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In this issue


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

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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.

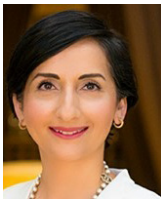
A final word on our own changes: we have just updated our logo as you will find out in this issue. This change comes be at a most interesting time when everything is changing and will continue to adapt to the new normality after the pandemic. A worldwide vaccination program is starting and after a while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

Contents

VOL. 25, ISSUE 2

Editors



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Expert Point of View

COVID-19 Special Issue

Contents

Gastro 2021

Calendar of Events

Message from the Editors

Mário Reis Álvares-da-Silva, MD, PhD

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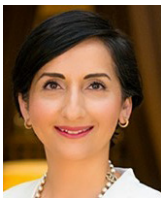

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The COVID-19 pandemic has taken a significant toll around the globe for our patients and each other. In this special issue devoted to COVID-19, we look at the impact and the management of the pandemic from a gastroenterologists' perspective among communities 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 digestives 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.

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

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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 suggest 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.[1, 2] 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 anticoagualtion 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 endosocopic procedures.[2, 3]

2. **Liver enzyme** elevation is frequent, detected in up to 40 % of patients, (29-40 %), concerning mostly transaminases.[1, 4] 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-

ment has been reported in one single study with up to 17% of 52 cases with systematic dosage.[4] However this study includes amylases and lipase abnormality without cut off, and only five of nine patients presented increase in lipase, without symptoms. Thus, severe or clinically significant pancreatic injury, related to the COVID-19 situation, seems infrequent at least in the acute phase.

4. Are there any **severe digestive complications** directly related to COVID-19? On published experience within and outside China, digestive symptoms are mild and biological abnormalities mostly remain into the < 5 N range.

The published experience, to date, suggests that most COVID-19-associated manifestations affecting the gastrointestinal, pancreatic and hepatobiliary systems are benign; there have been no reports of severe pancreatitis, hepatitis or digestive tract involvement that are clearly related to COVID-19 itself.

However, COVID-19 is a new 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

1. Cholankeril G, Podboy A, Aivaliotis VI, Tarlow B, Pham EA, Spencer S, Kim D, Hsing A, Ahmed A. High Prevalence of Concurrent Gastrointestinal Manifestations in Patients with SARS-CoV-2: Early Experience from California. Gastroenterology.
2. Cheung KS, Hung IF, Chan PP, Lung KC, Tso E, Liu R, Ng YY, Chu MY, Chung TW, Tam AR, Yip CC, Leung KH, Yim-Fong Fung A, Zhang RR, Lin Y, Cheng HM, Zhang AJ, To KK, Chan KH, Yuen KY, Leung WK. Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples from the Hong Kong Cohort and Systematic Review and Meta-analysis. Gastroenterology 2020.
3. Wu Y, Guo C, Tang L, Hong Z, Zhou J, Dong X, Yin H, Xiao Q, Tang Y, Qu X, Kuang L, Fang X, Mishra N, Lu J, Shan H, Jiang G, Huang X. Prolonged presence of SARS-CoV-2 viral RNA in faecal samples. Lancet Gastroenterol Hepatol 2020;5:434-435.
4. Wang F, Wang H, Fan J, Zhang Y, Zhao Q. Pancreatic injury patterns in patients with COVID-19 pneumonia. Gastroenterology 2020.

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

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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[1]. 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[2]. 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[3]. 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[4]. 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[5]. 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[6].

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 (See Table 1) should be taken for lower GI tract examinations[7]. 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[8] 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[9] 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[10]. 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[11].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 localized, 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 summarized 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.

Triage of all procedures should be done by trained medical personnel[12].

1.1 Triage referrals based on level of urgency.

1.2 Procedures which are not time-sensitive should be postponed.

1.3 Carry out regular subsequent monitoring of postponed patients to ensure that their condition does not become urgent.

Low resource: Same

2. **Reduce COVID-19 burden.**

Rationale: Hospitals and health care facilities are high risk areas for contracting COVID-19.

2.1 Keep patients away from health care facilities as much as possible.

2.2 Provide online or telephone care for patients prior to attending the hospital

2.3 Reschedule non time-sensitive procedures and follow up.

Low resource: Same

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[1]. 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[13].

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[6].

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[14].

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[14] 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 health care environment[15,16].

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[12].

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[18].

7.1 Review and observe staff practicing PPE donning and doffing PPE.

7.2 Make sure that staff have been fitted for respirators if possible[6]. 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[1].

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[20].

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

Rationale: The virus is detectable in the stool of infected patients[7]. 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[17]. 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[19].

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[20].

17. Wear work footwear
Rationale: There is ample evidence that the environment around an infected patient is contaminated. That includes the floor[21]. The virus can be tracked to other areas.

17.1 Change into work boots or dedicated washable shoes that are kept in the endoscopy unit staff changing room.

17.2 Wear disposable plastic, not cloth, longer length shoe covers.

17.3 Disinfect the boots worn in the endoscopy room in disinfectant bath at the end of the endoscopy session and do not take them out of the work area.

Low resource:

17.4 Shoe covers can be avoided by wearing boots which can be disinfected.

18. Ventilate the air in the endoscopy room.
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[1]. 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[22].
Low resource: Same

20. Endoscopy room cleaning staff

Society	WGO	AGA	APSDE	BSG	CAG	ESGE, ESGNA	SGEI, ISG, INASL
1.Triage	Yes	Yes	Yes	Yes	Yes	Yes	Yes
2. Reduce	Yes	NA	Yes	Yes	Yes	Yes	Yes
3. Screen, stratify risk	Yes	NA	Yes	Yes	Yes	Yes	Yes
4. Reduce risk from patients	Yes	NA	NA	NA	NA	Yes	Yes
5.Reduce risk to patients	Yes	NA	NA	NA	NA	Yes	Yes
6. Minimize staff exposure	Yes	Yes	Yes	Yes	NA	Yes	Yes
7. Train staff in PPE use	Yes	Yes	Yes	Yes	NA	Yes	Yes
8. No trainees in room	Yes	Review	NA	Yes	NA	NA	NA
9. Wash hands	Yes	NA	Yes	Na	NA	Yes	Yes
10. Respirator for Upper	Yes	Yes	Yes HRC	Yes FFP3	Yes	HRC only	Not specified
11. Respirator for lower	HR only	Yes	Yes HRC	Yes HR	No LRC	HRC only	Not specified
12. Use Surgical mask	LR, LRC only	No	Yes LRC	NA	Yes LRC	LRC only	Not specified
13. Double glove	No	Yes	No	No	Yes LRC	HRC only	NA
14. Wear Face shield or Goggles	Yes	NA	Yes	Yes*	Yes HRC	Yes	Yes
15. Wear Goggles or Face shield	Yes	NA	Yes	Yes*	Yes	Yes	Yes
16. Wear a Gown and hair cover	Yes	NA	Yes	Yes	Yes	Yes	Yes
17. Wear Work footwear	Yes	NA	NA	Yes	NA	NA	NA
18. Ventilation of endoscopy room	Yes	Yes	Yes HRC	NA	NA	Yes	Yes
19. Reprocessing staff wear PPE	Yes	NA	NA	NA	NA	Yes	NA
20. Cleaning staff wear PPE	Yes	NA	NA	NA	NA	NA	NA

Table 1.
Summary of evidence from selected National and International Societies compared to WGO recommendations.
Yes - Recommended, No - Not recommended, NA - indicates Not Addressed. HR - High Resource. LRC - Low Risk of COVID-19, HRC - High Risk of COVID-19.

WGO - World Gastroenterology Organisation.
AGA - American Gastroenterological Association[12], APSE – Asian Pacific Society for Digestive Endoscopy[23], BSG - British Society of Gastroenterology[24]. CAG - Canadian Association of Gastroenterology[25].
ESGE, ESGNA – European Society of Gastrointestinal Endoscopy, European Society of Endoscopy Nurses and Associates[14]. SGEI, ISG, INASL -Society of Gastrointestinal Endoscopy of India, Indian Society of Gastroenterology, Indian Society for Study of the Liver.[26]

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[6]. 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

1. Coronavirus (COVID-19) outbreak: what the department of endoscopy should know. Repici A, Maselli R, Colombo M. Gastrointest Endosc. 2020 Mar 14.
2. What is the efficacy of eye protection equipment compared to no eye protection equipment in preventing transmission of COVID-19-type respiratory illnesses in primary and community care? April 3, 2020. CEBM. https://www.cebm.net/covid-19/what-is-the-efficacy-of-eye-protection-equipment-compared-to-no-eye-protection-equipment-in-preventing-transmission-of-covid-19-type-respiratory-illnesses-in-primary-and-community-care/)
3. Can Cascades make guidelines global? Fried M, Krabshuis J. J Eval Clin Pract. 2008 Oct;14(5):874-9.
4. In Pursuit of PPE. NEJM. April 17, 2020. Artenstein AW
5. NEJM. 2020 Apr 15. Droplets and Aerosols in the Transmission of SARS-CoV-2. Meselson M
6. Transmission Potential of SARS-CoV-2 in Viral Shedding Observed at the University of Nebraska Medical Center. Joshua L. Santarpia, Danielle N. Rivera et al. https://www.medrxiv.org/content/10.1101/2020.03.23.20039446v2).
7. Cheung KS, Hung IF, Chan PP, Lung K, Tso E, Liu R, Ng Y, Chu MY, Chung TW, Tam AR, Yip CC, Leung K-H, Yim-Fong Fung A, Zhang RR, Lin Y, Cheng HM, Zhang AJ, To KK, Chan K-H, Yuen K-Y, Leung WK, Gastrointestinal Manifestations of SARS-CoV-2 Infection and Virus Load in Fecal Samples from the Hong Kong Cohort and Systematic Review and Meta-analysis, Gastroenterology 2020.
8. Personal protective equipment for preventing highly infectious diseases due to exposure to contaminated body fluids in healthcare staff. Verbeek JH, Rajamaki B, Ijaz S, Sauni R, Toomey E, Blackwood B, Tikka C, Ruotsalainen JH, Kilinc Balci FS. Cochrane Database of Systematic Reviews 2020, Issue 4
9. Use of personal protective equipment to protect against respiratory infections in Pakistan: A systematic review Abrar Ahmad Chughtai, Wasiq Khan. Journal of Infection and Public Health 12 (2019) 522–527
10. FDA. https://www.fda.gov/medical-devices/personal-protective-equipment-infection-control/n95-respirators-and-surgical-masks-face-masks
11. N95 Respirators and Surgical Masks. Posted on October 14, 2009 by Lisa Brosseau, ScD, and Roland Berry Ann. https://blogs.cdc.gov/niosh-science-blog/2009/10/14/n95/)
12. Sultan S, Lim JK, Altayar O, Davitkov P, Feuerstein JD, Siddique SM, Falck-Ytter Y, El-Serag HB, on behalf of the AGA, AGA Institute Rapid Recommendations for Gastrointestinal Procedures During the COVID-19 Pandemic, Gastroenterology 2020
13. Gastroenterology Practice in COVID -19 Pandemic. Xia L. Wu K https://www.worldgastroenterology.org/publications/e-wgn/gastroenterology-practice-in-covid-19-pandemic?utm_source=WGOBanner&utm_medium=Homepage&utm_campaign=COVID19Informationwebpage_COVID19_e-WGN_Article
14. ESGE and ESGENA Position Statement on gastrointestinal endoscopy and the COVID-19 pandemic. https://www.esge.com/esge-and-esgena-position-statement-on-gastrointestinal-endoscopy-and-the-covid-19-pandemic/
15. Covid-19: What is the evidence for cloth masks? Mahase E. BMJ 2020;369:m1422 doi: 10.1136/bmj.m1422 Published 7 April 2020.
16. A cluster randomised trial of cloth masks compared with medical masks in healthcare workers. C Raina MacIntyre, Holly Seale, Tham Chi Dung, https://bmjopen.bmj.com/content/bmjopen/5/4/e006577.full.pdf)
17. Virus Transfer from Personal Protective Equipment to Healthcare Employees' Skin and Clothing. Lisa Casanova, Edie Alfano-Sobsey, William A. Rutala et al. Emerging Infectious Diseases. www.cdc.gov/eid • Vol. 14, No. 8, August 2008).
18. Respiratory Protection Considerations for Healthcare Workers During the COVID-19 Pandemic Christopher R. Friese, Tener Goodwin Veenema, James S. Johnson et al. https://www-liebertpub-com.ezproxy.library.dal.ca/doi/full/10.1089/hs.2020.0036)
19. Characteristics of Ocular Findings of Patients with Coronavirus Disease 2019 (COVID-19) in Hubei Province, China. Pin Wu et al. JAMA. https://jamanetwork.com/journals/jamaophthalmology/fullarticle/2764083
20. Ontario Health. Optimizing the Supply of Personal Protective Equipment (PPE) during the COVID-19 Pandemic. https://www.wrh.on.ca/uploads/Coronavirus/Ontario_Health_Optimizing_PPE_During_COVID19_April_10_2020.pdf
21. Aerosol and Surface Distribution of Severe Acute Respiratory Syndrome Coronavirus 2 in Hospital Wards, Wuhan, China, 2020. Zhen-Dong Guo, Zhong-Yi Wang, Shou-Feng Zhang. CDC. https://wwwnc.cdc.gov/eid/ar-

ticle/26/7/20-0885_article

22. SAGES, SGNA, ASGE. Management of endoscopes, endoscope reprocessing, and storage areas during the COVID-19 Pandemic. https://www.sages.org/management-endoscopes-reprocessing-storage-covid-19/
23. Practice of endoscopy during COVID-19 pandemic: position statements of the Asian Pacific Society for Digestive Endoscopy (APSDE-COVID statements) 1234 Philip Wai Yan Chiu , Siew C Ng , Haruhiro Inoue et al. https://gut.bmj.com/content/gutjnl/early/2020/04/02/gutjnl-2020321185.full.pdf
24. British Society of Gastroenterology. https://www.bsg.org.uk/covid-19-advice/endoscopy-activity-and-covid-19-bsg-and-jag-guidance/
25. Canadian Association of Gastroenterology COVID-19: Advice from the Canadian Association of Gastroenterology for Endoscopy Facilities, as of March 16, 2020. Frances Tse, Mark Borgaonkar, Grigorios I. Leontiadis. https://www.cag-acg.org/images/publications/CAG-Statement-COVID-&-Endoscopy.pdf
26. Society of Gastrointestinal Endoscopy of India (SGEI), Indian Society of Gastroenterology (ISG), and Indian National Association for Study of the Liver (INASL) Joint Guidance from the Society of Gastrointestinal Endoscopy of India (SGEI), Indian Society of Gastroenterology (ISG), and Indian National Association for Study of the Liver (INASL) for Gastroenterologists and Gastrointestinal Endoscopists on the Prevention, Care, and Management of Patients with COVID-19. Mathew Philip, Sundeep Lakhtakia, Rakesh Aggarwal, Kaushal Madan, Vivek Saraswat, Govind Makharia. DOI https://doi.org/ 10.1055/s-0040-1709837 ISSN 0976-5042.

APPENDIX 1

Local manufacture of PPE in limited resource settings.

Optimal PPE for endoscopy: Hair covering, protective glasses, faceshield, 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[8]. 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.

https://www.themachinemaker.com/innovation/face-shield-mahindra-ford-innovation-covid19

https://www.dezeen.com/2020/04/03/mit-covid-19-face-shields-design/

https://www.youtube.com/watch?v=fsU3wyLELlI

Masks

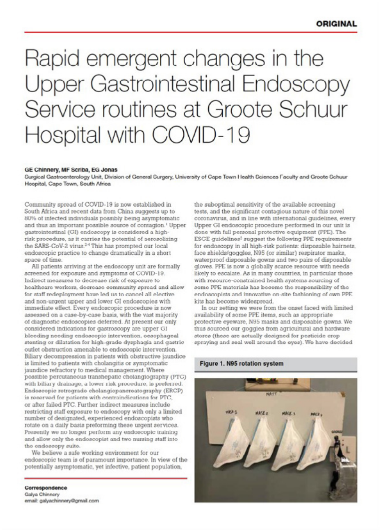
Respirators can be reused. (See Appendix on reuse). In low resource settings mask rotation is likely to be most applicable. If respirators are not available, surgical masks in combination with face shields may be used in specific circumstances as outlined in the Recommendations, together with modification of airflow (by fans or other means) to decrease exposure to aerosols and droplets, but the efficacy of this strategy is unknown. Cloth masks are acceptable for low-risk patients during pre-procedure assessment but are not adequate for healthcare staff during endoscopy procedures.

Boots

Plastic or rubber boots are widely available and can be disinfected post use.

Gowns and aprons. A method to manufacture disposable plastic covering has been described from South Africa.

http://ihpublishing.co.za/wp-content/uploads/2020/05/SAGES_Volume18_Issue1_digital.pdf


ORIGINAL

Rapid emergent changes in the Upper Gastrointestinal Endoscopy Service routines at Groote Schuur Hospital with COVID-19

Figure 1. N95 rotation system

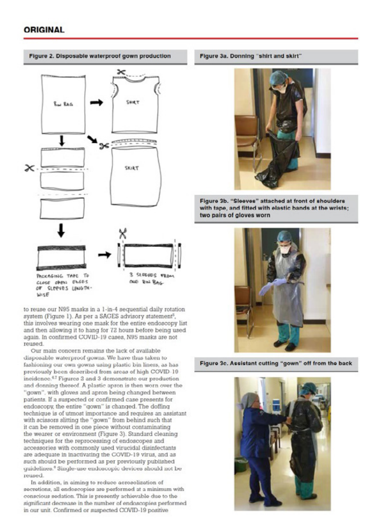

ORIGINAL

Figure 2. Disposable waterproof gown production

Figure 3a. Donning "shirt and skirt"

Figure 3b. "Sleeves" attached at front of shoulders with tape, and fitted with elastic bands at the wrists; two pairs of gloves worn

Figure 3c. Assistant cutting "gown" off from the back


ORIGINAL

Figure 3d. Careful doffing of "gown" as a single unit

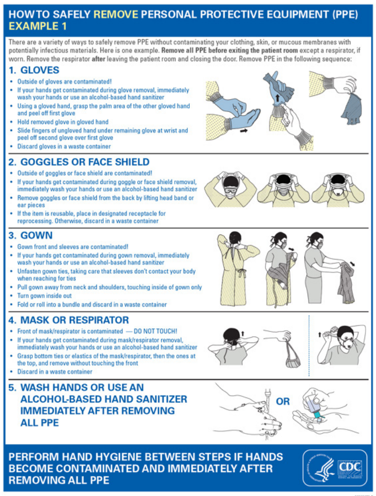
Figure 4. Plastic sheet with small hole allowing for endoscope passage only

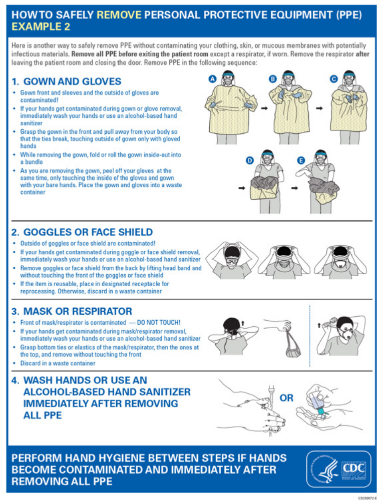
Figure 5. Endoscopy team making gowns

References

Appendix 2

The CDC has produced a visual guide to PPE use. **https://www.cdc.gov/coronavirus/2019-ncov/hcp/using-ppe**





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 corona virus 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)

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 reused, 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

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Doctors Cihan Yurdaydin, WGO Past President and Chair of Nominations and Saeed Hamid, Chair of the WGO Hepatology Interest Group, in collaboration with members of the WGO Hepatology Interest Group, present general clinical guidelines for patients with COVID-19 and Liver Disease.

Accompanying highlight slide sets can be viewed on the WGO website here: https://www.worldgastroenterology.org/publications/e-wgn/wgo-guidance-for-patients-with-covid-19-and-liver-disease

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Topics:

i. **Introduction and general approach to the patient with COVID-19 and elevated liver enzymes**

Ii. **Liver co-morbidities and COVID-19**
- iia. Chronic hepatitis B and C
- iib. Metabolic dysfunction-associated fatty liver disease (MAFLD) and COVID-19
- iic. Autoimmune liver diseases and COVID-19

Iii. **Practical aspects of caring for chronic liver disease patients in the COVID-19 era**
- iiia. How to follow chronic liver disease patients during COVID-19
- iiib. Performing procedures during COVID-19
- Iiic. Therapies under investigation for COVID-19 and potential hepatotoxicity

Iv. **Management of complications of liver disease:**
- iva. Screening and treatment of hepatocellular carcinoma (HCC)
- Ivb. Liver transplantation in the COVID-19 era

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

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 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 endothelitis 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

Table 1. A step-wise approach in COVID-19 patients suspected to have hepatobiliary disease

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

Determine need for further evaluation and urgency of intervention
- Conservative approach is the rule
  No invasive procedure
  Defer further imaging, use bedside ultra-sound if needed
- Exceptions
  Findings that may determine disease outcome ***and*** if diagnosed/treated have major implications
  Examples: Ascitic tap: decompensated cirrhosis vs malignancy and rule out Infection
  Ultrasonography: Common bile duct obstruction stones vs mass
  Liver biopsy: Autoimmune hepatitis? Can we treat without biopsy?
  EGD for upper GI hemorrhage

Table 2. Interpretation of liver test results in COVID-19 patients

Test	Comments
Hypoalbuminemia	Common in patients with systemic inflammatory response, usually not an indicator of liver failure
Prolonged INR or thrombocytopenia	Spontaneous coagulopathy / disseminated intravascular coagulation (DIC) may be present in 1/3 of sick patients (15, 21) Thromboembolic events likely common
High transaminases or bilirubin (> 3 x ULN)	Not typical for COVID-19, consider other causes
Anemia	GI bleeding: ulcer? Variceal hemorrhage?
Imaging	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)
GI symptoms including diarrhea	Common

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.

- 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 patient 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

1. Guan WJ, Hu Y, et al. Clinical characteristics of 2019 novel coronavirus infection in China. N Engl J Med 2020; published on line Feb 28 DOI:10.1056/NEJMoa2002032
2. Fan Z, Chen L et al. Clinical features of COVID-19-Related liver damage. Clin Gastroenterol Hepatol 2020 Apr 10: doi: 10.1016/j.cgh.2020.04.002
3. Cai Q, Huang D et al. Characteristics of Liver tests in COVID-19 Patients. J Hepatol 2020 Apr 13: doi.org/10.1016/j.jhep.2020.04.006.
4. Chen T, Wu D, Chen H, et al. Clinical characteristics of 113 deceased patients with coronavirus disease 2019: retrospective study. BMJ 2020;368:m1091 | doi: 10.1136/bmj.m1091
5. Schuttle A, Ciesek S, Wedemeyer H, Lange CM. Influenza virus infection as precipitating event of acute-on-chronic liver failure. J Hepatol 2019; 70:797-9
6. Wander P, Epstein M et al. COVID-19 Presenting as Acute Hepatitis. Am J Gastroenterol. 2020 Apr 15. doi: 10.14309/ajg.0000000000000660.
7. Xu Z, Shi L et al. Pathological findings of COVID-19 associated with acute respiratory distress syndrome. Lancet Respir Med. 2020;8:420-2
8. Lagana SM, De Michele S et al. COVID-19 Associated Hepatitis Complicating Recent Living Donor Liver Transplantation. Arch Pathol Lab Med. 2020 Apr 17
9. Wang Y, Liu S, Liu H, et al. SARS-CoV-2 infection of the liver directly contributes to hepatic impairment in patients with COVID-19. J Hepatol 2020 (in press)
10. Zhou P, Yang XL, Wang XG, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature 2020; published online Feb 3. DOI: 10.1038/s41586-020-2012-7.
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
12. Sena G, Gallelli G. An increased severity of peripheral arterial disease in the COVID-19 era. J Cardiovasc Surg 2020Apr 30;S0741-5214(20)31095-8. doi: 10.1016/j.jvs. 2020.04.489. Online ahead of print.
13. Bowles L, Platton S, Yartey N, et al. Lupus anticoagulant and abnormal coagulation tests in patients with Covid-19. N Engl J Med 2020 DOI: 10.1056/NEJMc2013656
14. Helms J, Tacquard C, Severac F, et al. High risk of thrombosis in patients in severe SARS-CoV-2 infection: a multicenter prospective cohort study. Intensive Care Med 2020 (in press).
15. Klok FA, Kruip MJHA, van der Meer NJM, et al. Incidence of thrombotic complications in critically ill ICU patients with COVID-19. Thromb Res 2020 April 10 (Epub ahead of print).
16. Llitjos JF, Leclerc M, Chochois C, et al. High incidence of venous thromboembolic events in anticoagulated severe COVID-19 patients. J Thromb Haemost 2020 April 22 (Epub ahead of print)
17. Li J, Fan JG. Characteristics and mechanism of liver injury in 2019 coronavirus disease. J Clin Transl Hepatol 2020; 8:13-7
18. Bowen DG, Warren A, Davis T, et al. Cytokine-dependent bystander hepatitis due to intrahepatic murine CD8+ T-cell activation by bone marrow–derived cells Gastroenterology Volume 123, Issue 4, October 2002, Pages 1252-1264
19. Chen G, Wu D, Guo W et al. Clinical and immunological features of severe and moderate coronavirus disease 2019. J Clin Invest. 2020 Apr 13. pii: 137244. doi: 10.1172/JCI137244.

20. Lippi G, de Oliveira MHS, Henry BM. Chronic liver disease is not associated with severity or mortality in Coronavirus disease 2019 (COVID-19): a pooled analysis. Eur J Gastroenterol Hepatol 2020
21. Bangash MN, Patel J, Parekh D. COVID-19 and the liver: little cause for concern. Lancet Gastroenterol Hepatol 2020.

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 oral 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:

1. Guan WJ, Zhong NS. Clinical Characteristics of Covid-19 in China. Reply. N Engl J Med 2020;382.
2. Zhang C, Shi L, FS W. Liver injury in COVID-19: management and challenges. Lancet Gastroenterol Hepatol 2020:1-3.
3. Chau TN, Lee KC, Yao H, Tsang TY, Chow TC, Yeung YC, Choi KW, et al. SARS-associated viral hepatitis caused by a novel coronavirus: report of three cases. Hepatology 2004;39:302-310.
4. Preliminary Estimates of the Prevalence of Selected Underlying Health Conditions Among Patients with Coronavirus Disease 2019 - United States, February 12-March 28, 2020. MMWR Morb Mortal Wkly Rep 2020;69:382-386
5. Schuttle A, Ciesek S, Wedemeyer H, Lange CM. Influenza virus infection as precipitating event of acute-on-chronic liver failure. J Hepatol 2019; 70:797-9

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

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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/m^2) 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

1. Eslam M, Newsome PN, Anstee QM, et al. A new definition for metabolic associated fatty liver disease: an international expert consensus statement [published online ahead of print, 2020 Apr 8]. *J Hepatol*. 2020;S0168-8278(20)30201-4. doi:10.1016/j.jhep.2020.03.039
2. Nseir WB, Mograbi JM, Amara AE, Abu Elheja OH, Mahamid MN. Non-alcoholic fatty liver disease and 30-day all-cause mortality in adult patients with community-acquired pneumonia. *QJM*. 2019;112(2):95–99. doi:10.1093/qjmed/hcy227
3. Prins GH, Olinga P. Potential implications of COVID-19 in non-alcoholic fatty liver disease [published online ahead of print, 2020 Apr 19]. *Liver Int*. 2020;10.1111/liv.14484. https://doi.org/10.1111/liv.14484
4. Ji D, Qin, E, Xu J, et al. Non-alcoholic fatty liver diseases in patients with COVID-19: A retrospective study . J. Hepatol 2020 DOI: https://doi.org/10.1016/j.jhep.2020.03.044
5. Zheng KI, Gao F, Wang XB, et al. Obesity as a risk factor for greater severity of COVID-19 in patients with metabolic associated fatty liver disease. Metabolism 2020, https://doi.org/10.1016/j.metabol.2020.154244

6. Xu L, Mao Y, Chen G. Risk factors for severe corona virus disease 2019 (COVID-19) patients : a systematic review and meta analysis. medRxiv preprint https://doi.org/10.1101/2020.03.30.20047415
7. Targher G, Mantovani A, Byrne CD, et al. Risk of severe illness from COVID-19 in patients with metabolic dysfunction-associated fatty liver disease and increased fibrosis scores [published online ahead of print, 2020 May 15]. *Gut*. 2020;gutjnl-2020-321611. doi:10.1136/gutjnl-2020-321611

IIC. AUTOIMMUNE LIVER DISEASE AND COVID-19

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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 cholangiopancreatography (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 cholangiopancreatograpy (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

1. Lleo A, Invernizzi P, Lohse AW, Aghemo A, Carbone M. Highlights for management of patients with Autoimmune Liver Disease during COVID-19 pandemia. J Hepatol. 2020 Apr 10. PubMed PMID: 32283134. PMCID: PMC7151539. Epub 2020/04/14. eng.
2. Fix OK, Hameed B, Fontana RJ, Kwok RM, McGuire BM, Mulligan DC, et al. Clinical Best Practice Advice for Hepatology and Liver Transplant Providers During the COVID-19 Pandemic: AASLD Expert Panel Consensus Statement. Hepatology. 2020 Apr 16. PubMed PMID: 32298473. Epub 2020/04/17. eng.
3. Boettler T, Newsome PN, Mondelli MU, Maticic M, Cordero E, Cornberg M, et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. JHEP Rep. 2020 Jun;2(3):100113. PubMed PMID: 32289115. PMCID: PMC7128473. Epub 2020/04/15. eng.
4. United States Department of Health and Human Services. Preliminary estimates of the prevalence of selected underlying health conditions among patients with coronavirus disease 2019 - United States, February 12-March 28, 2020. MMWR Morb Mortal Wkly Rep. 2020;69:382-6.
5. D'Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic. Liver Transpl. 2020 Mar 20. PubMed PMID: 32196933. Epub 2020/03/21. eng.
6. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet. 2020 Mar 28;395(10229):1033-4. PubMed PMID: 32192578. Epub 2020/03/21. eng.
7. Zhang C, Shi L, Wang F-S. Liver injury in COVID-19: Management and challenges. Lancet Gastroenterol Hepatol 2020 March 4. doi: 10.1016/S2468-1253(20)30057-1. [Epub ahead of print]
8. Congly SE, Sadler MD, Abraldes JG, Tandon P, Lee SS, Burak KW. Practical management of esophageal varices in the context of SARS-CoV-2 (COVID-19): The Alberta protocol. Can Liver J 2020 (in press).

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?

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- 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 lacking1,2. 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 system3. 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 though 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. Telemedicine 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 and 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

with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. JHEP Rep 2020 (2): 100113 .
2 Fix OK et al. Clinical best practice advice for hepatology and liver transplant providers during the COVID-19 pandemic: AASLD Panel Consensus Statement. Hepatology 2020, doi.org/10.1002/hep.31281.
3. Tapper EB & Asrani SK. COVID-19 pandemic will have a long-lasting impact on the quality of cirrhosis care. J Hepatol 2020 doi.org/10.1016/ j.jhep.2020.04.005.
4. Da BL, Im GY, Schiano TD. COVID-19 hangover: a rising tide of alcohol use disorder and alcohol-associated liver disease. Hepatology 2020; doi:10.1002/hep.31307
5. Szabo G, Saha N. Alcohol's effect on host defense. Alcohol Res 2015; 37:1509-70
6. Chick J. Alcohol and COVID-19. Alcohol and Alcoholism, 2020(00), 1–2 doi: 10.1093/alcalc/agaa039
7. Serper M et al. Telemedicine in liver disease and beyond: can the COVID-19 crisis lead to action? Hepatology 2020, doi.org/10.1002/hep.31276.
8. Xiao et al. Prevention of SARS-CoV-2 infection in patients with decompensated cirrhosis Lancet Gastroenterol Hepatol 2020 doi.org/10.1016/ S2468-1253(20)30080-7.

IIIB. PERFORMING PROCEDURES DURING COVID 19

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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 melaena). (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.

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). Please see recent WGO guidance on use appropriate use of PPE.
- Ensuring proper disinfection of equipment and the endoscopy room, minimize exposure in waiting and recovery areas and triage patients at entry, using well-trained staff.
- Clinicians should consider screening all patients undergoing endoscopy using a rapid COVID-19 test prior to the proceedure
- TIPS insertion should only be performed in life-threatening cases of refractory variceal bleeding.

References:

1. Xiao F, Tang M, Zheng X, Liu Y, Li X, Shan H. Evidence for Gastrointestinal Infection of SARS-CoV-2. Gastroenterology 2020.
2. Del Rio C, Malani PN. COVID-19-New Insights on a Rapidly Changing Epidemic. JAMA 2020.
3. Soetikno R, Teoh AY, Kaltenbach T, Lau JY, Asokkumar R, Cabral-Prodigalidad P, Shergill A. Considerations in performing endoscopy during the COVID-19 pandemic. Gastrointest Endosc 2020.
4. Musa S. Hepatic and gastrointestinal involvement in coronavirus disease 2019 (COVID-19): What do we know till now? Arab J Gastroenterol 2020.
5. Sultan S, Lim JK, Altayar O, Davitkov P, Feuerstein JD, Siddique SM, Falck-Ytter Y, et al. AGA Institute Rapid Recommendations for Gastrointestinal Procedures During the COVID-19 Pandemic. Gastroenterology 2020.
6. Repici A, Maselli R, Colombo M, Gabbiadini R, Spadaccini M, Anderloni A, Carrara S, et al. Coronavirus (COVID-19) outbreak: what the department of endoscopy should know. Gastrointest Endosc 2020.
7. Boettler T NP, Mondelli MU, Maticic M, Cordero E, Cornberg M,Berg T,. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID Position Paper. JHEP Reports 2020.
8. Chung RT, Reddy KR, Fix OK, Hameed B CLINICAL INSIGHTS FOR HEPATOLOGY AND LIVER TRANSPLANT PROVIDERS DURING THE COVID-19 PANDEMIC; AASLD Webinar, 26 March 2020.
9. An P, Huang X, Wan X, Xiao Y, Zhang J, Kang J, Liu J, et al. ERCP during the pandemic of COVID-19 in Wuhan, China. Gastrointest Endosc 2020.

IIIC. THERAPIES UNDER INVESTIGATION FOR COVID-19 AND POTENTIAL HEPATOTOXICITY

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Currently there are no drugs approved for COVID-19, although several drugs have been tested and many of them are still under investigation. Regarding patients with chronic liver disease, possible adverse events have to be considered. Drug-drug interactions in liver transplant patients should be kept in mind with certain immunosuppressive therapies where drug levels of calcineurin inhibitors (cyclosporine or tacrolimus), and mTOR inhibitors (sirolimus or everolimus) will have to be closely monitored. Moreover, patients with impaired liver function, including patients with Child-Pugh B/C cirrhosis, are at high risk of drug toxicities (1).

Remdesivir is a nucleoside analogue (NUC) that is approved in the US for emergency use for COVID-19, acts as a viral RNA polymerase inhibitor. It inhibits SARS-CoV-2 *in vitro* (2) as well as in case reports of patients with COVID-19 (3). A recent double-blind placebo controlled randomized study in 1063 patients confirmed beneficial findings of case reports (4). There is no experience so far in patients with liver cirrhosis. However, based on experience with NUCs in chronic hepatitis B and C, it might be considered as a safer drug than other drug classes (1). Liver toxicity with ALT elevation is a possible adverse event. No relevant drug-drug interactions are expected (5).

Other drugs currently under evaluation include chloroquine and hydroxychloroquine that interfere with the cellular receptor ACE2 and act as an endosomal acidification fusion inhibitor. These drugs have long been used for treatment

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. Hepatotoxicy 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 mTOR 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 the 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

1. Boettler, T., Newsome, P.N., Mondelli, M.U., Maticic, M., Cordero, E., Cornberg, M. and Berg, T., 2020. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. *JHEP Reports,* p.100113.
1. Wang, M., Cao, R., Zhang, L., Yang, X., Liu, J., Xu, M., Shi, Z., Hu, Z., Zhong, W. and Xiao, G., 2020. Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. *Cell research*, *30*(3), pp.269-271.
2. Holshue, M.L., DeBolt, C., Lindquist, S., Lofy, K.H., Wiesman, J., Bruce, H., Spitters, C., Ericson, K., Wilkerson, S., Tural, A. and Diaz, G., 2020. First case of 2019 novel coronavirus in the United States. *New England Journal of Medicine.*
3. Beigel JH, Tomashek KM, Dodd LE, et al. Remdesivir for the treatment of Covid-19- preliminary report. NEJM 2020 (in press)
4. COVID-19 Drug interactions. 2020 [cited March 16th 2020]; Available from: http://www.

covid19-druginteractions.org/
5. Geleris J, Yun Y, Platt J, et al. Observational study of hydroxychloroquine in hospitalized patients with Covid-19. NEJM 2020 (in press)
6. Abdel Galil SM. Hydroxychloroquine-induced toxic hepatitis in a patient with systemic lupus erythematosus: a case report. Lupus 2015; 24:638-40
7. Cao, B., Wang, Y., Wen, D., Liu, W., Wang, J., Fan, G., Ruan, L., Song, B., Cai, Y., Wei, M. and Li, X., 2020. A trial of lopinavir–ritonavir in adults hospitalized with severe Covid-19. New England Journal of Medicine.
8. Casado, J.L., Del Palacio, M., Moya, J., Rodriguez, J.M., Moreno, A., Perez-Elías, M.J., Belso, A., Dronda, F. and Moreno, S., 2011. Safety and pharmacokinetics of lopinavir in HIV/HCV coinfected patients with advanced liver disease. *HIV clinical trials*, *12*(5), pp.235-243.
9. Genovese, M.C., Kremer, J.M., van Vollenhoven, R.F., Alten, R., Scali, J.J., Kelman, A., Dimonaco, S. and Brockwell, L., 2017. Transaminase levels and hepatic events during tocilizumab treatment: pooled analysis of long-term clinical trial safety data in rheumatoid arthritis. *Arthritis & Rheumatology*, *69*(9), pp.1751-1761.
10. Chen, L.F., Mo, Y.Q., Jing, J., Ma, J.D., Zheng, D.H. and Dai, L., 2017. Short-course tocilizumab increases risk of hepatitis B virus reactivation in patients with rheumatoid arthritis: a prospective clinical observation. *International journal of rheumatic diseases*, *20*(7), pp.859-869.
11. Duan, K., Liu, B., Li, C., Zhang, H., Yu, T., Qu, J., Zhou, M., Chen, L., Meng, S., Hu, Y. and Peng, C., 2020. Effectiveness of convalescent plasma therapy in severe COVID-19 patients. *Proceedings of the National Academy of Sciences*.
12. Cai, Q., Yang, M., Liu, D., Chen, J., Shu, D., Xia, J., Liao, X., Gu, Y., Cai, Q., Yang, Y. and Shen, C., 2020. Experimental treatment with favipiravir for COVID-19: an open-label control study. *Engineering* (Beijing). 2020 Mar 18. doi: 10.1016/j.eng.2020.03.007. [Epub ahead of print]
13. Götte, M. and Feld, J.J., 2016. Direct-acting antiviral agents for hepatitis C: structural and mechanistic insights. Nature Rev Gastroenterol Hepatol, 13(6), p.338.
14. Elfiky, A.A., 2020. Anti-HCV, nucleotide inhibitors, repurposing against COVID-19. *Life Sciences*, p.117477.

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

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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 or high-risk HBV and MAFLD patients who are otherwise stable, routine HCC surveillance can be postponed for 2-3 months but probably no longer (4, 5). 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 telemedicine 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 care givers 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 telemedicine 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 measure while hoping for improvement in the COVID-19 infection (9). A detailed discussion of approaches to HCC in localities with limited resources is contained in the World Gastroenterology Organization's Global Guideline "Hepatocellular Carcinoma (HCC): a global perspective".

There are no published reports at this time on the various chemotherapies and immunotherapies being used to prolong life in advanced HCC patients so no recommendations are possible. The International Liver Cancer Association (ILCA) suggests that in patients with advanced HCC who require systemic therapies, oral tyrosine kinase inhibitors may be preferred to minimize nosocomial exposures when receiving infusion regimens (7).

The ultimate therapy remains liver transplantation, when that option is available to the patient and they are otherwise an appropriate candidate. However, COVID-19 may reduce access to both deceased and live donor liver transplantation. Again, delaying transplant to allow the COVID-19 to resolve or improve is preferred as mild cases will often resolve in 2-3 weeks. Experience is very limited regarding transplantation in patients who have COVID-19. There are two reports of liver transplant in HCC patients, both of whom survived and recovered, although with prolonged post-op courses and infectious complications when immunosuppression had to be increased due to rejection episodes (5, 10). This remains a last choice until curative therapies for COVID-19 become available and should be made only after careful discussion by 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

1. World Health Organization. Global Cancer Observatory. 2019 accessed at hhtp://gco.iarc.fr
2. Siegel, RL, Miller, KD, Jemal, A. Cancer statistics, 2019. CA Cancer J Clin. 2019; 69: 7-34.
3. Centers for Disease Control and Prevention, National Center for Health Statistics. Trends in liver cancer mortality among adults aged 25 and over in the United States, 2000-2016. NCHS Data Brief No. 314, July 2018 .Accessed at: http//bit.ly/2HpNzL4
4. Boettler T et al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. JHEP

Rep 2020 (2): 100113.
5. Fix OK et al. Clinical best practice advice for hepatology and liver transplant providers during the COVID-19 pandemic: AASLD Panel Consensus Statement. Hepatology 2020, doi.org/10.1002/hep.31281.
6. Iavarone M et al. Hepatocellular carcinoma in the time of COVID-19. Ann Oncol 2020, doi.org/10.1016/j.annonc.2020.04.007.
7. Tim Meyer, et al. Management of HCC During COVID-19: ILCA Guidance. April 8, 2020.
8. Rich, NE, et al. Hepatocellular carcinoma demonstrates heterogeneous growth patterns in a multicenter cohort of patients with cirrhosis. Hepatology 2020. February 4, doi: 10.1002/hep.31159.
9. Shiina,S. et al. Percutaneous Ethanol Injection for HCC: 20-year outcome and prognostic factors. Liver Int. 2012 32: 1434-1442.
10. Qin,J. et al. Perioperative Presentation of COVID-19 Disease in a Liver Transplant Recipient. Hepatology 2020; doi: 10.1002/HEP.31257.

IVB. LIVER TRANSPLANTATION IN THE COVID-19 ERA

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Coronavirus disease 2019 (COVID-19) caused by SARS-CoV-2 virus is impacting all aspects of hepatology, including the quality of our care (1). Liver transplantation is in the position where both donor and recipient risk must be considered. Developing hospital-specific policy for transplant can help with resource utilization while limiting risk to both patients and providers.

Pre-liver transplant

Patients with advanced liver disease are likely at higher risk for mortality if infected with SARS-CoV-2; however deferring management of complications of liver disease also places them at risk for severe consequences. Care should continue to follow clinical guidelines but it is important to limit contact with SARS-CoV-2 in all ways possible. Appointments should be conducted through virtual platforms when possible. Limit in-person visits to those with urgent issues such as those with new symptoms of decompensation or those with high liver enzymes.

High MELD/Acute

Evaluation for liver transplantation is traditionally encouraged when patients either meet minimal listing criteria, or have uncontrollable symptoms of advanced liver disease or liver cancer within Milan criteria. However, the COVID-19 pandemic is expected to affect both organ availability as well as peri-transplant risk. Individuals with a poor short-term prognosis that are likely to be transplanted quickly should continue to be evaluated and listed, especially those with high MELD and acute hepatic failure. Transplant for other indications must be a balance between the necessity of testing and the risk of SARS-CoV-2 exposure. This is especially true for liver cancer patients for whom listing must occur to start to accrue time toward allocation of points to allow them to be more competitive for transplant. Recipient age and co-morbid conditions must be balanced against potential benefit of evaluation.

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

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.
- There are few data to guide clinicians regarding transmission of SARS-CoV-2 through transplant.
- Post-transplant immune suppres-

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:

1. Tapper EB, Asrani SK. COVID-19 pandemic will have a long-lasting impact on the quality of cirrhosis care. J Hepatol. 2020 Apr 13. pii: S0168-8278(20)30217-8. doi: 10.1016/j.jhep.2020.04.005.
2. Fix O, Fontan R, Kwok R, McGuire B, Mulligan D, et al. Clinical Best Practice Advice for Hepatology and Liver Transplant Providers During the COVID-19 Pandemic: AASLD Expert Panel Consensus Statement. Hepatology Accepted. early release.
3. D'Antiga L. Coronaviruses and immunosuppressed patients. The facts during the third epidemic. Liver Transpl 2020 March 20. doi: 10.1002/lt.25756. [Epub ahead of print]
4. American Society of Transplantation. 2019-nCoV (Coronavirus): FAQs for organ donation and transplantation. Published March 20, 2020. https://www.myast.org/sites/default/files/COVID19%20FAQ%20Tx%20Centers%2003.20.2020- FINAL.pdf. Accessed April 2020.
5. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. Tobias Boettler, Philip N. Newsome, Mario U. Mondelli, Mojca Maticic, ... Thomas Berg JHEP|Reports June 2020 Page 100113 https://reader.elsevier.com/reader/sd/pii/S2589555920300471?token=4AB2685DDEEBAC836F4EDE9F139A95D24912157B246D9A10BC563E92A518F7D5E2E4F7529EB2E1299AAF243F06085B4D

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

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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-2in 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 (Comparative accuracy of oropharyngeal and nasopharyngeal swabs for diagnosis of COVID-19. Centre for Evidence-based medicine. https://www.cebm.net/covid-19/comparative-accuracy-of-oropharyngeal-and-nasopharyngeal-swabs-for-diagnosis-of-covid-19/. March 26, 2020). Furthermore, the PCR is not useful in identifying patients who are post infection and may be immune.

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 alClin 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

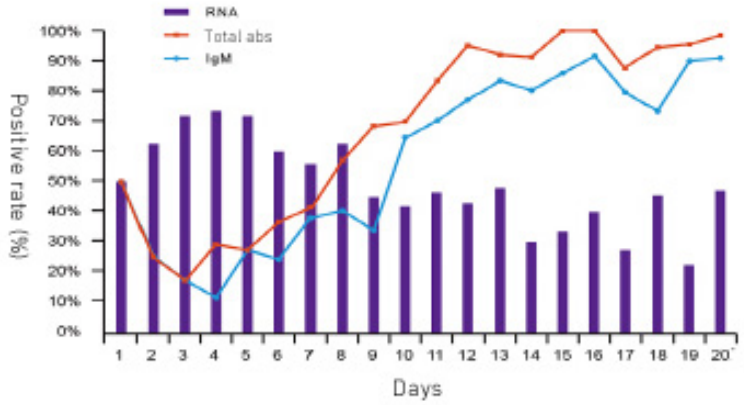

Figure 1. Positivity of PCR RNA obtained by oropharyngeal and/or nasal swabs, Total antibodies and IgM antibodies by days from onset of symptoms in SARS-CoV-2 in patients with COVID-19 (Data on file of Beijing Wantai Biological Pharmacy, submitted to National Medical Products Administration of China). N=380

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.

In practice, the kit demonstrates a detection rate of 30%-40% for patients with COVID-19 within the initial 7 days, 70% at 8-10 days, and 100% through 12 days. In contrast to the antibody detection, the PCR assay in the same cohort of COVID-19 patients showed 60%-70% of positivity within the initial 7 days and dropped to 40%-50% since then (Antibody responses to SARS-CoV-2 in patients of novel coronavirus disease 2019.Zhao J, Yuan Q, Wang H, Liu W, Liao X, Su Y, Wang X, Yuan J, Li T, Li J, Qian S, Hong C, Wang F, Liu Y, Wang Z, He Q, Li Z, He B, Zhang T, Fu Y, Ge S, Liu L, Zhang J, Xia N, Zhang Z.Clin Infect Dis. 2020 Mar 28. pii: ciaa344. doi: 10.1093/cid/ciaa344.).

Role of antibody testing in PCR negative patients

Days of onset	RNA negative	Ab positive in RNA negative
≤3 days	7	2
4-7 days	28	15
8-14 days	57	56
≥15 days	30	30

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)

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.

Approved indications of the antibody assay are:

1. Additional testing of suspect patients with negative nucleic acid test of SARS-CoV-2.
2. Antibody titering for patients recovered from COVID-19.

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 magneticluminescence, 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

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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

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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.[1] After that, telemonitor has been shown to facilitate chronic disease management, and many publications have been written for different specialties including gastroenterology and hepatology.[2-4]

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.[5,6]

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.[7]

Telemedicine is also ideal for chronic disease care management: inflammatory bowel disease, irritable bowel syndrome, liver disease, chronic pancreatitis, dyspepsia, and others.[8-10]

References

1. Arora, Sanjeev. Project ECHO: democratising knowledge for the elimination of viral hepatitis. The Lancet 2019: 4(2): 91-93.
2. Lee, T. Kim, L., Telemedicine in Gastroenterology: A value added service of patients. Clin Gastroenterol Hepatol 2020: 18(3): 530-3
3. Venkatesh R., Campbell, E., Thiim M., et al. E-consults in gastroenterology: An Opportunity for innovate care. J Telemedicine Telecare 2018; 25(3): 499-505.
4. Huntzinger M., Bielefeldt K., Expanding the Scope of Telemedicine in Gastroenterology. Federal Practitioner 2018: 26-31
5. Boettler, T., Newsome P., Mondenilli, M., et. Al. Care of patients with liver disease during the COVID-19 pandemic: EASL-ESCMID position paper. J Hepatol 2020: 2: 1 – 8.
6. Greenhalgh, T., Choon G., Car J. COVID-19: A remote assessment in primary care. BMJ 2020: 368: 1-5
7. Helsel, B., Williams J., Lawson K., et al. Telemedicine and Mobile Health Technology Are Effective in the Management of Digestive Diseases: A Systematic Review. Dig Dis Sci 2018: 63(3): 1392-1408.
8. Ateriya, N., Saraf A., Premlal V., et al. Telemedicine and virtual consultation: The Indian perspective. Natl Med J India 2018:31:215-18.
9. Tapper E., Asrani S. COVID-19 pandemic will have a long-lasting impact on the quality of cirrhosis care. J Hepatol 2020: S0168-8278(20)30217-8
10. Dorn Spencer. Gastroenterologist without borders: Using Virtual Care to reach beyond the clinic walls. Gastroenterology 2019: 157(2): 272-274.

Links:

https://giondemand.com/
http://webfiles.gi.org/docs/Toolbox/Essential_Guide_to_Telemedicine_in_Clinical_Practice.pdf https://gi.org/2020/03/20/top-five-things-gastroenterologists-should-know-about-telehealth/

Management of Patients with Inflammatory Bowel Disease (IBD)

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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

As patients with IBD often undergo endoscopy and this may pose a risk for SARS-CoV-2 infection to the patient and COVID-19 disease (by simply being in contact with a facility or health care providers who may be shedding the virus) or to health care providers (who are in close contact with patients who may be shedding the virus if they are infected with SARS-CoV-2 but are asymptomatic and hence are not aware of their infection status) the vast majority of endoscopies for patients with IBD have been postponed until the pandemic has passed. However, there may be instances where it is important to undertake an endoscopy in an IBD patient despite the ongoing pandemic. Approaches to endoscopy during the COVID-19 pandemic have been covered by reports from joint gastrointestinal professional societies (https://www.worldgastroenterology.org/about-wgo/covid-19/key-covid-19-resources#Endoscopy)

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*. The best way for IBD patients to reduce their risk of COVID-19 is to have their IBD treated and to stay away from health care facilities.

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

GASTRO 2021 PRAGUE
A Joint Meeting WGO/CSG

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.**

More information is available on the Gastro 2021 website: https://www.gastro2021prague.org.

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:

Joint Steering Committee	
WGO Representatives Naima Amrani, President Cihan Yurdaydin, Past President Guilherme Macedo, President-elect	**CSG Representatives** Julius Spicak, CSG Board Representative Ondrej Urban, CSG President Milan Lukas, CSG Past President
Joint Scientific Program Committee	
WGO Representatives Carolina Olano, Uruguay, Co-Chair Joost Drenth, The Netherlands Goeffrey Metz, Australia Gerhard Rogler, Switzerland David Sanders, United Kingdom	**CSG Representatives** Tomas Hucl, Czech Republic, Co-Chair Radan Bruha, Czech Republic Ilja Tacheci, Czech Republic

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://wcog2021.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

GIHep Singapore 2021

When: July 8 - 11, 2021
Location: Shangri-La Singapore
Country: Singapore
Organizer: Gastroenterological Society of Singapore
Website: www.gihep.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.apdwkl2021.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 Endoscopía Digestiva
Website: https://www.spge.org.py/

Congreso de las Asociaciones Colombianas del Aparato Digestive ACADI

When: September 9 - 11, 2021
Location: Estelar Santamar Hotel & Centro de Convenciones, Santa Maria, Colombia
Organizer: Asociación Colombiana de Gastroenterologia
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

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