru
- Naoya Sakamoto, Japan
- Murat Saruç, Turkey
- Michael Schultz, New Zealand
- Walid Sweidan, Palestine
- Lu Xia, China

**Managing Editor**

James Melberg, WGO Program Manager

**Art Production**

Jennifer Gubbin

**Editorial Office**

WGO Executive Secretariat
555 East Wells Street, Suite 1100
Milwaukee, WI 53202 USA
info@worldgastroenterology.org

---

**Expert Point of View**

**Special Edition of e-WGN: COVID-19 in the World of Gastroenterology**

Alejandro Piscoya, MD, MSc(Ed), AGAF

---

**Message from the Editors**

Mário Reis Álvares-da-Silva, MD, PhD
Anita Afzali, MD, MPH, FACG

---

**COVID-19 Special Issue**

**COVID-19 Situation in the World and Particular Role of the WGO**

Jean-Christophe Saurin, MD

---

**Personal Protection Equipment for Endoscopy in Low Resource Settings during the COVID-19 Pandemic: Guidance from the World Gastroenterology Organisation.**

Desmond Leddin MB, BCh, MSc, FRCPI, FRCPC, CAGF
David Armstrong MB, BCHir, FRCPC, CAGF, AGAF, FACG

---

**WGO Guidance for Patients with COVID-19 and Liver Disease**

Cihan Yurdaydin, MD
Saeed Hamid, MD

---

**Antibody Testing for SARS-CoV-2: Role in Management of the Disease**

Kai-Chun Wu, MD
Desmond Leddin, MB, MSc, FRCPI, FRCPC

---

**Personal Care and Stress Management**

Guilherme Macedo, MD
Filipe Vilas Boas, MD

---

**Telemedicine in Digestive Diseases During the COVID-19 Pandemic**

Alejandro Piscoya, MD, MSc(Ed), AGAF
Hugo Cedrón, MD

---

**Management of Patients with Inflammatory Bowel Disease (IBD)**

Charles Bernstein, MD

---

©2021 World Gastroenterology Organisation. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form without the prior permission of the copyright owner.
## Contents

<table>
<thead>
<tr>
<th>Section</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gastro 2021</td>
<td>43</td>
</tr>
<tr>
<td>Calendar of Events</td>
<td>44</td>
</tr>
</tbody>
</table>

©2021 World Gastroenterology Organisation. No part of this publication may be reproduced, stored in a retrieval system, or transmitted in any form without the prior permission of the copyright owner.
The COVID-19 pandemic has taken a significant toll around the globe for our patients and each other. In this special issue devoted to COVID-19, we look at the impact and the management of the pandemic from a gastroenterologists’ perspective among communities worldwide.

We include a selection of contributors with discussion of many relevant and important topics. Professor Jean-Christophe Saurin from France reviews the COVID-19 situation worldwide and specifically the role of the WGO. In an extensive review, Profs Kai-Chun Wu and Desmond Leddin outline the role of testing for antibodies against SARS-CoV-2 in the management of COVID-19. Next, Profs Desmond Leddin and David Armstrong from Canada very nicely summarize utilization guidance of personal protection equipment (PPE) and endoscopy, with many other global contributors. From Peru, Doctors Alejandro Piscoya and Hugo Cedrón shared the role of telemedicine and caring for our patients suffering from digestive diseases during the pandemic.

Doctors Cihan Yurdaydin, WGO Past President and Saeed Hamid, Chair of the WGO Hepatology Interest Group (HIG), in collaboration with HIG members, present general clinical guidelines for patients with COVID-19 and liver diseases. Dr. Charles Bernstein from Canada nicely summarizes management of the patient with inflammatory bowel disease.

As we are all working diligently to slow down the spread of disease and contain the crisis, let us not forget self-care and our own mental health. Doctors Guilherme Macedo and Filipe Vilas Boas from Portugal beautifully highlight the importance of personal care and stress management.

We hope this special e-WGN issue can help serve as a platform for shared experiences and lessons learned. Although we may not know what our lives will look like once the pandemic is over, or what the “new normal” of our world will be, we do know that we will be better and stronger together, as a global gastroenterology community.

Anita and Mario.
The COVID-19 pandemic represents a terrible challenge for health systems throughout the world and, in parallel, for individual patients for whom this can be a very aggressive disease with a high mortality, particularly for those with comorbidities. Research and publications are exceedingly active in this setting, most activity being focused on the pathophysiology of COVID-19, in addition to diagnostic, treatment and management strategies for this pandemic. One remarkable feature of the COVID-19 disease is the multiple clinical presentations and the numerous targets of the disease; the lungs have been considered the key target but skin (vasculitis), nose (olfactory disturbance and anosmia), central nervous system, heart (including cardiac arrhythmias), kidney (renal insufficiency) and the immune system are, also affected and, indeed, the immunological effects may be one major mechanisms underlying tissue injury. In addition, there is increasing recognition that COVID-19 is, also, associated with a spectrum of digestive, hepatic and pancreatic manifestations.

In general, first published experience suggests that the digestive tract manifestations of COVID-19 represent neither a life-threatening event nor a major prognostic factor. The questions that WGO should address to help the community of hepatologists and gastroenterologists are:

- Should we be aware of a significant risk of complications, during the acute or the late phase of COVID-19 disease, in one digestive organ, that should be checked during the illness?
- Does any specific digestive manifestation of the disease represent an important prognostic factor that deserves systematic evaluation?
- What are the relevant procedures that should be recommended for endoscopic intervention in order to protect the patients and the medical/nurse staff?
- What are the specific recommendations for patient care in COVID-19 situation with regard to our usual gastroenterology and hepatology situations and especially immunocompromised patients (liver disease, immunosuppression like transplanted patients, IBD).

National and international recommendations on patient management in the setting of COVID-19 are numerous, efficient and precise. They are also evolving as we learn each day from this disease, so that they will be updated regularly.

The WGO presents the latest version of these recommendations along with links to important supporting information. On the major questions for our specialty, the specific added value of WGO could be proposing alternatives, in different situations of high and limited resources, for the available investigation, treatment and management strategies.

What are the known gastroenterological manifestations of COVID-19?

It seems from available literature that these manifestations can be classified into 4 main topics:

1. **Digestive tract clinical manifestations** seem mostly diarrhea in 2-17% of cases in different series. Anorexia, more frequent, is probably not a specific digestive symptom. At this time no case of acute perforation or severe colitis has been reported. Unpublished experience in France reveals a high frequency of rectal bleeding in older patients, probably attributable to systematic anticoagulation in at-risk hospitalized patients; however, the underlying disease have not elucidated as only emergent endoscopies are being performed. Interestingly, series reporting the identification of virus in stools suggest that the stool excretion can persist for more than 30 days, often long after nasopharyngeal swabs have become negative; this is important information to take into account when considering lower endoscopic procedures.

2. **Liver enzyme elevation** is frequent, detected in up to 40% of patients, concerning mostly transaminases. At this time no severe hepatitis related to the virus has been described but data are lacking regarding the effect of the virus in patients with chronic liver disease. Clinical cohort studies are underway in most countries to clarify this point.

3. **Pancreatic biological involve-
disease for which there is not, yet, any active therapy and the direct and indirect effects of the coronavirus infection on the digestive system and the potential long-term sequelae have not been documented in detail. Patients requiring intensive care and mechanical ventilation are at risk of stress- and malnutrition-related digestive disease and further studies are urgently needed to understand this better. Furthermore, it is crucial to recognize how COVID-19 will affect our ability to manage digestive diseases in patients with suspected or confirmed disease and, also, how it will affect our ability to provide safe and effective care to all of our patients.

References

Desmond Leddin, MB, BCh, MSc, FRCPI, FRCPC, CAGF
Chair, WGO Clinical Research Committee
Dalhousie University
Halifax, Canada

David Armstrong MB, BChir, FRCP, CAGF, AGAF, FACG
Chair, WGO Guidelines Committee
McMaster University
Hamilton, Canada

Also:
• Raja Affendi Raja Ali, MD, FRCP, AGAF, Universiti Kebangsaan Malaysia, Kuala Lumpur, Malaysia
• Alan Barkun, MD, CM, MSc. McGill University, Montreal, Canada
• Amna Subhan Butt, MBBS. MSc, FCPS (Medicine) FCPS (GIl). Aga Khan University Hospital, Karachi, Pakistan
• Ye Chen, MD, PhD. Nanfang Hospital, Southern Medical University, Guangzhou, China
• Harshit S. Khara, MD, FACG, FASGE. Geisinger Medical Center, Danville, Pennsylvania, United States
• Justin Yeong Yeh Lee, MD, University Sains Malaysia, Penang, Malaysia
• Wai Keung Leung, MBChB, MD, MRCP, FRCP(Edin), FRCP(Lond), FHKCP, FHKAM(Med), Hong Kong University, Hong Kong
• Finlay Macrae, MD, MBBS, FRACP. The Royal Melbourne Hospital, Melbourne, Australia
• Govind Makharia, MBBS, MD, DNB. All India Institute of Medical Sciences, New Delhi, India
• Reza Malekzadeh, M.D, AGAF. Tehran University of Medical Sciences, Tehran, Iran
• Elias Makhoul, MD. University Hospital Notre Dame des Secours, Holy Spirit University of Kaslik Byblos Lebanon.
• Anahita Sadeghi, MD. Tehran University of Medical Sciences, Tehran, Iran
• Jean-Christophe Saurin MD, PhD. Hôpital Edouard Herriot, Lyon, France
• Sandie R. Thomson, ChM, FRCS, FRCP, MB, Groote Schuur Hospital, Cape Town, South Africa
• Andrew Veitch, MD. Royal Wolverhampton Hospitals NHS Trust and Nuffield Hospital, Wolverhampton, UK.
• Kaichun Wu, MD, PhD, Xijing Hospital of Digestive Diseases. Fourth Military Medical University Xi’an China

Purpose

We wish to provide guidance with regard to the utilisation of Personal Protection Equipment (PPE) for the prevention of infection from COVID-19 in health care workers performing gastrointestinal endoscopy, with special reference to low resource situations.

Background and Rationale

Endoscopic procedures will be indicated in some patients who are infected with COVID-19, or whose status is unknown. These procedures pose a transmission risk to the physicians, nurses and technicians involved. Prevention of infection of health care personnel is important in the management of the COVID-19 pandemic since the infection is associated with significant morbidity and mortality and health resources are finite. The procedures also pose a SARS-CoV-2 infection risk to the patient who may be exposed to the virus facility from staff, including the endoscopy personnel.

COVID-19 is spread by four means: contact with an infected surface or object, by droplets, by aerosols and probably by faeco-oral route. Endoscopy units are a suitable environment for disease transmission by all of these routes. Strategies to prevent infection need to be considered with regard to these modes of transmission in three phases: Pre, Intra, and Post endoscopic procedure. Health care worker protection involves more than PPE; hand washing, for example, to prevent contact transmission is an integral part of safe practice.

Ideally, appropriate and optimal PPE would be used in every procedure. However, PPE shortages have emerged as a key issue in the pandemic and this will be particularly problematic in developing world countries.
In order to optimize the use of PPE during this pandemic it is necessary to define both the level of risk and the appropriate PPE defence.

The World Gastroenterology Organisation (WGO) mission focuses on the developing world and low resource localities. WGO Cascades are guidelines formulated to outline options stratified by high, medium and low resource situations. In the current COVID-19 pandemic even traditionally high resource countries have faced equipment shortages requiring them to adopt strategies based on low resource realities. This cascade will outline the ideal resources when no equipment restrictions are in place, and the options for when restrictions on ideal practice occur.

**What is optimal PPE for Endoscopy?**
Upper endoscopy, including ERCP, is associated with the generation of aerosols from the upper GI tract and airways. SARS-CoV-2 is a pathogen which primarily infects the gastrointestinal and respiratory tracts. Aerosols containing the virus pose a risk of infection to medical personnel. In addition, surfaces and equipment in the endoscopy room environment may be contaminated by droplets and direct contact.

Although there is less data on the risk of transmission from lower GI tract procedures, SARS-CoV-2 virus can be detected in stool in up to 48% of COVID-19 patients and some have proposed that precautions should be taken for lower GI tract examinations. Infected patients will contaminate the environment with virus particles which can last for many hours.

In order to define what may be acceptable in low resource settings we first need to define what is optimal in non-restricted resource settings. A recent systematic review concluded that the evidence is limited because the studies simulated infection, and they had a small number of participants. The authors also stated that covering more of the body leads to better protection. However, as this is usually associated with increased difficulty in putting on and removing PPE, and the PPE is less comfortable, it may lead to more contamination and may even interfere with procedure effectiveness. Coveralls are the most difficult PPE to remove but may offer the best protection, followed by long gowns, gowns and aprons. Respirators worn with coveralls may protect better than a mask worn with a gown, but this form of PPE is more difficult to put on. More breathable types of PPE may lead to similar levels of contamination to coveralls but be more comfortable. A balance needs to be struck between the amount of PPE worn, comfort in use and contamination when it is being removed.

**What is the minimal PPE required for endoscopy in low resource settings?**
(See Appendix 1 for Local Manufacture of PPE)

Many developing countries struggle to provide even basic PPE; however there is a minimum requirement for PPE utilized during endoscopy beyond which medical team safety is compromised. Scrubs, hair covering, gowns, face shield, and/or googles, gloves and foot protection are basic requirements. These are not expensive and can be sourced or manufactured locally.

**Masks and Respirator Masks.**
Masks are a key component of PPE. A surgical mask is a loose-fitting, disposable device that creates a physical barrier between the mouth and nose of the wearer and potential contaminants in the immediate environment. Surgical masks differ in thickness and other properties that may affect ease of breathing and protective abilities. They are intended to help protect the wearer by blocking large-particle droplets, splashes, sprays or splatter that may contain viruses and bacteria and to help protect others by reducing their exposure to the wearer's saliva and respiratory secretions. Surgical masks do not provide complete protection because they do not filter very small particles and they do not fit very closely against the face.

A respirator mask is a protective device designed to achieve a very close facial fit and very efficient filtration of airborne particles. The ‘N95’ designation means that when subjected to careful testing, the respirator blocks at least 95 percent of very small (0.3 micron) test particles. If properly fitted, the filtration capabilities of N95 respirators exceed those of face masks. However, even a properly fitted N95 respirator does not completely eliminate all risk. Respirators capture particles through mechanical and electrostatic mechanisms. They are rated by their efficiency. N95, N99 and N100 capture 95%, 99% and 100% of particles respectively. Respirator masks cannot be made without specialized equipment.

The FFP2 mask is the equivalent of N95 and the FFP3 equates to N99. Cloth masks do not meet the minimum level of protection for health care workers and may result in a health care worker becoming infected and spreading disease. We do not recommend that cloth masks be used by health care providers in a health care setting.

For the purposes of this document respirator refers to N95, FFP2, FFP3 or higher levels of protection. PAPR (Powered Air Purifying Respirator) systems are effective but are not in widespread use.

**Variables used in the formulation of recommendations.**

Four inter-related variables guided the committee’s formulation of the
recommendations.

1. The Incidence of COVID-19 varies markedly from country to country and even within countries. Incidence numbers are determined by disease burden and by the extent of testing. It has become clear that the majority of infections are asymptomatic and will not be detected without population testing. There is no clear demarcation between high and low incidence. In the context of endoscopy, a single infected patient in a low incidence setting may result in considerable morbidity. Nevertheless, guidelines especially in resource constrained settings, need to accommodate the level of risk when distributing limited PPE resources.

2. The availability of PPE is related to disease burden since disease burden will result in increased utilization and to local resources. Countries vary markedly in their ability to provide PPE to health care providers. A high incidence of disease may precipitate shortages. Multiple items of PPE are required to perform endoscopic procedures safely. Shortages of even a single component may jeopardize safety.

3. The likelihood of a patient being infected with COVID-19 depends on the individual patient’s risk factors and clinical state and the background incidence of disease. Determination of whether a patient is infected or not is difficult without access to rapid PCR and antibody testing. There is currently no data on the sensitivity and specificity of questionnaires and temperature checks in the detection of COVID-19. A patient’s likelihood of infection with COVID-19 changes the level of PPE used and the frequency with which PPE is discarded.

4. There is disagreement on whether endoscopic procedures on the lower GI tract constitute the same level of risk as upper GI procedures which pose a higher risk of generating aerosols. It is not possible to formulate highly prescriptive recommendations in such a complex, dynamic situation especially given the paucity of evidence. Instead we have attempted to formulate recommendations which will act as guides and permit localised, customized decisions on PPE. These will be updated as experience and evidence evolves.

Comparison with other Societal recommendations.

Many national societies have prepared guidance for the use of PPE for endoscopy during the COVID-Pandemic. In order to give context to the WGO guidance the recommendations of some of these societies are summarised in Table 1 and contrasted with those of the WGO.

Methodology

The Research Committee of the WGO reviewed the literature and national guidelines with special reference to low resource countries. A literature search was conducted on PPE, and endoscopy in low resource settings. The literature results were shared with all members. Owing to resources and time constraints, no preliminary PICO-based statements were formulated; neither the level of evidence nor recommendations were formally graded, but the group followed a modified Delphi consensus process to produce the recommendations. Only low-very-low evidence for the most part was identified which might guide recommendations in this setting. The recommendations for low resource settings are, therefore, based on expert opinion. Much of the published literature on COVID-19 and endoscopy is in the form of preprints and may not have been peer reviewed. However, the guidance here is from a global group of seventeen clinical and research experts from developed, and developing, world countries.

When the committee members were not unanimous on a recommendation the issue was put to a vote with 60% in favor being taken as the threshold for acceptance of a recommendation.

Twenty headline recommendations were generated, and 57 sub recommendations, for PPE use in high and low resource situations. These cover PPE conservation and use of in Pre-procedure, Intra Procedure, Post Procedure and the return towards normal endoscopy unit function.

Recommendations

Pre-Procedure

1. Triage referrals. Reduce the number of endoscopies being performed, delay elective procedures. Rationale: A reduction in non-urgent procedures may reduce the risk of infection to non COVID-19 patients, and to medical personnel, and will conserve PPE.

2. Procedures which are not time-sensitive should be postponed. Rationale: Triage of all procedures should be done by trained medical personnel.

3. Carrying out regular subsequent monitoring of postponed patients to ensure that their condition does not become urgent. Rationale: Hospitals and health care facilities are high risk areas for contracting COVID-19.

4. Provide online or telephone care facilities as much as possible. Rationale: Reschedule non time-sensitive procedures and follow up.
3. **Screen all endoscopy patients for COVID-19 and stratify into low or high risk of infection.**
   Rationale: Screening patients and stratifying infection risk into higher and lower will allow conservation of higher-level PPE, such as respirators. On the other hand, it may induce a false sense of security since even with the most rigorous screening, asymptomatic infected patients may be classified as low risk, and treated as such, with subsequent risk to health personnel; even PCR testing carries a false negative risk that can be significant. Low risk patients are those from a low incidence area, with no history of contact or travel, no symptoms and no signs.

3.1 Stratify patients by risk level.
3.2 Perform screening by questionnaire and temperature checks.
3.3 If possible, supplement this with serological or PCR testing.

Low resource:
3.4 In areas of low incidence of infection, and with a low risk patient as determined by screening, it is reasonable to perform lower GI procedures with less than the highest level of PPE.
3.5 The minimum level of PPE even for a patient triaged as low risk includes scrubs, hair covering, long waterproof gown, boots, face shield, or goggles, reused respirator or surgical mask.

4. **Patients should wear masks on entry to the healthcare facility. Reduce the risk of transmission from infected, or potentially infected patients.**
   Rationale: Patients may be vectors for the disease and may infect other patients, health care providers, and contaminate the environment.

4.1 All patients should wear a surgical mask and disinfect their hands.
4.2 Keep a physical barrier, such as glass, between the nurse doing pre procedure interviews and the patient.
4.3 If a glass barrier is not available, the interviewer should wear eye protection.
4.4 The interviewer should wear a surgical mask and gloves for any contact with low risk patients and full PPE for contact with those suspected or known to be infected.
4.5 Caregivers and relatives should be prohibited from the endoscopy department unless necessary such as, for example, attending procedures on minors or accompanying patients who cannot give consent, or in the case of a language barrier.

Low resource:
4.6 As above from 4.1 – 4.5
4.7 Patients who are at low risk of COVID-19 can wear a cloth mask instead of a surgical mask. The effectiveness of cloth masks is questionable, but a clean, recently washed mask may offer some protection against droplet spread and limit contamination of the healthcare environment.

5. **Minimize the risk of patients acquiring infection.**
   Rationale: Health care facilities are high risk areas for transmission of infection to non-infected individuals. Infection could be acquired from a contaminated environment, other patients or from health care providers.

5.1 Practice physical distancing in the endoscopy unit. Space out chairs and recovery beds.
5.2 Arrange procedure start times to minimize congestion
5.3 Instruct staff to stay home if symptomatic or an unprotected contact with an individual with COVID-19.

Low resource: Same

6. **Minimize staff exposure.**
   Rationale: Usage of PPE can be reduced by minimising the number of personnel in the room. This will also help reduce infection in staff by minimising exposure to aerosol and contaminated surfaces and avoid possible simultaneous large-scale quarantining of staff with subsequent personnel shortage.

6.1 Keep the number of staff in the procedure room to a minimum.
6.2 Plan to bring into the room what you need before you start the procedure so that staff do not need to leave or enter.
6.3 Do not switch staff during the list, or during procedures as PPE will need to be removed. This wastes PPE and risks contamination.
6.4 Do as much documentation, as possible, outside the room, away from the patient.
6.5 Do not take personal belongings such as phones or stethoscopes into any procedural area as these may become contaminated.

Low resource: Same

7. **Train all staff in the correct use of PPE (Appendix 2)**
   Rationale: PPE is only effective if the right equipment is used in the right way for the right indication. Incorrectly donned PPE, such as an incorrectly fitted respirator, reduces PPE effectiveness and increases the risk of infection from COVID-19. Incorrect removal of PPE risks contaminating the user and the workspace. Correct procedure for donning and doffing is essential.

7.1 Review and observe staff practicing PPE donning and doffing.
7.2 Make sure that staff have been fitted for respirators if possible. See Appendix 1.
7.3 Emphasize the importance of meticulous hand hygiene.
7.4 Create an area adjacent to the
endoscopy rooms where PPE can be safely donned and doffed.

**Low resource:** Same

8. **Do not involve trainees in procedures on patients with a high risk of COVID-19.**

   **Rationale:** This will reduce trainee risk of infection, conserve PPE, and provide a physician reserve which may be utilised if necessary, if attending staff become ill. The difficulty is that many patients with COVID-19 are asymptomatic. Some patients, such as those with a positive RNA PCR, clearly have the disease and trainees should be excluded. Such a policy will also optimize effectiveness while minimizing procedural times and thus exposure of the personnel.

   **Low resource:** Same

**Intra Procedure**

9. **Wash Hands**

   **Rationale:** Contaminated hands may transfer the virus to eyes or mouth. Wash hands properly with soap for 20 seconds or use an alcohol based disinfectant, before and after each procedure, after contact with potentially infectious sources, before putting on PPE, and after removal of PPE. Gloves are not a substitute for proper hand hygiene.

   **Low resource:** Same

10. **Use a respirator for all upper procedures**  
    (See Appendix 3 for guidance on reuse)

    **Rationale:** Respirator masks represent optimal mask protection especially for aerosol generating procedures.

    **10.1 Do not discard the respirator between cases unless the endoscopy has been performed on a patient diagnosed with COVID-19 or highly likely to have the disease. See Appendix 3 for guidance on extended use or reuse of respirators.**

    Vote: 36% were in favor of changing the respirator between all cases even in low resource settings.

    **Low resource:**

    **10.2.** Where feasible collect used N95 respirators that are not visibly soiled or damaged so that they may be reprocessed for future use using appropriate sterilization and decontamination methods.

    **11. Use a respirator for lower GI procedures in high resource settings only**

    **Rationale:** The virus is detectable in the stool of infected patients.

    Lower GI tract procedures represent a risk of contamination of both the environment and the endoscopist. Aerosolization may be less than with upper procedures but may occur with removal of instruments from the biopsy channel. There is evidence of virus shedding into the air from infected patients simply by breathing. It is likely that the air in the endoscopy room will be contaminated further justifying the use of a respirator in this setting. Face shields may help extend the life of respirator stock by preventing contamination.

    Vote: 71% in favor.

    **11.1.** Do not discard the respirator between cases unless the procedure has been performed on a patient diagnosed with COVID-19 or highly likely to have the disease.

    **11.2.** Use a face shield and goggles with the respirator.

    **Low resource:**

    **11.3 Use a surgical mask during lower GI procedures on low risk patients.**

    Vote: 50% in favor of using respirators in lower GI procedures in low resource settings, this was not adopted.

    **12. Use surgical masks only in low risk patients in low resource settings.**

    **Rationale:** Surgical masks are made of non-woven materials such as cellulose polypropylene. They are designed to stop large droplet contamination from the user, but they are not designed to effectively filter particles less than 3 microns in size. COVID-19 has a diameter of 0.15 microns. As discussed above in Recommendation 3 the concept of low risk patients may not be valid.

    **Low resource:** Same

13. **Wear a single pair of gloves.**

    **Rationale:** For health care workers performing any GI procedure, regardless of COVID-19 status, some organizations recommend the use of double gloves compared with a single pair. There is some support for reduced contamination with double gloves\(^{11}\). The outer glove is removed, then the respirator and goggles are removed using the clean glove, and then the second glove is taken off.

    Vote: 57% voted for use of two pairs of gloves. The recommendation is for a single pair.

    **Low resource:**

    **13.1 In low resource settings, as for high resource settings, a single pair of gloves with meticulous hand washing is acceptable practice.**

    **50% voted for use of two pairs of gloves in this setting.**

    **13.2 Regardless of whether one pair, or two, are used it is important that there is no gap between glove and gown\(^{17}\). Gowns with thumb loops may help in this regard.**

14. **Wear a face shield.**

    **Rationale:** Face shields will protect the mask, eyes and face from splatter\(^{18}\) but will not protect from aerosols. Face shields are not difficult to manufacture. See Appendix on manufacture of face shields.

    Vote: 86% in favor.

    **14.1 Disinfect between each case.**

    **Vote 85% in favor**

    **14.2 Face shields do not need to be combined with goggles.**

    **Vote 21% in favor of combined**
goggle and face shield use. 

**Low resource:** Same

15. Wear Goggles
Rationale: COVID-19 infection may be acquired through the conjunctivae, certainly the virus can be found in tears. We do not know if aerosolized COVID-19 is infectious through the conjunctivae. If it is, only goggles will be protective from infection through the eyes and, a face shield alone may not suffice. It is likely that the virus can be transmitted through the conjunctivae if the eyes are touched by contaminated hands. This provides additional rationale for using goggles.

Vote: 86% in favor.

15.1 Use reusable, or disposable, goggles to prevent infection.

15.2 Disinfect the goggles between lists and after use in an infected patient.

Vote: 36% voted for disinfection between each case.

**Low resource:** Same

16. Wear scrubs, a gown and hair protection
Rationale: The objective of PPE is to create a barrier between the virus and the health provider. Contaminated clothes and skin and hair may lead to infection as contaminated hands touch the eyes or lips.

16.1 Wear scrubs and do not bring them out of the health center.

16.2 Wear a long waterproof gown.

16.3 Cover the skin of the neck and cover the hair.

16.4 Discard the gown between each case. This may help reduce infection to the health care provider from a contaminated gown, and transmission to non-infected patients, but will result in increased usage of PPE.

The committee voted 79% in favor of discarding gowns between use. 

**Low resource:**

16.5 In low risk patients, a disposable plastic apron can be worn over the gown. This can be discarded between cases, and the gown retained, allowing extended use of the gown. See Appendix 1 on local manufacture of gowns in situations of extreme shortage. The committee voted 50% in favor of discarding gowns in low resource settings.

16.6 Consider switching to reusable isolation gown options, wherever possible. These can be washed and disinfected in a hospital laundry.

**Rationale:** COVID-19 is shed into the air by infected patients. Aerosols containing the virus may be created during upper GI procedures. Aerosolized virus poses a risk to medical personnel. Reducing the concentration of virus in the air and preventing contamination of the air in adjacent rooms is a reasonable objective. Negative pressure rooms may help stop the spread of aerosols containing the virus to other areas of the facility. It is reasonable to use negative pressure rooms if available, but they are not essential. Negative pressure rooms are not widely available in low resource countries.

18.1 Use a negative pressure room if it is available.

18.2 When negative pressure rooms are unavailable, portable industrial-grade high-efficiency particulate air (HEPA) filters are a reasonable alternative to negative pressure rooms and can be used without a room filtration system.

18.3 Ensure that air conditioning is not in recycle mode.

18.4 Delay allowing a new patient in the room 30 minutes for negative pressure rooms) and 60 minutes in the absence of negative pressure rooms. Rooms differ in the amount of airflow and this should be determined for each unit. This will allow some time for aerosols of the virus to disperse.

**Low resource:**

18.5 If HEPA are not available, adequately ventilate the procedure room to the outside by opening windows or using a fan to blow air to the outside.

**Post Procedure**

19. Endoscopy reprocessing staff should utilize PPE.

Rationale: Reprocessing staff are exposed to contaminated scopes and should wear personal protective equipment (PPE) that includes gloves, gown, face shield, and surgical mask. Surgical mask may suffice since aerosol should be less than in the procedure room. While there is no data to support a requirement for the use of respirators in the reprocessing room, their use should be considered, if available.

**Low resource:** Same

20. Endoscopy room cleaning staff
should utilize PPE.

Rationale: The area where a procedure has been performed on a COVID-19 infected patient, the recovery area and washrooms will be contaminated. Aerosol should be reduced compared to procedure time so a surgical mask may be adequate for workers in this situation. Staff involved in the cleaning of endoscopy rooms should utilize PPE. This should include head cover, gown, surgical mask, eye-protection, foot coverings and gloves.

20.1 Given the contamination of the endoscopy environment it is necessary to perform meticulous cleaning of room after each procedure.

Low resource: Same

Returning to usual practice after the COVID-19

We have provided guidance with regard to the utilisation of Personal Protection Equipment (PPE) for the prevention of infection from COVID-19 in health care workers performing gastrointestinal endoscopy, with special reference to low resource situations. Once the initial phase of the pandemic is over it will be necessary to plan the reopening of endoscopy units and to revise triage criteria. This has implications for PPE and will be the subject of a separate report.

Acknowledgement.
The literature searches were carried out by Justus Krabshuis of the WGO “Ask a Librarian” service. This service is available for free for those interested in or working in the fields of Gastroenterology, Hepatology and Endoscopy in LMIC countries. We are very grateful for his help.

https://www.worldgastroenterology.org/forms/ask-a-librarian.php
References


APPENDIX 1

Local manufacture of PPE in limited resource settings.

Optimal PPE for endoscopy: Hair covering, protective glasses, face shield, N95 mask with covering surgical mask, scrubs, long disposable plastic gown, disposable foot coverings, gloves. Courtesy Dr Harshit S. Khara, MD. Clinical Associate Professor of Medicine, Geisinger Medical Centre, PA, USA.

What is currently felt to be optimal PPE is illustrated above. In extreme situations it may be necessary to innovate. The evidence base for the optimal equipment is weak. The evidence base for innovative equipment does not exist. The risk of performing procedures with novel fabricated PPE has to be weighed against benefit. Given WGO’s mission and focus on low-resource settings some of these innovations are described here but extreme caution is urged. If possible, consider referral to centres with adequate PPE before resorting to non-standard PPE.

Hair covering and scrubs
These can be manufactured from a variety of washable, synthetic and natural materials.

Face shields
These can be made from a variety of materials available in home or office.
Appendix 2


Appendix 3: Reuse of Respirators

Background: The nine types of certified particulate respirators that can be used by health care workers include: N95, N99, N100, R95, R99, R100, P95, P99, P100. Respirators are rated “N” if they are not resistant to oil, “R” if they are somewhat resistant to oil, and “P” if they are oil-proof.

It is worth noting that the coronavirus is 0.12 microns in diameter, about one tenth the size of an E.coli, and that N95 is designed to filter out 95% of particles with a median size of 0.3 microns in diameter. It follows that a mask rated at N95 or FFP2 is not necessarily sufficient to filter out COVID-19 and they should be used with a face shield. Degradation of the mask with loss of filtering ability will compromise safety.

The following is taken from the CDC but does not represent the whole document which should be reviewed.

(Recommended Guidance for Extended Use and Limited Reuse of N95 Filtering Facepiece Respirators in Healthcare Settings. [https://www.cdc.gov/niosh/topics/hcwcontrols/recommendedguidanceextuse.html](https://www.cdc.gov/niosh/topics/hcwcontrols/recommendedguidanceextuse.html))

There is no way of determining the maximum possible number of safe re-
uses for an N95 respirator as a generic number to be applied in all cases. Safe N95 reuse is affected by a number of variables that impact respirator function and contamination over time.

The CDC recommends discarding masks following aerosol generating procedures and any contaminated with fluids from patients.

Used respirators, which will be re-used, should be hung in a designated storage area or in a clean, breathable container such as a paper bag between uses.

To minimize potential cross-contamination, store respirators so that they do not touch each other and the person using the respirator is clearly identified. Storage containers should be disposed of or cleaned regularly.

Clean hands with soap and water or an alcohol-based hand sanitizer before and after touching or adjusting the respirator (if necessary, for comfort or to maintain fit).

Avoid touching the inside of the respirator. If inadvertent contact is made with the inside of the respirator, discard the respirator and perform hand hygiene as described above. Use a pair of clean (non-sterile) gloves when donning a used N95 respirator and performing a user seal check. Discard gloves after the N95 respirator is donned and any adjustments are made to ensure the respirator is sitting comfortably on your face with a good seal.

**Improving the safety of Reused Masks.**

A number of methods have been recommended to improve the safety of reused masks. The following is taken from SAGES. (SAGES. N95 Mask Re-Use Strategies. https://www.sages.org/n-95-re-use-instructions/).

**Mask rotation**

Acquire a set number of N95 masks, or equivalent, (at least 5 per the CDC), and rotate their use each day, allowing them to dry for long enough that the virus is no longer viable (> 72 hours). Proper storage for this technique requires either hanging the respirators to dry, or keeping them in a clean, breathable container like a paper bag between uses. Make sure the masks do not touch each other, and that you do not share your respirator with other people. A user seal check should be performed before each use.

**Hydrogen Peroxide Vaporization**

Hydrogen peroxide vapor (HPV) decontamination has been shown in pilot studies to allow multiple cycles of N95 processing with acceptable preservation of function. It is now approved by the FDA as an emergency method for N95 decontamination for healthcare personnel during the COVID-19 pandemic. This method of decontamination can only be used on N95 models that do not contain cellulose, such as the 1860. It is being utilized in industrial facilities such as Battelle (up to 20 cycles) as well as individual hospitals via Sterrad (up to 2 cycles) or Steris equipment (up to 10 cycles).

**UV treatment**

Proper UV treatment of N95 masks requires specific dosing protocols and full surface area illumination to ensure proper inactivation of viral particles with minimal mask degradation. Due to the precision required, home UV light use is not recommended. This method of decontamination has been implemented by some hospital systems in the United States.

**Moist Heat**

Moist heat (heating at 60-70°C and 80-85% relative humidity) has been shown to be effective for flu viruses, but there is limited data on the temperature, humidity, and time required to completely inactivate SARS-CoV-2 viral particles. Moreover, the parameters required to kill the virus may adversely affect filtration efficacy of the mask. Due to the dearth of specific data on a protocol to achieve both aims, this method is not currently recommended.

**Dry Heat**

Dry heating of the mask at 70°C for 30 minutes has been suggested as a method of decontamination which can adequately kill virus and preserve the filter integrity for re-use. Recent tests at the NIH utilizing SARS-CoV-2 specifically indicated that this method can be used for two cycles to kill the virus without compromising fit. Research efforts are ongoing to determine optimal parameters (temperature and duration), and this is not yet recommended by the CDC.
WGO Guidance for Patients with COVID-19 and Liver Disease

Cihan Yurdaydin, MD
WGO Past President and Chair of Nominations
Koc University Medical School
Istanbul, Turkey

Saeed Hamid, MD
Chair, WGO Hepatology Interest Group
Aga Khan University, Department of Medicine
Karachi, Pakistan

I. INTRODUCTION AND GENERAL APPROACH TO THE PATIENT WITH COVID-19 AND ELEVATED LIVER ENZYMES

Alice Lee (Australia), Qin Ning and Tao Chen (China), Dirk J van Leeuwen (USA)

The World Health Organization declared a global pandemic of the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) on March 11, 2020. To date, worldwide there have been approximately 5 million confirmed cases of coronavirus disease 2019 (COVID-19). Worldwide, many of us are overwhelmed by the increased demands that this infection has put on our healthcare systems and our personal work. This document is to summarize what we believe is currently the best way forward realizing that, depending on local circumstances, some recommendations may be difficult or even impossible to implement.

Elevated liver biochemistries are common in COVID-19 infection with a reported incidence of 14 to 76%. Elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are the most commonly reported pattern of liver derangement with slight elevations of bilirubin seen in about 10% of cases. Raised gamma-glutamyl transferase (GGT) levels are seen in up to 50% of cases, but alkaline phosphatase (ALP) is typically normal (1-3).

Significantly higher ALT and AST levels are reported in severe COVID-19. However, these increases in ALT and AST are usually quite mild and do not exceed 3 times the upper limit of normal (ULN). Serum AST was >40 IU/L in 52% of patients who died, but only in 16% patients who
obvious inflammatory cell infiltration lobular and portal activity but no microvascular steatosis, and mild steatosis in addition to mild to moderate features of acute cellular rejection (8). No viral inclusions were seen in any of the biopsy specimens. However, in a recent report, ultrastructural examination of liver tissues from 2 COVID-19 patients identified in the cytoplasm of hepatocytes typical coronavirus particles characterized by spike structure (9).

Histologically, massive hepatic apoptosis and a certain binuclear hepatocytes were observed. Immunohistochemical results showed scanty CD4+ and CD8+ lymphocytes. These ultrastructural and histological changes were considered indicative of a typical viral infection lesion (9). A proposed mechanism of direct liver injury is by direct cytotoxicity from viral replication in liver cells. However, the cell entry receptor of SARS-CoV-2, angiotensin converting enzyme 2 receptor (ACE2) (10), which is highly expressed in alveolar epithelial cells of the lung, is expressed only in 2.6% of hepatocytes. In contrast, although ACE2 is expressed on 58% of bile duct cells (11); ALP, a marker of bile duct injury, appears to be the least-affected of the liver enzymes. Thus, it remains unclear whether SARS-CoV-2 plays a direct role in producing liver injury (2-4).

ACE2 receptors are also expressed on vascular endothelial cells. One concern, therefore, may be that vascular diseases are increased in COVID-19 infection. An increase in peripheral arterial disease has been suggested (12). Furthermore, there are anecdotal reports of increased thromboembolism, particularly in critically-ill patients (13-16). However, according to the American Society of Hematology, the incidence of venous thromboembolism in COVID-19 patients is not established. It remains to be seen if thromboembolic events are secondary to severe illness and associated co-morbidities or if there is a specific link between COVID-19 infection and thromboembolic events. The frequency of ACE2 receptor expression is reported to be low in the liver vascular endothelium and endo-thelitis has not been noted in post-mortem liver biopsies of COVID-19 patients (17).

Systemic viral infections can cause transient elevation in transaminases as a result of general immune activation due to circulating cytokines without significant liver injury even in the most severe cases (“bystander hepatitis”) (18). However, in the absence of obvious inflammatory cell infiltration and typical liver cell necrosis, it is hard to conclude that bystander hepatitis occurs in COVID-19 patients.

Based on a study of the immunological characteristics of severe COVID-19 patients, serum concentrations of both pro-inflammatory cytokines and anti-inflammatory cytokines, including IL-2R, IL-6, TNF-α and IL-10 were increased in most severe cases and were markedly higher than in moderate cases, suggesting that cytokine storms might be associated with disease severity (19). However, a relationship between cytokine changes and hepatic inflammation has not been confirmed, suggesting that other contributors to liver injury should also be considered, such as hypoxic ischemic organ damage.

Possible drug-induced liver injury (DILI) should always be considered; an association with lopinavir/ritonavir appears to have been consistently reported (2, 3). However, other drugs may also be associated with liver toxicity.

It is also possible that the raised transaminases may actually be due to myositis which have been commonly reported in COVID-19 infection, this

recovered (4). AST is more frequently elevated compared to ALT. Lower platelet counts and albumin levels are seen in those with more severe disease; 65% of deceased but only 14% of recovered patients had albumin levels <32g/L. However, low albumin levels are not linked to liver failure, which has not been reported so far in COVID-19. The virus *per se* is unlikely to cause primary liver injury (1-4) and is not clearly associated with flares or progression of chronic liver disease. Acute on chronic liver disease reported for the influenza virus (5) has, so far, not been reported for SARS-CoV-2 infection.

In the era of SARS-CoV-2 infection, atypical presentations can occur, requiring isolation and testing. Acute hepatitis as the presentation of COVID-19 with dark urine, AST of 1230 IU/L, ALT of 697 IU/L (normal range <50), low albumin and raised ferritin of 6606 ng/mL (N<150) is reported in a patient with HIV infection on therapy. Viral screen was negative and previous liver tests were normal. Fever and chest X-ray changes were seen 18 hours after admission. An uneventful recovery occurred with normalisation of liver tests (6). Further data are required before recommending routine SARS-CoV-2 testing for SARS-CoV-2 as a potential cause of patients with acute hepatitis.

**Pathogenesis of liver abnormalities in COVID-19 disease**

The mechanisms of effects of SARS-CoV-2 on the liver are not well defined. Although direct viral cytopathic effects have been described with other coronaviruses (SARS, MERS), there was no data to support this in COVID-19. Findings on post mortem biopsies include moderate microvascular steatosis, and mild lobular and portal activity but no obvious inflammatory cell infiltration and/or typical liver cell necrosis were

found (7). Liver biopsy in an infant who developed COVID-19 post-liver transplant showed moderate acute hepatitis with prominent clusters of apoptotic hepatocytes, lobular lymphohistiocytic inflammation, and mild steatosis in addition to moderate features of acute cellular rejection (8). No viral inclusions were seen in any of the biopsy specimens. However, in a recent report, ultrastructural examination of liver tissues from 2 COVID-19 patients identified in the cytoplasm of hepatocytes typical coronavirus particles characterized by spike structure (9).

Histologically, massive hepatic apoptosis and a certain binuclear hepatocytes were observed. Immunohistochemical results showed scanty CD4+ and CD8+ lymphocytes. These ultrastructural and histological changes were considered indicative of a typical viral infection lesion (9). A proposed mechanism of direct liver injury is by direct cytotoxicity from viral replication in liver cells. However, the cell entry receptor of SARS-CoV-2, angiotensin converting enzyme 2 receptor (ACE2) (10), which is highly expressed in alveolar epithelial cells of the lung, is expressed only in 2.6% of hepatocytes. In contrast, although ACE2 is expressed on 58% of bile duct cells (11); ALP, a marker of bile duct injury, appears to be the least-affected of the liver enzymes. Thus, it remains unclear whether SARS-CoV-2 plays a direct role in producing liver injury (2-4).

ACE2 receptors are also expressed on vascular endothelial cells. One concern, therefore, may be that vascular diseases are increased in COVID-19 infection. An increase in peripheral arterial disease has been suggested (12). Furthermore, there are anecdotal reports of increased thromboembolism, particularly in critically-ill patients (13-16). However, according to the American Society of Hematology, the incidence of venous thromboembolism in COVID-19 patients is not established. It remains to be seen if thromboembolic events are secondary to severe illness and associated co-morbidities or if there is a specific link between COVID-19 infection and thromboembolic events. The frequency of ACE2 receptor expression is reported to be low in the liver vascular endothelium and endo-thelitis has not been noted in post-mortem liver biopsies of COVID-19 patients (17).

Systemic viral infections can cause transient elevation in transaminases as a result of general immune activation due to circulating cytokines without significant liver injury even in the most severe cases (“bystander hepatitis”) (18). However, in the absence of obvious inflammatory cell infiltration and typical liver cell necrosis, it is hard to conclude that bystander hepatitis occurs in COVID-19 patients.

Based on a study of the immunological characteristics of severe COVID-19 patients, serum concentrations of both pro-inflammatory cytokines and anti-inflammatory cytokines, including IL-2R, IL-6, TNF-α and IL-10 were increased in most severe cases and were markedly higher than in moderate cases, suggesting that cytokine storms might be associated with disease severity (19). However, a relationship between cytokine changes and hepatic inflammation has not been confirmed, suggesting that other contributors to liver injury should also be considered, such as hypoxic ischemic organ damage.

Possible drug-induced liver injury (DILI) should always be considered; an association with lopinavir/ritonavir appears to have been consistently reported (2, 3). However, other drugs may also be associated with liver toxicity.

It is also possible that the raised transaminases may actually be due to myositis which have been commonly reported in COVID-19 infection, this
should be considered if AST > ALT and if creatinine kinase (CK) is also elevated, as this is characteristic of myositis.

Transaminases > 3-5 x ULN, and/or elevation of bilirubin > 3 x ULN are believed to be uncommon in COVID-19 patients and should lead to consideration of other causes (20). It is important to remember that intensive care unit (ICU) patients often suffer from multiple conditions, which could explain abnormal tests secondary to disease complications.

Should all patients with COVID-19 get a set of liver tests done?
Outpatients with COVID-19 managed by home quarantine do not require routine liver tests. Patients admitted to hospital should have baseline liver tests, including ALT, AST, GGT, ALP and bilirubin. Liver enzymes should be monitored as COVID-19 progresses; if available, platelets, albumin, ferritin and CRP should also be monitored in severe cases.

Additional blood tests, including hepatitis B and C serology, should be considered to exclude other causes of liver disease, depending on the local context and available resources. Imaging is not routinely recommended, unless it is likely to change the management of the patient.

New onset liver test abnormalities during admission in COVID-19 patients should be managed in the same way as in COVID-19 negative patients, with particular consideration for excluding DILI. Patients with abnormal liver tests should not be excluded from receiving investigational agents to treat COVID-19, but close monitoring is recommended. Routine liver biopsy is not recommended.

After analysis of findings, assessment should include the urgency of implementation of any recommendations (Table 1). Test results need to be interpreted in the context of the patient's illness (Table 2).

**SUMMARY**

- Most commonly reported liver test abnormalities are elevated ALT and AST (14-76% of patients) - more common in severe disease and associated with worse outcome.
- Bilirubin increase in about 10%, alkaline phosphatase elevation infrequent.
- Mechanism of liver test abnormalities unknown: ACE2 receptors on cholangiocytes, and to a lesser extent, on hepatocytes; direct injury plausible recent data to support this.
- Possible mechanisms include drug induced liver injury (DILI), hypoxic hepatitis and an overactive immune-mediated pro-inflammatory response.

### Table 1. Determine Causes

<table>
<thead>
<tr>
<th>Test</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>COVID-19 infection per se</td>
<td></td>
</tr>
<tr>
<td>Complication of COVID-19 or treatment</td>
<td></td>
</tr>
<tr>
<td>Sepsis</td>
<td></td>
</tr>
<tr>
<td>Hypoxic injury and/or ventilator complications</td>
<td></td>
</tr>
<tr>
<td>Drugs including antibiotics and experimental therapy</td>
<td></td>
</tr>
<tr>
<td>Pre-existing liver disease that may not have been diagnosed (HAV, HBV, HCV, HEV, MAFLD, alcohol-related liver disease, auto-immune liver disease, other)</td>
<td></td>
</tr>
<tr>
<td>Concomitant medical problems.</td>
<td></td>
</tr>
<tr>
<td>Examples: Common bile duct obstruction (stones)</td>
<td></td>
</tr>
<tr>
<td>Malignancy of liver or biliary tract</td>
<td></td>
</tr>
<tr>
<td>Ascites</td>
<td></td>
</tr>
<tr>
<td>Thrombosis (Budd-Chiari), portal vein thrombosis</td>
<td></td>
</tr>
<tr>
<td>Exclude non-hepatic causes of abnormal liver tests</td>
<td></td>
</tr>
</tbody>
</table>

### Table 2. Determine need for further evaluation and urgency of intervention

<table>
<thead>
<tr>
<th>Test</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypoalbuminemia</td>
<td>Common in patients with systemic inflammatory response, usually not an indicator of liver failure</td>
</tr>
<tr>
<td>Prolonged INR or thrombocytopenia</td>
<td>Spontaneous coagulopathy / disseminated intravascular coagulation (DIC) may be present in 1/3 of sick patients (15, 21)</td>
</tr>
<tr>
<td>High transaminases or bilirubin (&gt; 3 x ULN)</td>
<td>Not typical for COVID-19, consider other causes</td>
</tr>
<tr>
<td>Anemia</td>
<td>GI bleeding: ulcer? Variceal hemorrhage?</td>
</tr>
<tr>
<td>Imaging</td>
<td>Chest-CT often done in some places: Could it help to assess liver/biliary tract disease? If indicated do US but avoid unnecessary imaging including US. (Not formally investigated)</td>
</tr>
<tr>
<td>GI symptoms including diarrhea</td>
<td>Common</td>
</tr>
</tbody>
</table>
• Consider myositis when AST is higher than ALT and accompanied by creatinine kinase elevation.
• Prolonged INR and thrombocytopenia may be secondary to disseminated intravascular coagulation. Thromboembolic events are common in COVID-19.
• Hypoalbuminemia may develop as a consequence of severe inflammatory response and is not indicative of liver failure.
• When ALT and bilirubin is > 3 x ULN consider other causes.

WGO recommendations:
• In this COVID-19 era, routine outpatient testing is not recommended – this applies to developed as well as developing countries.
• In patients with elevated ALT or AST, check for viral hepatitis causes. In developing countries, this may be particularly important, as patients may not have been tested before.
• Monitor COVID-19 progression with platelets, albumin, ferritin and CRP in severe cases dependent on availability.
• Routine investigation to exclude other aetiologies should take into consideration local context and availability.
• Routine imaging is not recommended unless it will alter management.

References
11. Chai X, Hu L, Zhang Y, et al. Specific ACE2 expression in cholangiocytes may cause liver damage after 2019-nCoV infection. bioRxiv 2020; published online Feb 4: doi.org/10.1101/2020.02.03.931766

II. LIVER CO-MORBIDITIES AND COVID-19:
A- Chronic hepatitis B and C
B- Metabolic dysfunction-associated fatty liver disease (MAFLD)
C- Autoimmune liver diseases

IIA. CHRONIC HEPATITIS B AND C AND COVID-19
Brian J McMahon (USA)
The COVID-19 pandemic has resulted in significant morbidity and mortality in the world since it began in late 2019. Mortality appears to be highest in persons with underlying chronic medical conditions. Currently, whether the novel coronavirus, SARS-CoV-2, causes direct liver injury is debated (1, 2). A more accepted concept is that the liver damage is collateral, caused by a cytokine storm induced by T cells and dysfunction of the innate immune response (2). However, three cases of viral hepatitis were found during the original SARS-1 outbreak early in this century (3). Thus, as more details on the pathogenicity of the SARS-CoV-2 coronavirus are uncovered, we may learn more about the virus’s effect on hepatocytes.

Currently, little is known about the independent contribution of chronic viral hepatitis B (HBV), with or without hepatitis D, and chronic hepatitis C (HCV) to the overall outcome in those persons who are infected with SARS-CoV-2. A study conducted early in the COVID-19 epidemic in China where the prevalence of chronic HBV is high, found no evidence that underlying chronic HBV infection increased adverse outcomes in persons with COVID-19 (1). A recent report from the Centers for Disease Control and Prevention (CDC) in the US found that 1% of hospitalized persons with COVID-19 has underlying liver disease (4). However, the etiology of the underlying liver conditions in these patients was not included in this report. Nevertheless, it is highly likely that those persons with chronic HBV or HCV who have advanced fibrosis or cirrhosis would be at an increased risk of more adverse outcomes if they were to develop COVID-19 disease. However, we currently have no solid evidence whether SARS-CoV-2 independently damages the liver in persons with underlying chronic hepatitis B, C, or D.

Since the global prevalence of chronic hepatitis B and C is high, though variable from country to country, we can make some generalized recommendations regarding approaches to persons with underlying chronic viral hepatitis who present with COVID-19 disease. First, all persons who are symptomatic with COVID-19 infection should have blood tests for AST, ALT, bilirubin and if any are elevated, they should be tested for hepatitis B surface antigen (HBsAg) and anti-hepatitis C antibody (reflexed to HCV RNA if positive). Those positive who have evidence of chronic viral hepatitis should have liver tests frequently monitored if they are hospitalized, as acute on chronic liver failure could be a theoretical risk as has been reported with influenza (5) but not so far with SARS-CoV-2. Furthermore, in patients with compensated liver disease non-invasive fibrosis markers may be used for assessment of advanced liver disease (fibrosis) or cirrhosis. Patients with decompensated cirrhosis should be further assessed with Child Pugh and MELD scores.

In persons with chronic viral hepatitis who have had a liver transplant and acquire COVID-19 disease, a flare of hepatitis could be related to the COVID-19 disease and not due to rejection of the transplanted liver, so clinicians should proceed with caution and thoroughly consider the aetiology of the rise in transaminases. Secondly, if persons with hepatitis B acquire COVID-19 and are on antiviral therapy, they should continue their medications. In these persons, an elevation of ALT/AST could be a direct result of the immunologic response to COVID-19 or a flare of their underlying HBV infection. An HBVDNA level should be done and if low (<2,000 IU/ml) or undetected, the cause of this flare could be considered a manifestation of the COVID-19 syndrome.

In the case of HCV infection, persons who are taking HCV direct acting antiviral medications (DAA) should continue these drugs and treatment should not be interrupted. In contrast, it would be prudent to stop interferon in persons receiving this medication to treat either HBV or HCV, as this could increase the severity of COVID-19, since severity appears to be associated, at least in part, with a cytokine storm response to the virus and interferon is a potent cytokine. Such patients should still be monitored carefully. Conversely, a prudent course of action would be to not start any patients with chronic HBV on interferon until this pandemic is over.

There is no evidence that HBV or HCV antiviral drugs have any additional adverse effects in persons with chronic viral hepatitis who acquire COVID-19 disease. However, for persons with active HCV infection who are not yet on DAA, it would be prudent to delay therapy until after their recovery from COVID-19 dis-
ease. While it is too early to tell, some HBV and HCV antiviral medications have recently been shown to bind to the SARS-CoV-2 RNA RdRp site on this virus, though the avidity of this binding appears to be less than, for example, sofosbuvir binding to HCV polymerase. Thus, it is conceivable that some medications for HCV and HBV, such as sofosbuvir, tenofovir and ribavirin may have some potential therapeutic activity against SARS-CoV-2 and clinical trials are underway.

In conclusion, more data are needed to determine if persons with chronic hepatitis B or C are at increased risk of adverse outcomes if they are infected with SARS-CoV-2, which causes COVID-19 disease. However, patients with chronic viral hepatitis who have advanced fibrosis or cirrhosis are, probably, at risk of more severe outcomes if infected with SARS-CoV-2 and they should, therefore, self-isolate to minimise the risk of developing COVID-19. Patients with chronic viral hepatitis should be counselled to wash their hands frequently, practise distancing, wear a facemask when going out and avoid crowds. It is also very important not to stop antiviral therapy in persons receiving DAA for hepatitis C or tenofovir or entecavir for HBV, as this could cause a viral rebound and subsequent flare of hepatitis. It is also important that patients with chronic HBV who are on oral antiviral medication have an adequate supply of their drugs, so they do not run out during the pandemic.

References:

SUMMARY
- It is unknown if patients with chronic hepatitis B and C, may be more susceptible to liver damage from SARS-CoV-2.
- It is not known whether patients with chronic HCV or HBV infection have a greater risk or not of severe disease after acquiring COVID-19.
- It is unknown whether patients on antiviral drugs for HCV or HBV are at less of a risk of severe outcomes after acquiring COVID-19.
- Some medication used to treat HBV or HCV such as sofosbuvir, tenofovir and ribavirin bind to the RdRp site on the CoV-SARS-2 virus and may have some potential therapeutic activity against SARS-CoV-2.

WGO Recommendations:
- In low income countries assessment for COVID-19 should include blood tests for AST, ALT, and if any are elevated, patients should be tested for HBsAg and anti-HCV (reflexed to HCV RNA if positive).
- In all patients with COVID-19 who are admitted to the hospital, test for hepatitis B and C: HBsAg and anti-HCV, with HCV RNA testing for those anti-HCV positive.
- Treat those diagnosed with HBV or HCV with DAAs, at least those with signs indicative of advanced liver disease.
- Do not stop antiviral medications for HBV or HCV in patients who present with COVID-19
- Avoid procedures during the COVID-19 illness that could put others at risk such as liver US or other advanced imaging unless there is a clinical suspicion.
- Provide 90-day supplies instead of 30-day supplies for HBV oral antiviral drugs and have a full course of DAA medications to complete HCV treatment if this has been started.

IIB. METABOLIC DYSFUNCTION ASSOCIATED FATTY LIVER DISEASE (MAFLD) AND COVID-19
Joost PH Drenth, (Netherlands)
The diagnosis of metabolic dysfunction-associated fatty liver disease (MAFLD), formerly called non-alcoholic fatty liver disease (NAFLD), is based on evidence of hepatic steatosis, in addition to one of the following three criteria: overweight/obesity, presence of type 2 diabetes mellitus, or evidence of metabolic dysregulation (1). Untreated MAFLD may progress to steatohepatitis, development of fibrosis and cirrhosis and ultimately hepatic decompensation and hepatocellular carcinoma.

Many patients with MAFLD possess a number of risk factors such as obesity, which may translate to a greater risk from respiratory infections. A nested case control study among 561 patients with community acquired pneumonia found a MAFLD prevalence of 36%. Presence of MAFLD increased 30-day mortality...
from pneumonia to 17% compared to 5.8% among patients without MAFLD. This association was greater in patients with advanced hepatic fibrosis (2).

The interaction between MAFLD and respiratory infections begs the question whether (i) MAFLD patients are at a greater risk to acquire COVID-19 and (ii) whether MAFLD patients follow a different disease course. There are a number of small cohort studies that shed light on this issue.

i. Risk to acquire COVID-19

It is unknown whether MAFLD patients are at a higher risk of COVID-19. There is speculation that patients suffering from metabolic dysfunction-associated fatty liver disease may be especially vulnerable to COVID-19. SARS-CoV-2 enters the cell through the angiotensin converting enzyme (ACE) 2 receptor. Liver injury and MAFLD up-regulate ACE2 and it is possible that liver injury, treatment with ACE inhibitors and metabolic syndrome may increase susceptibility to COVID-19 (3).

Interestingly MAFLD increases viral shedding time (17.5 ± 5.2 days vs. 12.1 ± 4.4 days p < 0.0001) compared to patients without MAFLD. Thus MAFLD patients are infectious for ~5 days longer (4).

ii. Different COVID-19 prognosis

A Chinese cohort study selected 66 MAFLD patients and divided the cohort into obese (BMI > 25 kg/m²) and non-obese patients. Obesity (n=45) increased the risk of severe COVID-19 disease course substantially (unadjusted OR 5.77, 95% CI 1.19-27.91; p=0.029). The association with obesity and COVID-19 severity remained significant even after adjusting for age, sex, smoking, diabetes, hypertension and dyslipidaemia (5).

A systematic review and meta-analysis from 20 articles (N=4062 participants) established that patients with a high BMI, and a combination of (metabolic) risk factors such as hypertension, diabetes and cardiovascular disease were more likely to develop critical illness. Diabetes mellitus increased the risk for severe disease by 3.04 (CI 2.01-4.60), hypertension by 2.31 (CI 1.68-3.18) and coronary heart disease by 2.76 (CI 1.39-5.45) (6). These data were confirmed by another study among 202 Chinese patients (MAFLD, n=76) (4). Patients with MAFLD had a higher risk of respiratory disease progression than those without MAFLD (44.7 vs. 6.6%), but also possessed a higher likelihood of abnormal liver biochemistry during admission (11.1% vs. 70%) (4). Another cohort study established that MAFLD patients with increased non-invasive liver fibrosis scores (FIB-4 score) are at higher likelihood of having severe COVID-19 illness, (7)

SUMMARY:

Patients with MAFLD have a number of risk factors such as obesity which may translate to a higher mortality from respiratory illnesses, including COVID-19.

It is unknown whether MAFLD patients are at a higher risk of acquiring SARS-CoV-2 infection.

However, liver injury and MAFLD up-regulate ACE2 and it is possible that liver injury, treatment with ACE inhibitors and metabolic syndrome may increase susceptibility to COVID-19.

Patients with MAFLD had a higher risk of respiratory disease progression than those without MAFLD (44.7 vs. 6.6%), but also possessed a higher likelihood of abnormal liver biochemistry during admission (11.1% vs. 70%).

Shedding time of SARS-CoV-2 is longer in patients with MAFLD when compared to those without MAFLD.

WGO Recommendations:

- The identification and monitoring of patients with metabolic disease to identify MAFLD stage and grade is pivotal during and after the COVID-19 crisis.
- Counselling of MAFLD patients to change lifestyle with a focus to curtail risk factors (such as obesity) that predict for a poor prognosis of COVID-19 is encouraged.

References


Patients with autoimmune liver diseases (autoimmune hepatitis, primary biliary cholangitis and primary sclerosing cholangitis), like all patients with chronic medical conditions, should avoid contact with anyone with symptoms, should respect physical distancing recommendations of public health officials and should wash their hands frequently to avoid contracting the virus. During the pandemic, follow-up of patients should be done with phone consultation or telehealth where available.

Our usual practices for diagnosis and follow-up of these patients may be affected by limited access to outpatient laboratory, diagnostic imaging tests, endoscopic retrograde cholangiopancreatoscopy (ERCP) and liver biopsy.

Autoimmune hepatitis

The diagnosis of autoimmune hepatitis (AIH) is typically confirmed with liver biopsy, but during the pandemic it is best to avoid invasive diagnostic procedures done within the hospital setting. Therefore, some experts have recommended starting empiric therapy (corticosteroids +/- azathioprine) for patients who present with elevated ALT, positive auto-antibodies and elevated immunoglobulin G levels, once other liver diseases have been excluded (1). Conversely, the AASLD expert panel warned against presuming that elevated liver tests in patients with AIH patients are due to a disease flare without biopsy confirmation (2).

AIH patients on immunosuppression may be at higher risk of acquiring infection and therefore should be prioritized for SARS-CoV-2 testing when presenting with fever, upper respiratory tract symptoms, other atypical symptoms (e.g. diarrhea or loss of smell and taste) (2,3). It is not recommended to lower immunosuppressive therapy in stable patients with AIH in an attempt to reduce the risk of contracting the infection, as this could result in disease flares that ultimately would require higher doses of corticosteroids to control (2,3). It is important that these patients receive pneumococcus and influenza vaccinations (3).

Early reports from the USA suggest that immune-compromised patients account for 6% of hospitalized patients and 9% of those admitted to ICU (4). From the emerging evidence, and from past experiences with other coronaviruses (SARS, MERS), it does not appear that immunosuppressed patients with COVID-19 are at higher risk of severe pulmonary disease (5). Acute respiratory distress syndrome (ARDS) is a leading cause of mortality in patients admitted to ICU. These patients may develop a cytokines storm with hyper-inflammation (high ferritin, increased IL-6) that resembles hemophagocytic lymphohistiocytosis (HLH). A series of 150 cases from Wuhan, China suggests that corticosteroids might exacerbate COVID-19-associated lung injury, leading experts to recommend against their use (6).

Therefore, if AIH patients on corticosteroids develop COVID-19, high-doses of prednisone should be avoided, recognizing that critically ill patients may require stress doses to avoid adrenal insufficiency (2). Patients with COVID-19 can also develop lymphopenia due to the viral infection, and if this is associated with fever or worsening respiratory status, consideration should be given to lowering the doses of azathioprine or mycophenolate mofetil (2).

Cholestatic liver diseases

It is not clear if patients with primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC), without underlying cirrhosis, are at increased risk of COVID-19 or if the virus worsens chronic cholestatic liver disease (7). Patients with PBC should be continued on their usual treatment, including ursodeoxycholic acid, and second-line agents (e.g. obeticholic acid or bezafibrate). PBC patients with established cirrhosis could have their hepatocellular carcinoma (HCC) surveillance deferred for several months during the pandemic (2). PBC patients may have varices at early stages of disease, but endoscopic surveillance should also be deferred, with use of non-selective beta-blockers being a preferred strategy during the pandemic (8). Magnetic resonance cholangiopancreatoscopy (MRCP) is best avoided in PSC patients unless it is likely to change management (e.g. suspected cholangiocarcinoma) (2). Although fever and worsening liver tests can be presentations of COVID-19, if this occurs in the setting of PSC, it is important to consider ascending cholangitis. These PSC patients should have blood cultures, be started on broad spectrum antibiotics, and ERCP may be indicated.

SUMMARY:

- Our usual practices for diagnosis and follow-up of patients with AIH may be affected by limited access to outpatient laboratory, diagnostic imaging tests, ERCP) and liver biopsy.
• AIH patients on immunosuppression may be at higher risk of acquiring SARS-CoV-2 infection.
• It does not appear that immunosuppressed patients with COVID-19 are at higher risk of severe pulmonary disease.
• However, some reports suggest that corticosteroids might exacerbate COVID-19-associated lung injury.
• It is not clear if patients with PBC or PSC, without underlying cirrhosis, are at increased risk of COVID-19 or if the virus worsens their liver disease.

WGO Recommendations:
• During the pandemic, follow-up of stable patients with AIH should be done with phone consultation or tele-health where available.
• Patients with AIH should be prioritized for SARS-CoV-2 testing when presenting with symptoms.
• It is not recommended to lower immunosuppressive therapy in stable patients with AIH in an attempt to reduce the risk of contracting the infection.
• However, if patients with COVID-19 develop lymphopenia, consider lowering the doses of azathioprine or mycophenolate mofetil.
• In new patients presenting with features of AIH, at first it appears better to avoid liver biopsy during the pandemic. However, starting empiric therapy cannot be recommended straight forward as concern exists that corticosteroids could be harmful to patients with COVID-19.
• If AIH patients on corticosteroids develop COVID-19, high-doses of prednisone should be avoided, keeping in mind that stress doses may be needed.

References

III. PRACTICAL ASPECTS TO CARING FOR CHRONIC LIVER DISEASE (CLD) PATIENTS DURING COVID-19

IIIA. How to follow CLD patients during COVID-19?
IIIB. Performing procedures during COVID-19
IIIC. Therapies under investigation for COVID-19 and potential hepatotoxicity

IIIA. HOW TO FOLLOW CHRONIC LIVER DISEASE DURING COVID 19?
Mario Reis Alvaro-da-Silva (Brazil)
• Liver disease patients often need to consult, undergo laboratory and imaging routine tests, and therefore, make extensive use of the health system. However, during the pandemic, this population is paradoxically exposed to two risks: staying at home and suffering the consequences of not carrying out their exams and clinical reviews or attending hospitals and laboratories and running the risk of becoming infected with SARS-CoV-2. Thus, some liver medical societies have tried to guide doctors on these issues, based on expert opinions, since knowledge about COVID-19
and the liver is still lacking.1,2. Probably, physicians will have to deal, in the future, with the varied consequences of COVID-19 in liver disease patients, balancing the risks of treatment in patients at risk of COVID-19, the risk of under treatment in patients with advanced or progressive liver disease and the risks of iatrogenic COVID-19 in patients exposed to the health care system.3 Patients with stable, compensated liver diseases should postpone medical visits and routine labs. Telemedicine or phone visits should be encouraged in such cases.1,2,4,5 Furthermore, self-isolation and distancing may lead to increased alcohol consumption, which may be associated with dreadful consequences in patients with alcohol-associated liver disease (ALD). Actually, it is speculated that patients with ALD may be amongst the populations that are most severely impacted during the COVID-19 era (6) for a couple of reasons: (i) they have a depressed immune system which make them susceptible to viral and bacterial infections (7); (ii) co-morbidities including obesity with metabolic syndrome are common; (iii) their inability to attend regular visits by providers and social isolation leads to psychological decompensation and increased drinking or relapse drinking; (iv) they are often smokers and have chronic respiratory disease. It is suggested that the reasons mentioned above may put these patients at higher risk for severe COVID-19 infection (6). These patients may also be less willing to adopt suggested precautions for COVID-19 prevention.

Patients with severe alcoholic hepatitis probably should not receive standard corticosteroid treatment, in particular in areas where COVID-19 is frequent (6). One concern is that patients with ALD or alcoholic hepatitis will not seek medical care unless their situation is critical and that a substantial increase of patients with alcoholic decompensated cirrhosis will occur. Increase in alcohol consumption as well as alcohol relapse in patients with alcohol use disorder is expected to facilitate this trend. In the post COVID era liver transplantation centers may need to apply more flexible approaches to such patients. Finally and tragically, due to some terrible misunderstandings some people have started drinking alcohol to prevent COVID-19 (8). In Iran, some 180 people died after consuming ‘moonshine’ or industrial alcohol, including methanol, in March this year in the belief that it would protect them from the COVID-19 outbreak. This myth of alcohol being preventive against COVID-19 is by no means confined to Iran and has been observed in many geographical destinations ranging from Eastern Europe to the Far East.

SUMMARY:

- CLD patients are paradoxically exposed to two risks: staying at home and suffering the consequences of not carrying out their exams and clinical reviews or attending hospitals and laboratories and running the risk of acquiring nosocomial SARS-CoV-2.
- Staying at home is associated with increased alcohol drinking. In patients with ALD this may lead to hepatic decompensation.
- Patients with ALD may be prone to acquire SARS-CoV-2 and to go through a severe course of COVID-19.
- Given the nature of the pandemic, physicians and patients will have to deal with these risks for some time in the future.

WGO Recommendations

- Patients with stable, compensated liver diseases should postpone medical visits and routine labs.

Telemmedicine or phone visits should be encouraged in such cases

- In low-income countries, telemedicine or phone visits may not be possible. Outpatient visits may be used to differentiate patients with compensated vs. decompensated liver disease.
- Outpatient visits should be limited to those with high MELD scores.
- In persons with decompensated cirrhosis who have complications that need laboratory monitoring such as ascites management, visits for blood draw and clinical evaluation may be needed but should be kept to a minimum.
- Telemedicine approaches should take into account patients with alcohol use disorder such patients should be approached.
- Routine prescriptions should be sent by mail and should be given to cover extended durations.
- Treatment of severe alcoholic hepatitis with corticosteroids should be decided and followed on a case-by-case basis, liberal use of high dose steroids should better be avoided, and whenever possible patients should be hospitalized.
- Liver biopsies should be restricted to cases in which it becomes unavoidable in order to make a definitive diagnosis
- Hospitalizations, if needed, should be as short as possible, preferably in private rooms: keep doors closed and windows open, limit medical and nursing staff
- Phone communication and tele-medicine is encouraged; limit imaging exams to those likely to change management
- SARS-CoV-2 testing should be done in patients who present with acute decompensation of CLD, or acute on chronic liver failure.

References:
1. Boettler T et al. Care of patients
5 Szabo G, Saha N. Alcohol’s effect on host defense. Alcohol Res 2015; 37:1509-70

### IIIB. Performing Procedures During COVID 19

Guilherme Macedo, Rui Gaspar (Portugal)

The COVID-19 pandemic has created several challenges to healthcare services across the world, especially when caring for vulnerable patients. On the one hand, we should minimize physical contact between patients with chronic liver disease (CLD) and medical staff to reduce viral dissemination; on the other hand, we should continue to give the best medical care to these challenging patients.

Patients with CLD, particularly those with advanced or decompensated cirrhosis, often require therapeutic or prophylactic interventions. There is general agreement that procedures should not be performed in patients with CLD unless they are strictly necessary.

### Endoscopy:

Human-to-human transmission occurs mainly through respiratory secretions and aerosols but the virus can, also, be transmitted via feces and contaminated environmental surfaces (1-3).

Endoscopy is a high-risk procedure as healthcare providers will be exposed to respiratory and/or gastrointestinal fluids (3). Thus, it is very important to strictly select the emergent procedures, and consider postponing other procedures to the end of the outbreak.

In order to minimize the risk of acquiring SARS-CoV-2 infection when performing endoscopic procedures, several measures should be taken: healthcare workers should always use personal protective equipment (PPE) which includes N95 masks, double gloves, hairnet, waterproof gowns and protective eyewear (4-6). Although not always available, if possible, procedures should be performed in negative pressure rooms on known COVID-19 positive patients (5).

Guidance regarding the use of PPE, particularly in resource restrained countries, is being issued by WGO.

Patients with CLD need to be protected against acquiring SARS-CoV-2 infection. Risk of infection to patients can be minimized by ensuring disinfection of equipment and the endoscopy room, minimizing exposure in waiting and recovery areas and triaging patients at entry to detect possible SARS-CoV-2 infection.

### Portal hypertension:

In patients with liver cirrhosis we should use non-invasive risk assessment for the presence of varices in order to stratify patients during the SARS-CoV-2 pandemic.

Pure screening of gastric and esophageal varices in patients with cirrhosis should be rescheduled as endoscopy is considered high-risk for the endoscopy team, because it is an aerosol-generating procedure. Therefore, it is of paramount importance to identify high-risk patients, in whom variceal banding should continue to be performed such as patients with large varices and red spots, recent variceal bleeding, signs of significant portal hypertension (large volume ascites, thrombocytopenia < 100 x 10^9/mL) or with signs of active bleeding (hematemesis or melena). (7, 8)

### Endoscopic retrograde cholangiopancreatography (ERCP):

ERCP is also considered an aerosol-generating procedure. Consequently, all the procedures should be reviewed by experts and rescheduled after the outbreak if not urgent/essential.

ERCP should be performed in cases of cholangitis, acute biliary pancreatitis, sepsis or high suspicion of cholangiocarcinoma (4, 7-9).

### Paracentesis:

Till now, there are no reports of the presence of SARS-CoV-2 in peritoneal fluid. Despite that, paracentesis should be performed with appropriate PPE and the patient should also wear a surgical mask.

In the vast majority of cases, there are few life-threatening situations where paracentesis is strictly necessary. Beyond cases of suspicion of spontaneous bacterial peritonitis, not only for the diagnosis but also to evaluate the response to the antibiotics at day 3, paracentesis should also be performed in cases of refractory large...
volume ascites.

**Transjugular intrahepatic portosystemic shunt (TIPS):**
There are no reported cases of TIPS insertion in COVID-19. As a risky and time-consuming procedure, which may also need admission to intermediate or intensive care units, TIPS insertion should only be performed in life-threatening cases of refractory variceal bleeding. (8)

**SUMMARY:**
- Endoscopy is a high-risk procedure as healthcare providers will be exposed to respiratory and/or gastrointestinal fluids.
- Patients with CLD also need to be protected against acquiring SARS-CoV-2 infection in the endoscopy unit.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.

**WGO Recommendations:**
- Interventional procedures, such as endoscopy and ERCP, should not be performed in patients with CLD unless they are strictly necessary, such as those with high risk varices or cholangitis.
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.
- Endoscopy should always be performed using appropriate personal protective equipment (PPE).
- Pure screening of gastric and esophageal varices in patients with stable cirrhosis should be rescheduled.

**References:**
of malaria, amoebiasis and autoimmune conditions. Initial reports of hydroxychloroquine, in conjunction with azithromycin, leading to viral load reduction in COVID-19 patients have not been confirmed (6). Special consideration regarding those medications is to exclude G6PD deficiency before application, and to consider interactions with immunosuppressive drugs: close monitoring of drug levels is required for calcineurin or m-TOR inhibitors (5) and the risk of severe QT prolongation induced by the two drugs, more commonly seen with hydroxychloroquine, should be considered. Hepatotoxicity due to hydroxychloroquine has been described but is rare (7).

Lopinavir/ritonavir are approved protease inhibitors (PIs) for second-line HIV treatment. Many centres have discontinued their experimental use as there is no proven efficacy in vivo in severe COVID-19 (8). Drug interactions with immunosuppressive drugs are well studied. Close monitoring for calcineurin inhibitor drug levels is recommended, while m-TOR inhibitors should not be co-administered (5). Patients with decompensated cirrhosis should not be treated, based on the experience with PIs in HCV. The risk of lopinavir-associated hepatotoxicity in patients with very advanced liver disease is low (9).

Tocilizumab is a humanised monoclonal antibody against interleukin-6 receptor that works by damping cytokine release syndrome observed in COVID-19 patients. Liver toxicity in the form of ALT elevations is frequent but clinically apparent liver injury with jaundice seems to be rare (10). HBV reactivation is a considerable adverse event in case of its administration (11). Moreover, it is should not be used in patients with decompensated cirrhosis (1).

Convalescent plasma shows a potential therapeutic effect and has low risk in the treatment of severe COVID-19 patients (112). There is no experience with convalescent plasma therapy in COVID-19 patients with chronic liver disease (1).

Favipiravir is a guanine analogue, that is an RNA-dependent RNA polymerase (RdRp)- inhibitor, approved for influenza in Japan. Studies have revealed that favipiravir showed better treatment outcomes in COVID-19 patients in terms of their disease progression and viral clearance (13). ALT and AST elevation is a possible side effect, while no data in cirrhosis are available (1).

The possibility of using sofosbuvir ± ribavirin in COVID-19 infection has been suggested. Sofosbuvir, a nucleotide analogue, was originally approved for the treatment of HCV infection. It inhibits HCV RdRp, which is essential for viral replication, and acts as a chain terminator (14). In the case of COVID-19, in vitro data also show binding to SARS-CoV-2 RdRp (15). It is safe, based on the experience of its use in patients with chronic hepatitis including patients with decompensated cirrhosis. However, ribavirin should be used cautiously as it may cause severe haemolytic anaemia (1).

SUMMARY:
- Currently there are no drugs approved for COVID-19, although many are under investigation.
- Patients with impaired liver function are at high risk of drug toxicities, particularly patients with Child-Pugh B/C cirrhosis.
- Drug-drug interactions in liver transplant patients should always be kept in mind with certain immunosuppressive therapies.
- Remdesivir potentially reduces length of hospital stay and has received provisional fast-track approval from the US FDA. Liver toxicity with ALT elevation is a possible adverse event.
- Favourable data have been reported for favipiravir from Japan.
- Chloroquine and hydroxychloroquine, as well as lopinavir/ritonavir seem to have no role in COVID treatment.

WGO Recommendations:
- No recommendation can be currently made with regards to treatment of COVID-19.
- Evolving treatment data should be thoroughly evaluated by experts, bearing in mind issues of efficacy, safety, local access and affordability.
- Abnormal liver tests should not be a contraindication to using COVID-19 experimental therapies if needed.

References
Editorial | COVID-19 Special Issue | Gastro 2021 | Calendar of Events

WORLD GASTROENTEROLOGY NEWS MARCH 2021

DOI: 10.15860/gastro.2021.03.03.0017

https://www.covid19-druginteractions.org/


IV. MANAGEMENT OF COMPLICATIONS OF LIVER DISEASE:
IVA. Screening and treatment of HCC
IVB. Liver transplantation in the COVID-19 era

IVA. SCREENING AND TREATMENT OF HCC

Douglas R. LaBrecque, (USA) and Mark Sonderup (South Africa)
The World Health Organization continues to report that hepatocellular carcinoma (HCC) is the fifth most common tumor, globally, and the second most common cause of cancer-related death (1). Although the incidence and mortality rates of most common cancers continue to decrease due to earlier diagnosis and marked advances in treatment, incidence and mortality rates from HCC continue to rise (2, 3).

In patients with cirrhosis and a suspect nodule, or an elevated AFP, should continue to undergo imaging exams to avoid missing HCC (6).

In the era of COVID-19, all patients being evaluated for the diagnosis and management of HCC must first be screened for COVID-19 (5, 6, 7). Those without COVID-19 should be treated according to local protocols, with added steps taken to limit risks of COVID-19 exposure during therapy. Use of teledicine rather than in-person visits, choosing therapies that require minimal intervention or use of anesthesiologists, surgeons, interventional radiologists, or infusion therapies, in order to reduce risks to the patient and caregivers whose efforts are focused on the severely-ill COVID-19 patients, are recommended (5, 7).

If the patient is being referred from an outside institution or practitioner, the initial COVID-19 screen should be completed prior to the patient being seen. In addition, before an in-person evaluation, except for a very urgent presentation, a full review of all outside records and diagnostic imaging studies should be completed and, when possible, a visit by teledicine or, minimally, by telephone interview, should be completed with a full review by a multidisciplinary team (MDT) at the recipient institution.

The standard of care for HCC patients is evaluation by a MDT comprised of transplant surgeons, hepatologists, oncologists, body image and interventional radiologists, pathologist, psychologist/psychiatrist, and social worker (5, 7). In the era of COVID-19, the presence of infectious disease specialists and pulmonologists are especially critical, along with pharmacologists/pharmacists, in evaluating and making recommendations concerning the care of these very complex patients.
The following comments refer to patients found to be COVID-19 positive.

Except in the case of patients with extensive tumor burden and/or multiple lesions, it may be reasonable to allow one or two months of close monitoring of the HCC with AFP and imaging in order to provide time to determine the severity of the COVID-19 disease before initiating treatment. A high percentage of COVID-19 patients will resolve their infection in a matter of weeks. Data are insufficient to determine whether HCC increases the risk of COVID-19 severity or of effects of COVID-19 on HCC progression. The slow median doubling time of HCC supports a rationale for a short delay in initiating treatment for the HCC (8), including a minor delay in radiological surveillance given the demands on many medical centers due to COVID-19 (5).

Non-surgical treatment approaches are recommended in most cases to reduce stress and risks to the patient as well as to other patients and staff in the OR and ICU (5, 7).

Depending on local capabilities, TACE/TARE, RFA or SBRT would be the first-line of therapy (5, 7). In those requiring urgent therapy, but with active COVID-19 infection, TARE may be preferable to reduce the risk of immunosuppressive effects of chemoembolization on COVID-19 recovery. Lacking the facilities to perform these therapies, ultrasound guided percutaneous ethanol injection (PEI) is an appropriate temporizing option in the MDT and with the patient and patient's family.

SUMMARY:

- The SARS-CoV-2 pandemic is likely to affect screening for HCC, and regular care of patients with already diagnosed HCC.
- Data are insufficient to determine whether HCC increases the risk of COVID-19 severity or whether COVID-19 affects HCC progression.
- In patients with concomitant COVID-19, the slow median doubling time supports a rationale for a short delay in initiating treatment for the HCC.
- Oral tyrosine kinase inhibitors may be preferred to minimize nosocomial exposures associated with receiving infusion regimens.
- Experience is very limited regarding transplantation in patients who have COVID-19.

WGO Recommendations:

- Routine HCC surveillance can be postponed for 2-3 months in patients who are otherwise stable.
- All patients being evaluated for the diagnosis and management of HCC must first be screened for COVID-19.
- Include ID specialists and pulmonologists in the MDT for HCC care.
- Non-surgical treatment approaches are recommended in most cases, depending on local availability. PEI can be a viable option in low and middle income countries, when other options are not available.
- Preferably use oral tyrosine kinase inhibitors to avoid nosocomial exposures associated with receiving infusion regimens.
- Delaying transplant to allow the COVID-19 to resolve is preferred if possible.

References

4. Boettler T et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. JHEP
There are few data to guide clinicians regarding transmission of SARS-CoV-2 through transplant. Testing organ donors for the presence of virus is recommended and those that are positive should be ineligible for donation (3, 4). Recipients should also be screened prior to transplant with rapid COVID-19 PCR testing; however, results could be misleading or contribute to delays. If a potential recipient has symptoms concerning for COVID-19, a CT chest without contrast can also be performed to look for opacities consistent with infection (4).

**Post-liver transplant**
Routine post-transplant monitoring should continue, but in-person visits should be minimized. Patients should be encouraged to practise social distancing which includes telework options.

Post-transplant immune suppression has not been shown to be a risk factor for mortality with SARS-CoV-2 although more data are needed. Prophylactic reduction in immunosuppression is not recommended but preventive measures (social distancing, hand washing etc.) should be strongly emphasized (5).

Immune suppressed patients infected with COVID-19 should have immunosuppression reduced to the lowest levels, especially if more than 6 months post-transplant (5)

**SUMMARY:**
- The COVID-19 pandemic is expected to affect both organ availability as well as peri-transplant risk.
- Elective procedures have been deferred which includes living donor liver transplantation (LDLT) for all but pediatric indications (2). However, in areas of the world where LDLT represents the majority of transplantations done, LDLT for patients with high MELD score and ALF in selected transplantation centers may be considered. Access to LDLT will need to be dynamically assessed as locations begin to reopen.
sion has not been shown to be a risk factor for mortality with SARS-CoV-2, although more data are needed.

WGO recommendations:
• Listing for liver transplantation should be restricted to patients with a poor short-term prognosis such as patients with high MELD score, acute liver failure or liver cancer within Milan criteria.
• LDLT for patients with high MELD score and ALF may be considered in areas of the world where LDLT represents the majority of transplantations done. Access to LDLT will need to be dynamically assessed as locations begin to reopen.
• Testing organ donors for the presence of virus is recommended, and those that are positive should be ineligible for donation.
• Recipients should also be screened for SARS-CoV-2 by rapid PCR testing. If found positive transplantation may be postponed until after recovery from SARS-CoV-2 infection.
• Post-transplantation immunosuppression (PTIS) regimens should not be changed. However, in patients diagnosed with COVID-19, reduction of PTIS should be considered.

Reference:
Antibody Testing for SARS-CoV-2: Role in Management of the Disease

Kai-Chun Wu, MD
Councilor at Large, WGO Promotion of Education in Asia-Pacific Region; State Key Laboratory of Cancer Biology; National Clinical Research Center for Digestive Diseases and Xijing Hospital of Digestive Diseases; Air Force Medical University; Xi’an, China

Desmond Leddin, MB, MSc, FRCP, FRCPC
Chair, WGO Clinical Research Committee
Dalhousie University
Halifax, Canada

Summary
Detection of viral RNA by PCR has become a mainstay of disease detection. However, this technique has several limitations including the requirement for technical expertise, the occurrence of false negative results and an inability to detect individuals who may be immune.

Antibody testing has a role to play in supplementing PCR in diagnosis, screening of contacts and possibly in the determination of population immunity. Sensitivity varies with the stage of infection; it is low in the first week and then rises. Antibodies are highly specific.

Combined PCR and antibody testing may be the optimal strategy for initial diagnosis given the dynamics of the infection and host response and the limitations of PCR testing.

Significant questions remain with regard to the performance of individual test methods and the degree of immunity associated with the antibody response.

Purpose
The purpose of this report is to outline the role of testing for antibodies against SARS-CoV-2 in the management of COVID-19.

Rationale and background
In addition to clinical judgment, supplemented if possible by chest CT, two testing strategies have emerged to aid in diagnosis of the disease. A third approach is to combine PCR and antibody testing.

a) PCR testing
PCR detects viral RNA and has become a mainstay of diagnosis. However, this method has several limitations. Viral RNA is usually obtained from a nasopharyngeal swab, but the virus is predominantly a lower respiratory pathogen. It may not be present in sufficient quantity in the upper respiratory tract leading to false negative results. The virus may be present in low titer in the incubation period. Technically the test requires expertise and sophisticated laboratory equipment which may be in short supply especially in the developing world. False negative tests may occur.

b) Antibody testing
A humoral response with production of antibodies to pathogens is part of the normal host response. SARS-CoV-2 exhibits a number of antigenic sites. Most attention has focused on the spike and nucleocapsid proteins. IgM and IgG antibodies to these sites can be detected by a number of methods including ELISA and immunochromatographic testing.

Several groups have published their results of the time profile of antibody detection. In the initial report from Wuhan the serology of 34 patients was reported (Ai Tang Xiao, Chun Gao, Sheng Zhang, Profile of Specific Antibodies to SARS-CoV-2: The First Report, Journal of Infection (2020). Accepted March 11 2020. doi: https://doi.org/10.1016/j.jinf.2020.03.012). IgM and IgG were analyzed by chemiluminescent immunoassay. With the exception of two patients tested in the first week after infection, all included patients had IgM and
IgG tests two weeks after symptom onset. IgM and IgG both rose towards week 2 with IgM. A subsequent report (Wanbing Liu, Lei Liu, Guomei Kou, Yaqiong Zheng, Yinjuan Ding et al. JCM Accepted Manuscript Posted Online 30 March 2020 J. Clin. Microbiol. doi:10.1128/JCM.00461-20) of 214 patients, confirmed with the disease by positive PCR from pharyngeal swabs, outlined the results of ELISA testing for IgM and IgG antibodies to recombinant nucleocapsid (rN) and spike (rS) proteins. The positivity rates for rN based IgM and/or IgG was 80.4% and for rS 82.2%. The positivity rate for IgM dropped after 35 days and for both assays was less than 60% in the first 10 days after infection.

It appears, therefore, that infection with the virus is associated with a detectable immune response. IgM levels decrease after about a month indicating that it may be a useful marker of more recent infection. IgG may be a reliable marker of past infection as levels persist for longer.

c) Combined PCR and antibody testing.

In another report from Shenzhen, China (Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019. Juanjuan Zhao, Quan Yuan, Haiyan Wang et al.Clin Infect Dis. 2020 Mar 28. pii: ciaa344. doi: 10.1093/cid/ciaa344.) the results of total antibodies, IgM and IgG were reported in 173 patients. The presence of antibodies was <40% in the first week after onset of symptoms and rapidly increased to 100%. In contrast, RNA detectability decreased from 66.7% in samples collected before day 7 to 45.5% between days 15-39. The authors concluded that combining RNA and antibody testing significantly improved virus diagnosis. Specificity was estimated at over 99% by testing serum from healthy individuals obtained before the outbreak of SARS-CoV-2.

The value of combining antibody and RNA PCR testing was confirmed in a further report which stated that the detection rate increased to 98.6% for combined testing compared to 51.9% for a single PCR. (Profiling Early Humoral Response to Diagnose Novel Coronavirus Disease. COVID-19, Li Guo, Lili Ren, Siyuan Yang et al.Clin Infect Dis. 2020 Mar 21. pii: ciaa310. doi: 10.1093/cid/ciaa310. [Epub ahead of print]). The authors also commented on the cross reactivity of the antibodies with SARS-CoV-1 but not other coronaviruses.

Utility of antibody testing

1. Diagnosis of infection. Antibody testing is useful in the diagnosis of acute infection especially as time increases from onset. It may add to the diagnostic rate in patients with negative PCR.

2. Screening of contacts and reduction of quarantine. Currently contacts of patients diagnosed with the disease are asked to remain in quarantine. This is a particular problem for health care providers many of whom may be unnecessarily removed from work due to a shortage of testing. Antibody testing adds a diagnostic test which may reduce time lost.

3. Possible identification of immune populations. PCR becomes negative as the virus is lost from an individual. A negative PCR does not indicate if the person has been infected and may be immune. Antibody testing may allow mass testing of the population and identification of individuals who have recovered from infection. This clearly will become important as restrictions are removed and populations begin to resume normal life. Antibody testing will also allow ongoing surveillance of the population to determine population immune status and will allow detection of both potentially immune and susceptible.

Quality control

There are number of concerns with regard to antibody testing. The performance characteristics of tests may vary. It is important to know the sensitivity, specificity, and reproducibility of each test method. Most importantly, we do not yet know if the presence of antibodies is associated with immunity from reinfection and the duration of any immunity conferred.

Current Practice in China

This section summarizes our experience in Xijing and three other institutions in China. The antibody assay we are using in the Xijing Hospital of Fourth Military Medical University is a product of Beijing Wantai Biological Pharmacy, which has been approved in early March by National Medical Products Administration of China and received a European Conformity (CE) certificate. The product covers 28 provinces with over 200,000 tests done in China, and 23 countries with 35,000 tests done over the world.

This is a chemiluminescent immunoassay based on double-antigen sandwich principle for specific antibody capture in the serum or plasma. The antigens used in the system are recombinant proteins containing the receptor-binding domain (RBD) of the spike protein of SARS-CoV-2. Total antibodies are detected by applying 2 RBD proteins as the immobilized and
HRP-conjugated antigen. The IgM μ chain capture method (IgM-ELISA) is used to detect the IgM antibodies. The assay takes 29 minutes to give the first result and the speed of detection can reach 200 tubes per hour if using automatic device of Caris200, Huawei Medical LLC, Beijing, China.

The sensitivity and specificity of the kit is 94.8% and 99.7% respectively according to a previous study of 386 patients with confirmed COVID-19 and 1859 healthy controls.

Relationship of PCR and antibody positivity following infection.

The IgM positivity (not quantification) curve does exactly track the total antibody curve in the initial 20 days. We know from other published study that the IgG response is different, about 19% in the first 7 days since onset and rise to 80% by 30 days (Clin Infect Dis. 2020 Mar 28. pii: ciaa344. doi: 10.1093/cid/ciaa344.). We assume the COVID patients had not previously been exposed to SARS-CoV-2 as this virus is new to humans. One possible explanation could be the cross-reactivity to other coronavirus although the assay claimed a 99% specificity with over 1800 healthy subjects as controls. The fall to 50% in antibody response from first day of onset to days 3-4 post onset may not mean anything as there were too few chances to have patients’ blood taken for antibody analysis at day 1 of onset.

Of concern, 40% of patients had detectable RNA in swabs 20 days post onset. We do not know how this relates to the risk of them transmitting infection but, if verified, this finding has implications with regard to the duration of isolation of affected patients.


As shown above, the antibody assay is complementary to the PCR assay to identify those false negative patients at early phase of infection. In the first eight days post infection antibodies added an approximately 50% diagnostic gain in PCR negative patients. After eight days, antibodies were detected in nearly 100% of PCR negative patients.

Role of antibody testing in PCR negative patients

<table>
<thead>
<tr>
<th>Days of onset</th>
<th>RNA negative</th>
<th>Ab positive in RNA negative</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤3 days</td>
<td>7</td>
<td>2</td>
</tr>
<tr>
<td>4-7 days</td>
<td>28</td>
<td>15</td>
</tr>
<tr>
<td>8-14 days</td>
<td>57</td>
<td>56</td>
</tr>
<tr>
<td>≥15 days</td>
<td>30</td>
<td>30</td>
</tr>
</tbody>
</table>

Table 1. Days since onset of symptoms in PCR negative patients and antibody status at different time points of COVID-19 in clinically confirmed patients (Data on file of Beijing Wantai Biological Pharmacy, submitted to National Medical Products Administration of China).

Approved indications of the antibody assay are:
1. Additional testing of suspect patients with negative nucleic acid test of SARS-CoV-2.

Potential Indications.
1. Initial diagnosis of COVID-19. First test for suspect or clinically diagnosed patients with COVID-19. If the total antibody is positive, no matter what the result of the PCR assay, the patient is managed as confirmed case. If the total antibody is negative, nucleic acid assay is performed and antibody is rechecked in a week’s time.
2. As a screening test for the asymptomatic patients with close contact.
3. As a check on the immune status of a confirmed patient positive with a positive PCR. A positive antibody result may indicate that an appropriate immune response has been activated. According to recently published studies, a high titer of antibodies may be associated with increased severity of patients with COVID-19, indicating strong immune response in the severe patients.

4. As a test for asymptomatic subjects at the end of 14 days quarantine. If the total antibody is positive, a nucleic acid assay is recommended, and the close contacts should be traced and watched.

We have started the SARS-CoV-2 antibody assay in my hospital mainly for screening for COVID-19 in every patient prior to his admission to hospital. We also perform this assay to screen patients before elective endoscopy. It becomes a useful complement to the PCR and reduces the heavy burden on the clinical lab doing PCR testing by doing 400-500 tests of SARS-CoV-2 antibody assay every day.

As of March 16, 2020, eight different kits from seven biopharma companies of SARS-CoV-2 antibody assay have been approved by the National Medical Products Administration of China. Among them, there is one kit for total antibody and IgM by chemiluminescence, 2 kits for IgG or IgM by magnetic luminescence, 5 for total antibody or IgM/IgG by colloidal gold technique. They are used in many institutes or hospitals in China for research or clinical purpose. Comparative data on test characteristics and performance is awaited.
Personal Care and Stress Management

Guilherme Macedo, MD
President-Elect of WGO and Chair of the WGO Foundation
Centro Hospitalar Sao Joao
Porto, Portugal

Filipe Vilas Boas, MD
Centro Hospitalar Sao Joao
Porto, Portugal

This pandemic has been highlighting the importance of mental health in professionals engaged in the different overwhelming challenges they nowadays deal with while coping with COVID 19 outbreak. Their increased vulnerability is also related to the extensive media coverage, which amplifies fear and uncertainty, especially as there is no vaccine or definitive treatment so far.

Many gastroenterologists, beyond being faced with unpredictable new needs such as limiting GI-specific care, entire reorganization of their schedules and patient management rules - either in Endoscopy Units or outpatient clinics - have also been reassigned, in multiple occasions, to unexpected tasks. Some (young faculty members mainly) with recent ICU or critical care experience, are being additionally trained for ICU care, and backfill positions previously under internal medicine management. GI trainees and specialists have been redeployed to Internal Medicine and Infectious Disease wards.

Though adequate training on infection control for staff, with clear protocols to follow, might mitigate and facilitate an adaptive stress response, the role of a both supportive and communicative supervisor/leader must be emphasized. Burn out is as importantly to be prevented as to be readily identified so that timely intervention can be provided. Leveraging your medical staff to the top of their competences and humanity will be a rewarding experience for everyone involved and promote a safety culture environment.
Telemedicine in Digestive Diseases During the COVID-19 Pandemic

Alejandro Piscoya, MD, MSc(Ed), AGAF
Chair, WGO Publications Committee; Chief of Gastroenterology, Hospital Guillermo Kaelin de la Fuente, EsSalud; Research Associate, Universidad San Ignacio de Loyola; Lima, Peru

Hugo Cedrón, MD
Clínica Anglo Americana
Lima, Peru

Technology in medicine has become an integral part of medical practice. It has transformed the way in which patients and health-care professionals interact. First, it was used to shared knowledge and experiences from specialists to primary-care providers, the main experience developed by ECHO Institute in the fight against hepatitis C. After that, telemonitor has been shown to facilitate chronic disease management, and many publications have been written for different specialties including gastroenterology and hepatology.

The COVID-19 pandemic has forced to change the way how to practice medicine, and looked for new ways to provide and support care to the patients. The COVID-19 pandemic has forced us to avoid gathering of people, as physical distancing is needed. Although face-to-face contact is the basis for the physician-patient relationship and allows physicians to assess the overall condition, it also carries a risk of infection not only for the patients, but also for physicians.

Telemedicine and teleconsults give access to healthcare services, avoid driving time, avoid both waiting time and the gathering of people to decrease the COVID infection risk. Telemedicine allows enhanced patient-to-physician communication, allowing select patients at risk of developing more severe disease to go to the emergency room for physical evaluation, and to finally ensure prescription.

Telemedicine is also ideal for chronic disease care management: inflammatory bowel disease, irritable bowel syndrome, liver disease, chronic pancreatitis, dyspepsia, and others.

References

Links:
https://giondemand.com/
https://gi.org/2020/03/20/top-five-things-gastroenterologists-should-know-about-telehealth/
Management of Patients with Inflammatory Bowel Disease (IBD)

Clinicians caring for patients with IBD are uncertain if persons with active IBD or persons with IBD on immunomodulatory medications are at any greater risk of either acquiring the infection or of having a more complicated course of the infection. There has been some consensus reached among a group of international IBD experts under the auspices of the International Organization for the Study of IBD (IOIBD) (https://www.ioibd.org/). There has also been a position statement published by the American Gastroenterological Association on approaches to patients with IBD (https://www.gastrojournal.org/article/S0016-5085(20)30482-0/fulltext). There are few key questions regarding patients with IBD and risk for COVID-19 that are recurrently being asked by patients and health care providers. These include:

Who is at greatest risk for getting a COVID-19 infection?
The risk categories in short are as follows:
1. High Risk: Over the age of 65 years OR under 65 years AND either moderate or severely flaring, using high doses of prednisone, or moderate to severe malnutrition
2. Medium Risk: Under the age of 65 years and immunocompromised with an immunosuppressive or biologic
3. Low Risk (i.e. same as the general population): Under the age of 65, IBD is in remission, and not immunocompromised

To learn more, click here (https://crohnsandcolitis.ca/covid19).

Are my IBD medications safe to take during a COVID-19 pandemic? Should a patient continue taking his/her IBD medications?
Even though it is considered medium risk to be on immunomodulating medications like immunosuppressives (i.e. azathioprine, 6-mercaptopurine or methotrexate) or a biologic drug, the consensus is that patients with IBD should not stop their drugs because of concerns that a flare of IBD will pose a greater risk. Further, the early data accrual (constantly updated through the SECURE website can be accessed at https://covidibd.org/map/) does not suggest that persons using these drugs are actually at increased risk. Hence, our recommendations are for IBD patients to continue to take their IBD medications. Patients should not discontinue their IBD medications.

When patients with IBD ask if they should avoid work, what should I tell them? If a healthcare worker has IBD and is taking an immunosuppressant, should that person continue working?
It depends on the patient’s risk (and exposure at work). If a patient is over age 65 or on immunomodulating drugs then it may be prudent for them to avoid the workplace; as the safest place will be in self isolation at home. If the patients are health care workers or providing essential services and they feel well, it is likely safe for them to work however; we would recommend that they avoid very high-
risk situations (i.e. hospital work in an Emergency Department or ICU or on a ward with COVID-19 patients). It is possible that persons who want to continue to work may be able to switch roles at their workplace with less exposure. Each case is unique and requires discussion with between the healthcare provider and the patient and potentially with the employer.
Gastro 2021

The World Gastroenterology Organisation (WGO) is pleased to co-host its biyearly international conference, Gastro 2021, with the Czech Society of Gastroenterology (CSG), in Prague, Czech Republic.

Gastro 2021 will take place from 9 – 11 December 2021. The conference, as currently planned, will be in a hybrid format with sessions offered on-line for those unable to travel to Prague.


This event is also co-organized jointly by the Czech Society of Hepatology, Czech Society of Gastrointestinal Oncology, and Czech Society of Surgery.

We are pleased to present the Joint Steering Committee and Joint Scientific Program Committee:

<table>
<thead>
<tr>
<th>Joint Steering Committee</th>
<th>CSG Representatives</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WGO Representatives</strong></td>
<td><strong>CSG Board Representative</strong></td>
</tr>
<tr>
<td>Naima Amrani, President</td>
<td>Julius Spicak</td>
</tr>
<tr>
<td>Cihan Yurdaydin, Past President</td>
<td>Ondrej Urban, CSG President</td>
</tr>
<tr>
<td>Guilherme Macedo, President-elect</td>
<td>Milan Lukas, CSG Past President</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Joint Scientific Program Committee</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>WGO Representatives</strong></td>
<td><strong>CSG Representatives</strong></td>
</tr>
<tr>
<td>Carolina Olano, Uruguay, Co-Chair</td>
<td>Tomas Hucl, Czech Republic, Co-Chair</td>
</tr>
<tr>
<td>Joost Drenth, The Netherlands</td>
<td>Radan Bruha, Czech Republic</td>
</tr>
<tr>
<td>Goeffrey Metz, Australia</td>
<td>Ilja Tacheci, Czech Republic</td>
</tr>
<tr>
<td>Gerhard Rogler, Switzerland</td>
<td></td>
</tr>
<tr>
<td>David Sanders, United Kingdom</td>
<td></td>
</tr>
</tbody>
</table>

9 - 11 December 2021
Calendar of Events

Due to uncertainties of scheduling from the COVID-19 situation, please check the WGO Meetings and Events Calendar for the latest updates at https://www.worldgastroenterology.org/meetings-and-events/meetings-and-events-calendar

WGO RELATED EVENTS

World Digestive Health Day (WDHD) 2021: Obesity: An Ongoing Pandemic
When: May 29, 2021
Location: Virtual online worldwide events
Organizers: World Gastroenterology Organisation and The International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO)
Email: info@worldgastroenterology.org
Website: https://www.worldgastroenterology.org/wgo-foundation/wdhd/wdhd-2021

Gastro 2021 Prague
When: December 9 -11, 2021
Location: Prague, Czech Republic
Organizers: World Gastroenterology Organisation and the Czech Society of Gastroenterology
Website: https://www.gastro-2021prague.org/

World Congress of Gastroenterology 2022
When: December 2022
Location: Dubai, United Arab Emirates
Organizers: WGO and the Emirates Gastroenterology and Hepatology Society
Website: http://wco2021.org

CALENDAR OF EVENTS

ALEH 2021
When: April 21 -24, 2021
Location: Online virtual meeting
Organizers: Latin American Association for the Study of the Liver (ALEH)
Website: https://congresoaleh.com

National Congress of Romanian Society of Gastroenterology and Hepatology
When: May 13 -15, 2021
Location: Mamaia, Romania
Email: info@congres-gastro.ro
Website: http://www.srgh.ro

Digestive Disease Week (DDW) 2021
When: May 21 -23, 2021
Location: Virtual online conference
Host Country: USA
Organizers: AASLD, AGA, ASGE and SSAT
Email: administration@ddw.org
Website: www.ddw.org

Curso Internacional FAGE 2021
When: June 12, 2021
Location: Cordoba, Argentina
Organizer: Federación Argentina de Gastroenterología
Website: http://www.fage.org.ar/

International Symposium on Viral Hepatitis and Liver Disease (ISVHLD)
When: June 17 - 20, 2021
Location: Taipei International Convention Center, Taipei, Taiwan
Organizers: ISVHLD / GHS and the Taiwan Association for the Study of the Liver
Website: ghs2020taipei.com

International Liver Congress™ 2021
When: June 23 - 26, 2021
Location: Online virtual conference
Organizer: EASL
Website: https://easl.eu/event/the-international-liver-congress-2021-2

GHeP Singapore 2021
When: July 8 -11, 2021
Location: Shangri-La Singapore
Country: Singapore
Organizer: Gastroenterological Society of Singapore
Website: www.ghep.org.sg

Panamerican Digestive Disease Week 2021
When: July 14 -16, 2021
Location: Online virtual meeting
Host Country: Uruguay
Organizer: OPGE
Website: https://sped2021.com

Asian Pacific Digestive Week 2021
When: August 19 - 22, 2021
Location: Kuala Lumpur Convention Centre, Kuala Lumpur, Malaysia
Organizers: Asian Pacific Association of Gastroenterology and Malaysian Society of Gastroenterology & Hepatology
Website: https://www.apdwkd2021.org/

Congresso Brasileiro de Doenças Funcionais do Aparelho Digestivo 2021
When: September 4 -7, 2021
Location: Online virtual conference
Host Country: Brazil
Organizer: Federação Brasileira de Gastroenterologia (FBG)
Website: https://fbg.org.br/
XV Congreso Paraguayo de Gastroenterología y Endoscopia Digestiva
When: September 8 - 10, 2021
Country: Paraguay
Organizer: Sociedad Paraguaya de Gastroenterología y Endoscopia Digestiva
Website: https://www.spge.org.py/

Congreso de las Asociaciones Colombianas del Aparato Digestivo ACADI
When: September 9 - 11, 2021
Location: Estelar Santamar Hotel & Centro de Convenciones, Santa Maria, Colombia
Organizer: Asociación Colombiana de Gastroenterología
Website: www.gastrocol.com

Australian Gastroenterology Week (AGW) 2021
When: September 12 - 14, 2021
Location: Brisbane, Australia
Organizer: Gastroenterological Society of Australia (GESA)
Website: https://agw.gesa.org.au/

UEG Week 2021
When: October 3 - 5, 2021
Location: Online virtual conference
Organizer: UEG
Website: https://ueg.eu/week/ueg-week-2021

XXVII United Russian Gastroenterology Week
When: October 18 - 20, 2021
Country: Russia
Organizer: Russian Gastroenterological Association
Website: http://www.gastro.ru

ACG 2021
When: October 24 - 27, 2021
Location: Las Vegas, Nevada, USA
Organizer: American College of Gastroenterology
Website: https://acgmeetings.gi.org/

JDDW 2021 - Japan Digestive Disease Week 2021
When: November 4 - 7, 2021
Location: Kobe, Japan
Organizer: Organization of JDDW
Website: http://www.jddw.jp/english/index.html

Semana Nacional de Gastroenterología 2021
When: November 12 - 16, 2021
Location: Guadalajara, Mexico
Organizer: Asociación Mexicana de Gastroenterología
Website: https://www.gastro.org.mx/eventos

Korean Digestive Disease Week
When: November 18 – 20, 2021
Location: Online virtual meeting
Organizer: The Korean Society of Gastroenterology
Email: info@kddw.org
Website: http://www.kddw.org

APASL 2022
When: March 30 - April 3, 2022
Location: Seoul, Korea
Organizers: APASL and Korean Association for the Study of the Liver
Website: http://www.apasl2022seoul.org/

JDDW 2022 - Japan Digestive Disease Week 2022
When: October 27 - 30, 2022
Location: Fukuoka, Japan
Organizer: Organization of JDDW
Website: http://www.jddw.jp/english/index.html

JDDW 2023 - Japan Digestive Disease Week 2023
When: November 2 - 5, 2023
Location: Kobe, Japan
Organizer: Organization of JDDW
Website: http://www.jddw.jp/english/index.html

JDDW 2024 - Japan Digestive Disease Week 2024
When: October 31 - November 3, 2024
Location: Kobe, Japan
Organizer: Organization of JDDW
Website: http://www.jddw.jp/english/index.html

WGO Member Societies Submit Your Event
Are you a WGO Member Society wanting to share your event with WGO readers? Visit http://www.worldgastroenterology.org/forms/submit-event.php to submit your event for publication in WGO’s website conference calendar as well as the quarterly e-WGN calendar of events!
The Biocodex Microbiota Institute is the first international reference platform offering expertise on human microbiota, intended for both health professionals and the public.


In a nutshell:
• A Website in 6 Languages
• More than 500,000 visitors in 2019
• 9 Newsletters
• 10 Thematic folders
• 15 Videos
• More than 300 Current Topics
• 10 new articles per month

DONATE TODAY
Contributions to The WGO Foundation support and expand the educational, training, research, and awareness programs and initiatives of WGO by strengthening the reach of WGO to areas in the world that benefit directly from the education offered through programs such as Training Centers, Train the Trainers, World Digestive Health Day (WDHD), Global Guidelines, and meetings such as the World Congress.

DONATE HERE