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In this issue

Need for Endoscopic Interventions and a Multimodality Approach in the Era of Living Donor Liver Transplantation in South Korea

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Liver Transplantation in South Korea

Liver transplantation (LT) in South Korea differs markedly from that in Western countries in terms of etiology and method. The rate of living donor liver transplantation (LDLT) is more than twofold higher than that of deceased-donor LT (DDLT). South Korea has the largest number of living donors per million people among Asia–Pacific countries and ranks second worldwide in terms of the number of living donors per million people (IRODaT 2019). Since the performance of the first LDLT in South Korea in 1997, the rate of LDLT has steadily increased. South Korea is the world leader in LDLT, with the largest annual number of transplantation surgeries, 22.9 per million people. This is more than tenfold that in Japan and Hong Kong, which have the highest frequencies of LT worldwide (IROaT 2019).[1] Due to the shortage of brain-death donors in South Korea, DDLT is performed in patients with a high MELD score. In South Korea's family-centered culture, this surgery has become a source of hope for patients with end-stage liver disease.[2]

South Korea has developed innovative surgical techniques, which are now the standards at most centers worldwide. South Korean physicians established right-lobe LDT some years ago. LDLT is now commonly performed in South Korea for the treatment of hepatocellular cancer and end-stage liver cirrhosis.

Biliary complications after LDLT differ from those after DDLT

Biliary stricture and bile leak are the primary targets for endoscopic and percutaneous interventions. Biliary complications are the most common complications after DDLT and LDLT.

Biliary Stricture

LDLT is technically more complex and challenging than DDLT and has a higher incidence of biliary complications. Bile duct strictures are the most common biliary complication after LT, accounting for approximately 40% of all biliary complications. Bile duct stricture reportedly occurs in up to 5% of DDLT cases, compared to 7.3–60% for right-lobe grafts and 24% for left-lateral-segment grafts for LDLT.

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In recent years, duct-to-duct reconstruction has been preferred over hepaticojejunostomy in LDLT, because of its simplicity, rapid gastrointestinal recovery, and preservation of physiological biloenteric continuity. A duct-to-duct anastomosis can be easily approached endoscopically, mostly by ERCP, rather than hepaticojejunostomy. However, when this is performed, the site is higher (at the hilum) than in DDLT. In LDLT, the angle between the bile duct of the received liver and the extrahepatic bile duct is acute, which is associated with a risk for ischemia and traction in surrounding tissues. As the transplanted liver becomes hypertrophic, an anastomotic stricture is possible. A post-LT anastomotic biliary stricture (ABS) is typically caused by an improper surgical technique, including excessive use of electrocoagulation, tension at the level of the anastomosis, and inappropriate bile duct dissection, as well as by small-caliber bile ducts, localized ischemia, infection, or fibrotic healing, with most cases occurring within 12 months after LT. The ABS after LDLT is more frequent and challenging than DDLT for the above reasons.[3]

Non-anastomotic strictures (NAS) typically result from hepatic artery injury or thrombus, causing irreversible biliary fibrosis as a result of ischemia. Other causes include prolonged cold ischemia or ABO-type incompatibility.

Bile Leak

Bile leak is the second most common biliary adverse event following LT and results in significant morbidity among LT recipients. A bile leak is a risk factor for biliary strictures and vice versa. Bile leaks occur in up to 25% of LT cases, typically one day to six months after the operation. The leak can occur from the anastomosis, biliary drainage tube tract, liver cut surface, or cystic duct remnant. Anastomotic leak is the most common type. The frequency of bile leak is 7.5% after DDLT and 9.5% after LDLT.[4]

Endoscopic management is the initial treatment modality for biliary complications

Biliary Stricture

The mainstay of ABS and NAS management is ERCP therapy. Most patients require several ERCP sessions at three-month intervals, with stenting and dilation for more than one year. Plastic stents should be exchanged regularly to avoid occlusion-causing cholangitis. The stricture resolution rate for patients with ABS treated with plastic stents via ERCP is 80%. The rate of recurrence depends on the duration of stenting; less than one year of stenting has a 78% stricture resolution rate, compared to 97% for more than one year.

There have been attempts to overcome the limitations of periodic plastic stent replacements using temporary single-session self-expanding metal stents (SEMSs).[5,6] However, because SEMSs have high migration rates and variable results, they do not yield a consistently superior resolution of ABS compared to maximal plastic stent therapy. In South Korea, for the treatment of proximal benign biliary stricture, a modified fully covered SEMS is used, which has a mid-waist to prevent migration and a long string to facilitate removal using standard endoscopic grasping forceps. The waist, at the central portion, prevents migration of the stent. The stent is available at diameters of 6.8 and 10 mm and lengths of 4, 5, and 6 cm, enabling clinical use according to the anatomical situation. The short removable fully covered SEMS is an

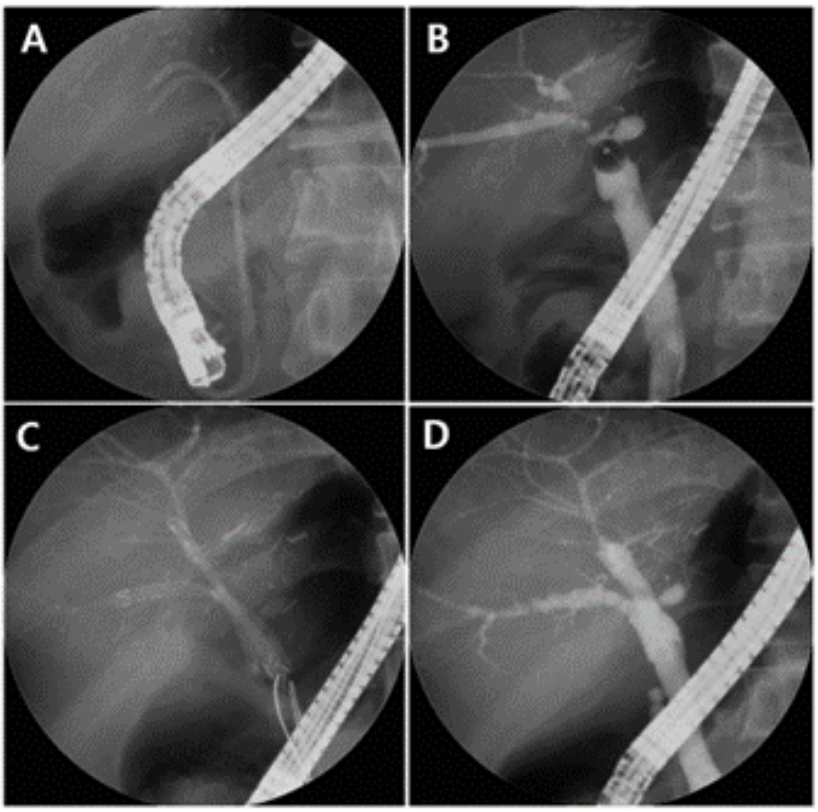

Figure 1

effective treatment for ABS after LT that is not amenable to treatment by conventional procedures with plastic stents (Fig. 1). In addition, a plastic stent should be inserted if obstruction of a branch of the intrahepatic bile duct by a fully covered SEMS is suspected. The fully covered SEMS is a novel salvage treatment option for ABS after LDLT.

Dilation of NAS typically requires a smaller balloon than ABS. The efficacy of ERCP or percutaneous treatment for NAS is less than that for ABS, and NASs require a longer duration of treatment. In addition, there is a higher rate of stent failure due to migration or occlusion. NAS strictures that occur in the intrahepatic region of the biliary tree are difficult to access endoscopically.

Bile Leak

The most widely accepted treatment in patients with duct-to-duct biliary anastomosis is early ERCP-guided endoscopic therapy. Usually, a sphincterotomy is performed, and a transpapillary stent is placed for two to three months to divert bile from the leak. This decreases the transpapillary pressure gradient, which can exacerbate bile leaks. A longer duration of stent placement than in cholecystectomy cases are recommended because of delayed healing in the setting of immunosuppression. The fully covered SEMS can effectively treat refractory or bile leaks with a large defect.

Given the anatomy, bile leaks after Roux-en-Y in LDLT are rarer and difficult to treat by ERCP. If unable to obtain biliary access endoscopically, a percutaneous internal-external drainage can be performed to treat bile leaks. Surgery will be necessary if these measures are unsuccessful.

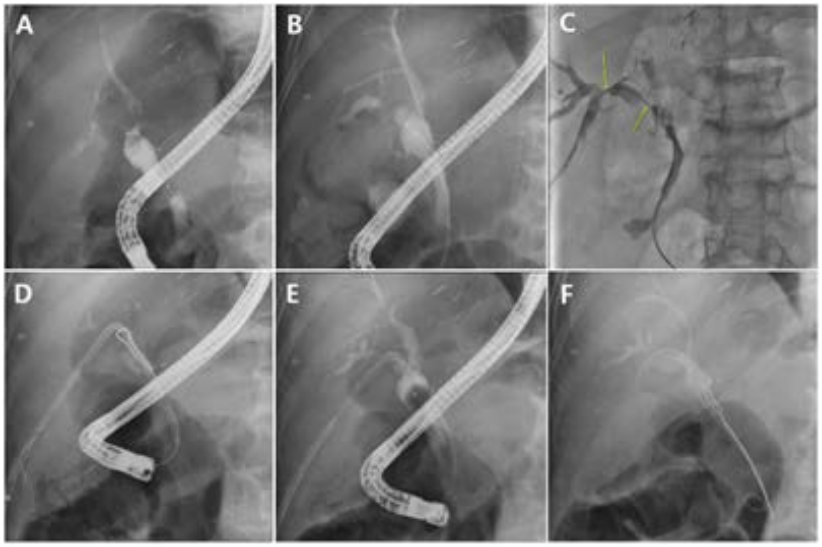

Figure 2

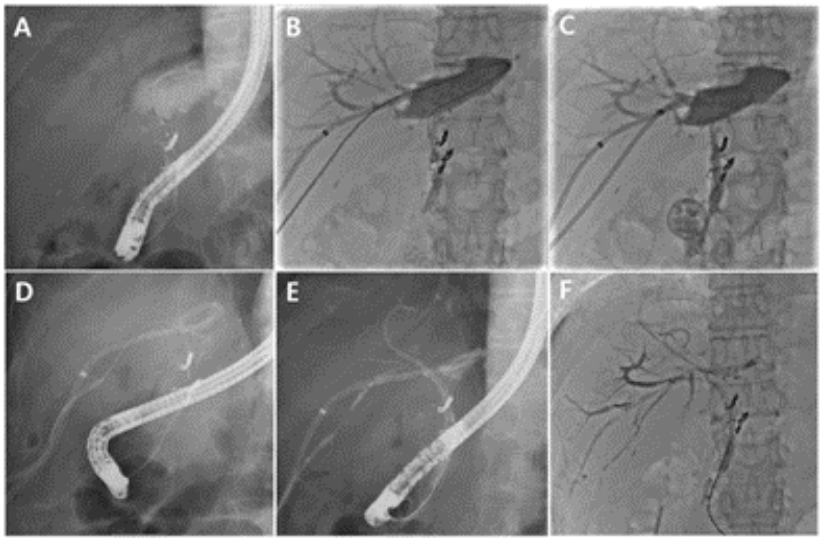

Figure 3

Treatment of complex complications after LDLT requires a multimodality approach

Advantages and Need for Collaboration between Percutaneous and Endoscopic Approaches Under Challenging Cases

In terms of treating biliary strictures, the donor bile duct and narrowing are smaller and more anatomically challenging in LDLT. These features are more prominent in LDLT than in DDLT patients. ERCP is a feasible first treatment modality for post-LDLT biliary stricture, but in failed cases, particularly with a pouched anastomosis, percutaneous transhepatic biliary drainage (PTBD) can be attempted. Stricture type is a determinant of successful guidewire passage rather than the procedure equipment or procedure time. Among the pouched, triangular, and intermediate forms of the distal side of the bile duct anastomosis, the pouched form has the lowest endoscopic success rate (25%).[7] If contrast medium readily passes into the intrahepatic duct in a pouched-form case, we spend

more time than typical attempting to pass the guidewire. Spending too much time on ERCP in patients with a pouched-form anastomosis is undesirable. If the results fall short of expectations, we convert to a percutaneous approach (Fig. 2).

The success rate of PTBD for resolving a bile duct anastomosis stricture in pouched-form cases is 60% on the first attempt, but the total success rate, including repeated PTBD, is 87%. Therefore, PTBD is useful for cases of failed endoscopic therapy for a post-LDLT biliary stricture. We attempt a second PTBD because we believe that the major reason for the failure of the first PTBD is not the tightness of the anastomotic stricture area but a tortuous and kinked anastomotic stricture because of the compression effect of the transplanted liver. To pass a guidewire through a stricture, PTBD is more effective than ERCP, because torque can be applied on a short guidewire using a variably shaped pathfinding catheter during PTBD. In addition, PTBD has advantages over ERCP in terms of patient comfort (e.g., being in the supine position during the procedure) and offers a more exact biliary anatomy. If PTBD succeeds, one may exchange the PTBD catheter for an internal stent using the rendezvous method.

Cooperation with intervention radiology is frequently necessary when treating complicated or refractory bile leaks after LDLT. Additional percutaneous stenting is mandatory if the biliary defect is large and per-oral, stenting cannot effectively bridge the bile leak. If the per-oral approach fails to enable selective cannulation of the leak area, the percutaneous method is typically effective (Fig. 3), e.g., for bile leaks in patients with multiple anastomoses of the bile ducts.

Magnet Compression Anastomosis for the Treatment of Total Biliary Obstruction

Endoscopic and percutaneous procedures have high success rates in post-LT ABS. However, recanalization is impossible using conventional endoscopic and percutaneous methods in cases of a severe stricture or complete obstruction that prevents the passage of the contrast medium and guidewire. In such cases, surgical revision must be performed or external drainage catheters must be maintained.

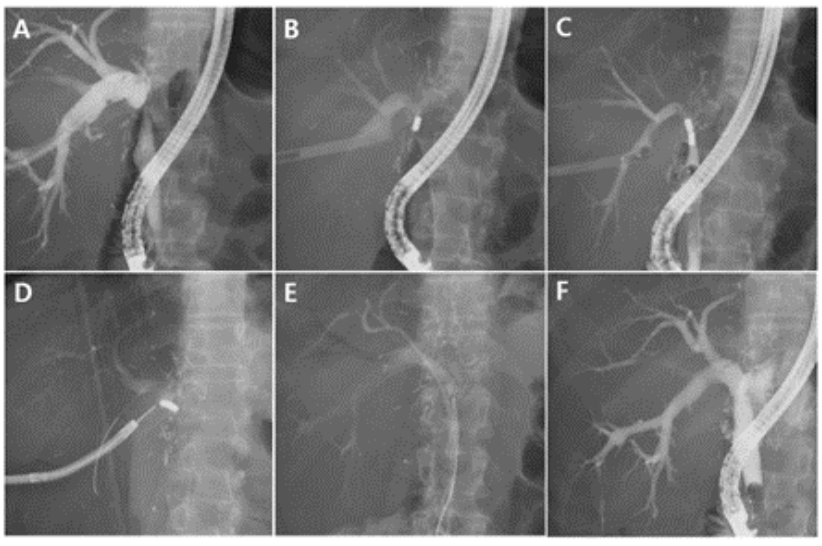

Figure 4

Surgical revision of BBSs is associated with high morbidity and mortality rates. Moreover, there is a high rate of recurrent strictures requiring further interventions following surgical revision. Catheter-related complications can arise when percutaneous external drainage catheters are maintained, compromising the patient's quality of life.

Magnet compression anastomosis (MCA) was developed as a nonsurgical alternative for patients with BBSs in whom conventional endoscopic or percutaneous methods failed (Fig. 4).[8, 9, 10] The attractive force from the two magnets on both sides of the ABS creates compression, which induces ischemia in the ABS tissue. As the two magnets approach each other, complete necrosis of ABS tissues occurs, and a new fistula is formed to complete the recanalization. MCA is safe and in animal studies has been found to be equivalent or superior to anastomoses created by traditional suturing or stapling techniques. Our institution has performed MCA on more than 70 patients after LDLT, with a success rate of more than 90% and a low rate of stricture recurrence. Two magnet-delivery routes are needed to perform this procedure, typically one PTBD and one ERCP. An appropriate percutaneous magnet delivery route is key for procedure success, which makes cooperation with intervention radiology essential.

Conclusion

In South Korea, there are more biliary complications after LDLT than after DDLT, with biliary stricture being the most common. ERCP is a feasible initial treatment modality for post-LDLT complications, and PTBD can be used in failed cases.

In the future, most LTs will be LDLT; DDLT is becoming rare worldwide. As experience with LDLT accumulates and the surgical technique improves, the incidence of

biliary tract complications after LDLT may decrease. However, after LDLT one or more biliary complications is inevitable, the treatment of which—particularly of complicated and refractory biliary complications—requires a multimodality approach.[11]

Figure legend

Figure 1. Fully covered self-expandable metal stent (FCSEMS) for the treatment of refractory anastomotic biliary stricture

(A) The patient was referred to our hospital with two plastic stents. **(B)** Cholangiogram showing multiple tight anastomotic strictures in the posterior and inferior intrahepatic ducts. **(C)** FCSEMSs were sequentially inserted into the stricture sites. **(D)** After an indwelling time of 3 months, the retrieval strings were grasped using biopsy forceps to remove the FCSEMSs. The cholangiogram demonstrates the resolution of multiple strictures.

Figure 2. Percutaneous treatment of pouch-type anastomotic biliary stricture (ABS) after living donor liver transplantation

(A) ERCP cholangiography showing pouch-type ABS. **(B)** Guidewire passing through the pouch-type ABS; ERCP was attempted but failed. Only the right posterior duct was successfully cannulated. **(C)** Guidewire was successfully passed through the ABSs (yellow arrows) using the percutaneous approach. Percutaneous transhepatic biliary drainage (PTBD) catheter was placed in the ABS. **(D)** Successful guidewire insertion with ERCP in the pouch-type ABS using the rendezvous method. **(E)** After passing the guidewire through the ABS, the PTBD catheter was removed. **(F)** Fully covered self-expandable metal stent (FCSEMS) was inserted into the ABS, and a plastic stent was placed in the right posterior duct to prevent bile duct obstruction by the FCSEMS membrane.

Figure 3. Percutaneous bile leakage treatment after living donor liver transplantation (LDLT)

(A) Cholangiogram showing bile leakage after LDLT. Selective cannulation of the anastomosis site with ERCP was not possible. **(B)** A percutaneous catheter was inserted to drain the leaked bile. Another PTBD catheter at B6 was used to pass a guidewire through the common bile duct (CBD). Selective cannulation of the CBD using the guidewire was successful. **(C)** The percutaneous transhepatic biliary drainage (PTBD) catheter remained indwelling across the bile leak area. **(D)** A guidewire was successfully passed with ERCP in the leaking bile duct 1 month later using the rendezvous method. **(E)** Fully covered self-expandable metal stent (FCSEMS) was inserted into the leaking bile duct, and a plastic stent was placed to prevent blockage by the stent membrane. **(F)** After FCSEMS insertion, the amount of leaked bile decreased, and the percutaneous drainage catheter could be removed.

Figure 4. Magnetic compression anastomosis in a benign biliary stricture patient after living donor liver transplantation

(A) Percutaneous transhepatic biliary drainage (PTBD) catheter was inserted and dilated up to 16 Fr. We preferred an indwelling fully covered self-expandable metal stent (FCSEMS) at the ampulla because of the ease of magnet delivery in ERCP. **(B)** A magnet grasped with a polypectomy snare was delivered into the common bile duct (CBD) with ERCP. **(C)** The proximal magnet was delivered through the 18 Fr. sheath PTBD tract. Magnet alignment could be confirmed during the procedure. **(D)** The approximated magnets were removed after for weeks using a percutaneous transhepatic cholangioscopy. **(E)** After magnet removal, the indwelling FCSEMS remained at the new fistulous tract for six months. **(F)** The FCSEMS was removed and fistula formation was evident.

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Message from the Editors

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To our WGO community,

We welcome you to go through our September issue of *e-WGN*. In the last few months, through a pro-active role played by the editorial board and our secretariat, we have been able to reach potential contributors with positive response. Our September issue, as you would notice, have articles from different geographical locations with its inherent diversity. We have also developed a portal for submission of manuscripts by authors, making the process smoother.

We are very happy to note that a new WGO Training Center related to gastroenterology, hepatology and endoscopy was inaugurated in Brazil on 15 July with the presence of WGO President Prof. Macedo. We are sure this new academic platform will help the physicians of South America to enhance their knowledge.

Drs. Lee and Russel, through their article "Elimination Goals in the Pacific Island" have disclosed the challenges faced in the Pacific region for prevention and treatment of gastrointestinal diseases. It is heartening to note that local physicians have united to meet the challenge and control diseases such as hepatitis B by increased availability of antiviral drugs and using measures to reduce vertical transmission.

Dr. Lee from Seoul has shared his experience of liver transplantation in the featured Expert Point of View article of this issue. South Korea is a world leader in liver transplantation. The program differs from Western countries in terms of technique as well as the fact that living donor liver transplantation (LDLT) is almost twice that of deceased donor liver transplantation. (DDLT). This difference has a consequence of higher and more complex types of post-transplant biliary complications. The nature and treatment of these complications depicted by Dr. Lee is going to be very informative for physicians working at centers with a predominant LDLT program. During his conversation with Dr. Kaul (Rochester, USA), the story of liver transplantation and treatment of biliary complication as seen in Korea has been nicely revealed.

In another Expert Point of View article, Dr. Akash Roy (India) has projected the global burden of non-alcoholic fatty liver disease. In this article, he has discussed the preparatory strategies of various countries. Additional components of preparedness that are highlighted include awareness, integration, investment and development of infrastructure and drugs. It is interesting to note the different reported rates of preparedness of various Asian and European countries. We feel this article can help various countries to prepare themselves with appropriate policy.

Articles from Chicago, USA by Drs. Bhagwat, Post and Reau have looked at various global guidelines on the treatment approach to hepatitis B. The authors have discussed the geographical differences in approaching this virus, noting a more permissive use of therapy in some Asian countries. There seems to be a changing paradigm with a more liberal use of antiviral therapy.

As usual, we have also tried to include a calendar for future gastroenterology related international meetings. We hope this information will help our readers to plan their schedule.

We hope you would find September issue to be worth browsing through. We also welcome your feedback to improve *e-WGN* further to fulfill your expectations.

Mahesh and Anita

Non-Alcoholic Fatty Liver Disease: Global Scenario, Challenges, and Preparedness

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Introduction

Non-alcoholic fatty liver disease (NAFLD) has emerged as the most common and rapidly growing chronic liver disease globally with an estimated pooled prevalence of 32.4%. Additionally, an overall incidence of 46.9 cases per 1000 person-years.[1] Regional variations remains a variable of the disease's prevalence, with the highest prevalence in the Middle East and South America and the lowest in Africa.[2] NAFLD is most commonly associated with the components of metabolic syndrome, the most common being obesity and diabetes mellitus.[2, 3] In people with obesity and type 2 diabetes, NAFLD prevalence ranges as high as 50-70%.[4, 5] Given these associations with obesity and type 2 diabetes and the exponential increment in these entities in conjunction with a globally aging population, the burden of NAFLD is projected to grow further.[6] Because of such projected modeling of an incremental disease burden, developing strategies and policies to ensure adequate preparedness to combat the disease becomes imperative. Herein, we delve into a brief overview of the global scenario, challenges, and preparedness for tackling NAFLD.

Global Scenario

Over the past two decades, one of the key issues has been the variations in the reported prevalence of NAFLD, with differences arising out of geography, ethnicity, type of population studied, reporting, selection bias, and lack of uniformity in definitions. Albeit, the exponential evolution is reflected in the temporal change in NAFLD prevalence, which has increased by more than 50% from 25.26% (21.59-29.33) in 1990-2006 to 38.00% (33.71-42.49) in 2016-2019.[7] The prevalence varies geographically, with the highest pooled prevalence being in Latin America (44.3%), followed by the Middle East and North Africa (MENA) (36.5%), South Asia (33.8%), Southeast Asia (33.1%), North America (31.2%,), East Asia (29.71%), Asia Pacific (28.0%), Western Europe (25.1%).[7] In sync with the prevalence of NAFLD, the global prevalence of

Figure 1: Roadmap for Preparedness for NAFLD

non-alcoholic steatohepatitis (NASH) is estimated to be 5.27%, with the highest prevalence being in Latin America (7.1%), followed by MENA (5.8%), South Asia (5.4%), Southeast Asia (5.3%), North America (5.0%), East Asia (4.7%) Asia Pacific (4.5%) and Western Europe (4.02%). When we look at subgroups, the prevalence of NAFLD goes up to 40%-60% in overweight and obese subjects and around 10% in lean subjects, with lean NAFLD being higher in Asians.[8] NAFLD in people with diabetes appears to be most worrisome, with an overall global prevalence of 55.5% (95% CI 47.3-63.7) 37.3%, and 17% prevalence of NASH and advanced fibrosis, respectively.[9] Lastly, beyond the adult population, NAFLD has also emerged as a growing problem associated with the pediatric population, with an overall pooled prevalence of 7.6%, which alarmingly increases to 34% in subjects with pediatric obesity.[10]

Challenges

Against the backdrop of the epidemiological burden, it is essential to identify the key challenges in the holistic management of NAFLD. The foremost challenge remains the need for more awareness regarding the entity and its relationship with poor metabolic health. While the impact of alcohol or viral hepatitis on liver health is well understood, the impact of lifestyle choices and metabolic co-morbidities leading to poor liver health in NAFLD has glaring gaps. Recent systematic reviews and surveys indicated a lack of sufficient communication between healthcare providers and patients, and obesity and diabetes are more concerning to the patients than NASH.[11, 12] The lack of awareness and comprehension of the gravity of the problem transcends beyond patient-healthcare providers to overall governmental policy decisions. This is reflected in the need for additional focus on NAFLD in governmental health policies. The paucity of awareness is compounded by the variations in reported prevalence, lack of uniform diagnostic codes, good quality data on natural history with endpoints such as cirrhosis and hepatocellular carcinoma, and new controversies arising out of name changes to metabolic dysfunction associated fatty liver disease (MAFLD).[13] The culminating point of these variations and lacunae in knowledge is the development of hurdles and stumbling blocks toward objective disease burden and outcome assessment. This in turn affects the development of uniform policy decisions in management. As the disease burden is of enormous magnitude, it also becomes imperative to develop appropriate referral pathways for specialist care from primary healthcare settings. There, however, still needs to be uniformity amidst guidelines recommended by various societies for appropriate referral pathways, which is again driven by demographic and epidemiological variations in different countries. Lastly, NAFLD being a hepatic reflection of metabolic dysregulation, there is an urgent need for concordance and consensus between different specialties, including primary care, endocrinology, cardiology, gastroenterology, and hepatology in terms of diagnosis, risk stratification, referral pathways, and management.[14]

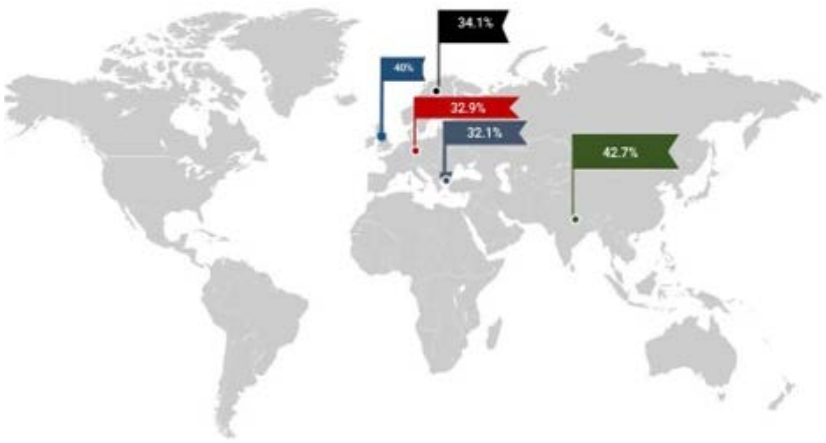

Figure 2: Top 5 Countries based upon NAFLD Preparedness Index (Based upon Lazarus et al. J Hep 2022)

Preparedness

In the background of above-outlined burden and challenges, it becomes important to focus on strategies directed towards a holistic approach to NAFLD (Figure 1).

One of the crucial elements to address the challenges is to increase awareness amongst the public and health care providers to raise NAFLD to a similar pedestal as diabetes and obesity as markers of metabolic ill health. Furthermore, educating primary care providers about making appropriate diagnoses and ensuring effective clinical care pathways and referrals is important. In addition, interdisciplinary models of communication and management involving primary care, specialty, and subspecialty domains for uniformity in management need to be established.

To achieve these core goals for holistic care, it becomes imperative to incorporate NAFLD as one of the non-communicable diseases and explicitly delineate the bidirectional relationship with diabetes mellitus, obesity, and other components of metabolic health. An effort to implement these strategies calls for adequate preparedness and planning. In 2019,

a survey of 29 European countries was conducted addressing public health response strategies for NAFLD.[15] Alarmingly, none of 29 participating countries had written strategies or action plans for NAFLD and only one-third reported having national clinical guidelines specifically addressing NAFLD. Only five countries reported having referral pathways, and only one-fourth had funded awareness campaigns.[15] A follow-up survey assessed the preparedness index of countries based on four key domains of policies, guidelines, epidemiology, and care management.[16] No countries were found to have yet attained a high level of preparedness. The United Kingdom (UK) scored best, although falling within the midlevel preparedness band, followed by Spain, and Denmark. While Spain scored highly in the epidemiology indicator category, UK was the only country that scored highly for care management.[16] This concept was further expanded on a global scale involving 102 countries.[17] The highest-scoring countries were India (42.7) and the United Kingdom (40), with almost a third of the countries scoring zero out of 100 (Figure 2).

One-third of the countries had national NAFLD clinical guidelines, while no country had a national or sub-national strategy directed specifically towards NAFLD.[17] These findings indicate glaring deficiencies in preparatory strategies and policies addressing NAFLD. Such deficiencies call for urgent implementation of goal-directed measures across healthcare systems with a bottom-up approach starting from primary healthcare level up to subspecialty level care in the backdrop of specific national policies.

Conclusion

NAFLD is a major global public health challenge. Although several strides have been made in the understanding and management of the disease, its translation into acceptance as a public health challenge has several areas of deficiency. Globally countries lack appropriate preparatory strategies to combat the evolving epidemic of NAFLD. Holistic approaches involving increased awareness, infrastructure development, interdisciplinary collaboration and strategic action plans at national levels are urgently required for comprehensive care.

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Should Society Guidelines Move Towards More Permissive Therapy for Chronic Hepatitis B Virus Infections?

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Chronic infection with hepatitis B virus (HBV) is associated with high morbidity and mortality worldwide through progression to hepatocellular carcinoma (HCC) and cirrhosis. As of 2019, it was estimated that 316 million people globally have chronic HBV infection.[1] HBV is an important cause of HCC; over 50% of HCC cases worldwide are attributable to the virus. The global burden of HBV infection is unevenly prevalent throughout the world. The Asian continent has prevalence rates estimated as high as 4%, while disease rates are under 1% in North America.[2] Due to the high burden of disease caused by HBV, the World Health Organization (WHO) published a global health sector strategy in 2016 calling for HBV elimination that aimed for a 95% reduction in new cases and 65% reduction in deaths by 2030. This review aims to compare expert guidelines published in the last five years considering newer research that suggests use of more permissive therapy.

The natural course of HBV infection is categorized by five major phases (Table 1), and the stage of infection guides treatment recommendations.

The goal of treating chronic HBV is to improve clinical outcomes in patients, including preventing progression of chronic hepatic inflammation to cirrhosis, reducing risk of HCC, and improving rates of survival. The Reveal-HBV study demonstrated that increased HBV DNA portends increased risk of disease progression to HCC and cirrhosis, even at levels as low as 1,000 IU/mL to 10,000 IU/mL.[3] In fact, newer data show that the patients with greatest risk of HCC may be those with moderate serum levels of HBV DNA (1,000,000 IU/mL).[4] Treatment has traditionally been limited to patients with chronic hepatitis, or those patients with increased liver enzymes and viremia about a threshold of 2,000 IU/mL. However, in the last five years, several national and regional expert societies have up-

Table 1. Clinical and Pathological Characteristics of Stages of Hepatitis B Infections

Phase I	HBeAg positive (HBeAg+) chronic HBV infection	Also referred to as "immune tolerant" phase. Patients initially have high levels of HBV DNA in their serum and can infect others but are not yet showing signs of hepatic inflammation.
Phase II	HBeAg+ chronic hepatitis	Over time, immune response to infected hepatocytes increases, resulting in hepatic inflammation and fibrosis. Patients can still infect others.
Phase III	HBeAg negative (HBeAg-) chronic HBV infection	Over time, there is less active inflammation and more fibrosis in hepatocytes. As a result of the immune response, patients lose the ability to infect others.
Phase IV	HBeAg-chronic hepatitis	Patients cannot infect others but have progressive levels of liver inflammation that can lead to HCC and/or cirrhosis.
Phase V	HBsAg negative (HBsAg-) phase	A group of patients exhibit loss of HBsAg, resulting in a greatly decreased risk of progression to cirrhosis and HCC. This is also called a "functional cure."

HBeAg: Hepatitis B Envelope Antigen; HBsAg: Hepatitis B surface antigen

Table 2. Clinical and Pathological Differences in Hepatitis B Phases

Phase	HBeAg+		HBeAg-		HBsAg-
	Chronic infection	Chronic hepatitis	Chronic infection	Chronic hepatitis	Occult infection
Hepatic Necroinflammation	-/+	++/+++	+	++/+++	+
Hepatic Fibrosis	none/minimal	variable	present	variable	variable
HBV DNA	++++	+++	++	+	+
ALT normal +++			normal	+	variable
HBsAg	+	+	+	+	-
HBeAg	+	+	-	-	-
Anti-HBeAg	-	-	+	+	+
Anti-HBsAg	-	-	-	-	+

dated guidelines with more permissive criteria to determine which patients are eligible for treatment. Regarding treatment options, the consensus is to recommend the use of a nucleoside analogue with high barrier to resistance, making entecavir (ETV), tenofovir alafenamide (TAF), and tenofovir disoproxil fumarate (TDF) first line oral therapies. Well-chosen patients may still consider pegylated interferon alpha, the only finite therapy for HBV, though efficacy is low.

One aspect of variation between published guidelines lies in the definitions of the phases of HBV infections. National associations vary in their limits for treatment of HBV DNA, vary in the definition of abnormal liver enzymes, and inconsistently include age and other factors as indications for treatment (Table 3). Some guidelines use additional standards in defining phases of infection, like quantitative HBsAg measurement. Finally, some publications do not define phases at all. For that reason, differentiating which patients should be treated instead of monitored closely is a special challenge.

Most of the guideline variation, however, stems from differences in treatment approaches for chronic infection. Earlier guidelines recommend a more conservative approach to treatment in HBeAg positive chronic infection (previously called the immune tolerant phase).[5, 6, 7, 8] Previous literature had suggested that in this phase of infection, patients, especially younger and healthier ones, did not mount a robust immune response to HBV and thus were not undergoing hepatic necroinflammation that eventually causes progression to HCC and cirrhosis. Additionally, patients in the HBeAg positive chronic infection phase could possibly undergo spontaneous seroconversion of HBsAg without any need for treatment, which is known to be associated with a favorable prognosis and can occur at rates as high as 40% over 25 years.[9] Available antiviral treatment has low efficacy in accelerating rates of HBsAg seroclearance in patients with HBeAg positive chronic infection, and there is a high rate of viral relapse once treatments are stopped, indicating necessity of long-term treatment.[10] To complicate factors, many studies that evaluate treatment and seroconversion rates contain inadequate sample sizes of patients with true HBeAg positive chronic infection, so accurate evidence is limited.[11] Additionally, since the presence of HbeAg is implicated in the development of fibrosis and HCC the loss of this antigen was thought to be associated with lower cancer risk.[12]

Newer research highlights the risks of a conservative approach. The development of fibrosis, previously thought to be mainly associated with HBeAg positive chronic hepatitis, is now being shown to be present in all stages.[13] The risk of fibrosis development increases with length of chronic infection and with age.[14] Emerging research shows that treatment of HBeAg positive chronic infection may delay the progression of fibrosis.[15] Integration of HBV into the host genome has been found to occur with viral replication, even in HBeAg negative infection. Viral suppression through pharmaceutical treatment can disrupt cycles of viral replication, resulting in decreased integration. Unsurprisingly given this newer data, recent outcomes research is showing that patients in HBeAg positive chronic infection and chronic hepatitis have comparable rates of mortality and HCC.[16] Inconsistent expert recommendations will lead to under treatment, while simple guidelines will help facilitate a decrease in morbidity from HBV.

Discussion

The goals for treatment of HBV are to promote seroclearance and decrease disease progression to HCC and

Table 3. Differences in definitions and treatment recommendations for chronic infection

Group	Year	HBeAg+ chronic infection definition	Populations in which HBeAg+ individuals should be treated	HBeAg- chronic infection definition	Populations in which HBeAg- individuals should be treated
AASLD [17]	2018	HBV DNA: Very high (typically > 1,000,000 IU/mL) Liver enzymes: Normal or minimally elevated ALT and/or AST* Histological findings: no fibrosis and minimal necroinflammation *ULN defined by AASLD to be ALT of 35 IU/L for male patients and 25 IU/L for female patients	HBV DNA: >20,000 IU/mL Liver Enzymes: ALT ≥2× ULN Histological findings: evidence of significant histologic disease	HBV DNA: Often normal Liver enzymes: Normal or elevated ALT and/or AST levels Histological findings: chronic hepatitis with variable necroinflammation and/or fibrosis	HBV DNA: ≥2,000 IU/mL Liver enzymes: ALT ≥ 2x ULN
CASLD [5]	2018	HBV DNA: often > 10,000,000 IU/mL Liver enzymes: ALT normal* Histological findings: normal *ULN defined as <30 IU/L for male patients and < 19 IU/L in female patients	None	HBV DNA: often <2,000 IU/mL, sometimes >2,000 IU/mL Histological findings: Normal or mildly abnormal non-invasive fibrosis assay	None
INASL [6]	2018	HBV DNA: >20,000 IU/mL Liver enzymes: ALT < 40 IU/L or 40-80 IU/L with minimal histological findings Histological findings: minimal inflammation and fibrosis	Age: >30 years Other considerations: Extrahepatic manifestations of HBV, family history of HCC or cirrhosis with HBV >2,000 IU/mL	HBV DNA: <2,000 IU/mL or 2,000 to 20,000 IU/mL with histological findings of minimal necroinflammation and fibrosis	None
BSH [8]	2020	Not defined	Age >30 years Other considerations: Family history of HCC or cirrhosis, extrahepatic manifestations of HBV	Not defined	None
JSH [18]	2020	HBV DNA: Not defined Liver enzymes: ALT within ULN* Histological findings: few abnormal findings *ULN defined by JSH as ≤30 IU/L	HBV DNA: ≥2,000 IU/mL AND Liver enzymes: ALT ≥ 31 U/L Other considerations: Clinical decompensation	HBV DNA: <2000 IU/mL Liver enzymes: Persistently normal ALT levels	None

Group	Year	HBeAg+ chronic infection definition	Populations in which HBeAg+ individuals should be treated	HBeAg- chronic infection definition	Populations in which HBeAg- individuals should be treated
CSH [19]	2021	HBV DNA: > 20,000,000 IU/mL Liver enzymes: ALT with persistent or recurrent increase from normal limits* Histological findings: Obvious necroinflammation, or fibrosis, or both Other considerations: HBsAg >10,000 IU/mL *ULN not defined by CSH	Histological findings: Liver biopsy with G ≥2, or S ≥2, or both Other considerations: Age > 30 years old and any of the following: -Family history of HBV-related cirrhosis or liver cancer -Histological findings of obvious liver inflammation or fibrosis in those with persistently normal ALT levels - HBV-related extrahepatic manifestations	HBV DNA: <2,000 IU/mL Liver enzymes: ALT within ULN* Histological findings: Liver biopsy with histological activity index score <4 Other considerations: HBsAg <1,000 IU/mL	Histological findings: Liver biopsy with G ≥2, or S ≥2, or both Other considerations: Age >30 years and any of the following: -Family history of HBV-related cirrhosis or liver cancer -Histological findings of obvious liver inflammation or fibrosis in those with persistently normal ALT levels - HBV-related extrahepatic manifestations
KASL [20]	2022	HBV DNA: Generally >10,000,000 IU/mL Liver enzymes: Persistently normal ALT* Histological findings: Minimal or absence of hepatic necroinflammation *ULN defined as ALT of 34 IU/L for male patients and 30 IU/L for female patients	HBV DNA: ≥20,000 IU/mL Other considerations: Clinical decompensation	HBV DNA: <2,000 IU/mL Liver enzymes: Persistently normal ALT Histological findings: Minimal or absence of hepatic necroinflammation	HBV DNA: ≥2,000 IU/mL Liver enzymes: ALT level ≥2x ULN Other considerations: Clinical decompensation
US Expert Opinion [21]	2022	HBV DNA: usually 10,000,000 IU/mL Liver enzymes: ALT <ULN* *ULN not defined by this Opinion	HBV DNA: >2,000 IU/mL AND elevated ALT Other considerations: HBV DNA>2,000 IU/mL and ALT within ULN* - consider risk factors for developing HCC, age, lifestyle, and desire to undergo treatment	Not defined	HBV DNA: >2,000 IU/mL AND elevated ALT Other considerations: HBV DNA>2,000 IU/mL and normal ALT - treat if fibrosis present

AASLD: American Association for the Study of Liver Diseases; CASLD: Canadian Association for Study of Liver Disease; INASL: Indian National Association for Study of the Liver; BSH: Brazilian Society of Hepatology; JSH: Japan Society of Hepatology; CSH: Chinese Society of Hepatology; KASL: Korean Association for the Study of the Liver; US: United States; ULN: Upper limit of normal; ALT: alanine transaminase

cirrhosis. Emerging research shows that the chronic infection phases are not benign; rather, chronic infection is implicated in the development of catastrophic complications of HCC and cirrhosis. Patients with cirrhosis and viral replication, especially in the HBeAg positive chronic infection phase, could benefit from treatment. Treatment is of utmost importance in patients with older age, family history of HCC and cirrhosis, and extrahepatic manifestations of HBV. However, more permissive therapy is challenging due to imperfect efficacy and the need for long term therapy, which could result in higher costs over time.

Guidelines for the management of chronic HBV published in the last five years are greatly varied. There are inconsistencies in definitions of HBV infection phases, patient populations indicated for treatment, and timing of treatment. There is also variation in defining the normal limit of ALT. Some recent guidelines recommend more permissive indications for HBV antiviral treatment initiation, using recent evidence that early HBV chronic infection can still contribute to morbidity and mortality. However, it is worth noting that guidelines formed by expert opinion are not as limited by the need for high quality data to support recommendations. Regional differences are also evident as more permissive guidelines are found in Asian countries that have higher rates of endemic HBV. However, the expert opinion recently published in Clinical Gastroenterology and Hepatology for treatment recommendations in the United States[22] has one of the most permissive guidelines,

recommending treatment in all patients with HBV DNA >2,000 IU/mL and elevated ALT, and in certain cases patients with elevated HBV DNA and normal ALT (see Table 3), though it does not clearly define the upper limit of normal ALT. The importance of standardizing guidelines continues to increase as national borders become more fluid. Standardization would also allow better characterization of treatment eligibility and success rates in individuals.

The quest for functional cure would not only help clarify populations at risk and the impact of antiviral therapy but will also continue to modify for whom and when treatment should be considered. Developments in pharmacologic agents that increase treatment efficacy and maintenance of seroconversion would favor greater adoption of more permissive treatment guidelines. Specific treatment regimens that can optimize the delay of progression to fibrosis should also be comparatively studied. Finally, studies that evaluate treatment regimens for hepatitis B would benefit from a robust population of patients with HBeAg positive chronic infection. Guidelines published in the last five years are becoming more and more permissive based on pharmacological and epidemiological developments. Updated guidelines would help translate recent research into practice.

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The Role of Endoscopy and Multidisciplinary Care in Patients Undergoing Living Donor Liver Transplantation: A Conversation with Dr. Dongki Lee, Vice-Chair of the WGO Endoscopy Committee

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In this issue of *e-WGN*, Dr. DongKi Lee discusses the status of living donor liver transplantation in South Korea, as well as the several attributes of multidisciplinary care that are required for successful and positive outcomes in this complex cohort of patients. Dr. Lee discusses the evolution of LDLT as well as contrasting the nuances of LDLT with the more traditional deceased donor liver transplantation paradigm.

More specifically, in this article Dr. Lee has discussed the role of ERCP and endoscopy in managing pre- and post-liver transplant patients who undergo LDLT. He emphasizes the algorithmic approach for management of pre- and post-transplant issues and suggests care pathways across interdisciplinary service lines depending on the clinical issue at hand. He also discusses a novel biliary stricture management approach using magnetic compression anastomosis (MCA) and his team's fairly significant experience using this technique at his institution.

I had the opportunity to discuss this review as well as Dr. Lee's own personal journey and professional involvement with the living donor liver transplantation program and his thoughts on the current state of liver transplantation in South Korea. We hope that the readers of *e-WGN* will find this Q&A format discussion helpful as an appendix to the main review article published in this issue.

Vivek Kaul (VK): Can you tell us about your career pathway and how you became involved with a multidisciplinary team taking care of liver transplant patients?

DongKi Kee (DL): After acquiring the Gastroenterology Board Certification 30 years ago, I devoted myself to treating pancreas and biliary disease. Interventional ERCP has developed as a significant specialty since when I first started.

After succeeding in the first magnetic compression anastomosis (MCA) case 16 years ago, I recognized that we could apply this treatment to total biliary occlusion after living donor liver transplantation (LDLT), and from then on, patients with unresolved biliary complications after LDLT were referred from other parts of the country to us. Recognizing that cooperative spirit between endoscopy, radiology and surgery is desperately needed to treat these patients, a multidisciplinary team has been developed here and is very active.

(VK): What clinical and administrative roles do you serve at your institution?

(DL): I am in charge of the pancreas and biliary disease section of the Department of Gastroenterology. Previously, I served at Gangnam Severance Hospital Cancer Center as Chair of the Department of Internal Medicine.

(VK): What are the most common indications for liver transplantation in South Korea?

(DL): The most common indications for liver transplantation in Korea are hepatocellular carcinoma (HCC), alcoholic decompensated liver cirrhosis, and HBV or HCV-induced decompensated liver cirrhosis.

(VK): Why is living donor liver transplantation more common than cadaveric liver transplantation in South Korea?

(DL): Due to cultural reasons, there are not many deceased donor-based liver gifts. The number of deceased donations is increasing in recent years because of continuous education and advisement. About 500 deceased donors contribute to the organ pool yearly, but many patients are waiting for liver transplantation. Therefore, approximately 1200-1300 LDLT cases

are performed annually in our country. In addition, close family relationships in Korea are such that offspring often donate their partial liver graft to their parents.

(VK): Are there any differences in the type of patients that proceed on the living donor transplant pathway compared to the cadaveric pathway in terms of indications or other clinical criteria in your country?

(DL): There is no difference in indications or other clinical criteria between LDLT and deceased donor liver transplantation (DDLT) in liver transplantation in Korea. When in need of liver transplantation, patients are asked whether they have a potential living liver donor, and if so, LDLT is an option. If they do not have a living donor available, then we consider DDLT.

(VK): Why are complications in living donor liver transplantations different and more unique than those seen in cadaveric transplantation?

(DL): Compared to DDLT, LDLT is more challenging to perform from a surgical surgical technique perspective and therefore has higher potential for surgical complications. LDLT causes more complications due to the smaller diameters of the bile duct, hepatic artery, and portal vein than DDLT. Mainly, the biliary complication occurs in 20-30% of LDLT patients due to poor blood supply of the bile duct.

In particular, in LDLT, duct-to-duct anastomosis between donor and recipient is located at the proximal level compared to DDLT, so the incidence of anastomotic site complications, including stricture and bile leak, is high. There is also the possibility of anastomotic stricture due to hypertrophy of the recipient liver after surgery.

(VK): Have you had any significant problems, failures or complications with the magnetic compression anastomosis approach?

(DL): Over the past 16 years, our institute has performed MCA on 120 patients with complete biliary obstruction after various HPB surgeries. To my knowledge, this is the largest single center experience globally for this procedure in a clinical setting. Almost all patients have been successful recently, except for a few cases at the beginning of the procedure. We built much know-how and tips to overcome the difficulties of the current system. Safety issues, as well as procedure success, are considered essential. The most challenging part of the procedure is securing the proper percutaneous tract for magnet delivery and effective per-oral magnet delivery up to the stricture site. Therefore, close cooperation between an expert endoscopist and the interventional radiologist is vital for this procedure. This team has been well established, and there has been no significant complication following the process so far.

(VK): What are the key and essential concepts and resources that are needed when an institution is contemplating setting up a living donor liver transplantation program?

(DL): The safety of living liver donors is paramount in the liver transplant program. The resources and infrastructure needed are similar to a similar sized DDLT program, but as stated above the close collaboration between radiology, surgery and GI endoscopist is very critical for the success of the program and good patient outcomes.

Message from the Co-Chairs

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We are pleased to provide you and your patients with resources to support the 2023 WDHD campaign *Your Digestive Health: A Healthy Gut From the Start*. These four sites give practical information for adults, children, patients, and providers about healthy diet and other healthy habits

Diet Guidelines for Adults and Children

This site from the Harvard T.H. Chan School of Public Health has a downloadable Healthy Living Guide for 2022/2023 with tips and strategies for healthy eating and healthy living. The Healthy Eating Plate for adults has been translated into over 25 languages. The Kid's Healthy Eating Plate has wonderful visuals and graphics. This is a very user-friendly format.

Healthy Eating for Children

This site emphasizes the important role of caregivers of children in learning healthy eating habits, such as three meals a day and one to three healthy snacks a day. The best foods are whole, fresh, and unprocessed. The site addresses sugar, juices and water, salt, fats, and gives advice for picky eaters and vegetarian diets and even what snacks are healthy.

Advice for Parents of Healthy-Weight Children

From the UK's National Health Service, this site gives advice for parents of healthy-weight children. Advice includes role modeling, physical activity, child size portions, and how to pack a healthy school lunch. There are links for information on how to help children lose weight and also how to gain weight.

Dietary Guidelines for Americans

The Dietary Guidelines for Americans (DGA) 2020-2025 is a PDF resource that can be downloaded and shared. It has been prepared by a scientific advisory committee and is evidence based. DGA is now working on the 2025-2030 version. This is a rigorous multi-year program and addresses every part of the life span: infants and toddlers, children and adolescents, adults, pregnant women, and older adults. Many resources are translated into Spanish. Their motto is "make every bite count."

WGO Salutes Women in Leadership in our Member Societies

Argentina
Dr. Maria Giovanna Porfilio Gularte
President; Federacion Argentina de Gastroenterologia

Argentina
Dr. Estela Veronica Parra Wirth
Secretary; Federacion Argentina de Gastroenterologia

Argentina
Dr. Josefina Sobrero
Secretary; Sociedad Argentina De Gastroenterologia (SAGE)

Azerbaijan
Dr. Gulnara Aghayeva
President; Azerbaijan Gastroenterologists and Hepatologists Society

Azerbaijan
Dr. Sevda Aghayeva
Secretariat; Azerbaijan Gastroenterologists and Hepatologists Society

Belarus
Dr. Julia Gorgun
Secretary; Byelorussian Gastroenterology Association

Belgium
Dr. Isabelle Colle
President; Vlaamse Vereniging Voor Gastroenterolgie

Bosnia
Dr. Renata Tamburic
Secretary; Association of Gastroenterologists & Hepatologists of Bosnia & Herzegovina

Canada
Dr. Laura Sly
Secretary; Canadian Association of Gastroenterology

Chile
Dr. Claudia Defilippi
President; Sociedad Chilena de Gastroenterología

Chile
Dr. Pamela Yaquich
Secretary; Sociedad Chilena de Gastroenterología

Colombia
Dr. Viviana Parra Izquierdo
Secretary; Asociación Colombiana de Gastroenterologia

Cote d'Ivoire
Dr. Therèse Ndri Yoman
President; Société Ivoirienne de Gastro-entérologie et D´endoscopie Digestive (SIGEED)

Cote d'Ivoire
Dr. Marie Jeanne Lohoues-Kouacou
Secretary; Société Ivoirienne de Gastro-entérologie et D´endoscopie Digestive (SIGEED)

Cuba
Dr. Mirtha Infante Velazquez
President; Sociedad Cubana de Gastroenterologia

Czech Republic
Dr. Martina Pfeiferova
Secretariat; Czech Society of Gastroenterology

Democratic Republic Congo
Dr. Jacqueline Nkondi Nsenga
Secretary General; Congolese Association of Gastroenterology, D.R. Congo

Democratic Republic
Dr. Claralí Almonte Núñez
Vice President; Sociedad Dominicana de Gastroenterologí

Democratic Republic
Dr. Yirania Rodríguez
Secretary General; Sociedad Dominicana de Gastroenterología

Estonia
Dr. Riina Salupere
President; Estonian Society of Gastroenterology

Finland
Dr. Tuire Ilus
Secretary General; Finnish Society of Gastroenterology

Ghana
Dr. Mary Afihene
President; Ghana Association for the Study of Liver and Digestive Diseases

Guatemala
Dr. Regina Liggoria
Vice President; Asoc. Guatemalteca de Gastroenterología, Hepatología Y Endoscopía Gastrointestinal

Iceland
Dr. Sunna Gudlaugsdottir,
President; The Icelandic Gastroenterology Society

Iraq
Dr. Nawal Mehdi Firhan Alkhalidi
Vice President; Iraqi Society of Gastroenterology

Italy
Dr. Patrizia Burra
Secretary General; Società Italiana Di Gastroenterologia Ed Endoscopia Digestiva

Lithuania
Dr. Ilona Savlan
Secretary General; Lithuanian Society of Gastroenterology

Montenegro
Dr. Brigita Smolovic
President; Gastroenterohepatology Association of Montenegro (GAM)

Netherlands
Dr. W.M.U. van Grevenstein
Vice President; Nederlandse Vereniging Voor Gastro-enterologie

Nicaragua
Dr. Martha Josefa Sequeira Suarez
Secretary; Sociedad Nicaragüense Gastroenterología Y Endoscopia Digestiva (SONIGED)

Ireland
Dr. Deirdre McNamara
President; Irish Society of Gastroenterology

Lithuania
Dr. Goda Sadauskaite
President; Lithuanian Society of Gastroenterology

Mali
Dr. Sanra Déborah SANOGO ep. SIDIBE
Secretary General; Societe Malienne Des Maladies de L'Appareil Digestif (SOMMAD)

Netherlands
Dr. Janneke Van Der Woude
President; Nederlandse Vereniging Voor Gastro-enterologie

New Zealand
Dr. Catherine Stedman
President; New Zealand Society of Gastroenterology Inc.

North Macedonia
Dr. Dafina Nikolova
Secretariat; Macedonian Society of Gastroenterohepatology

Norway
Dr. Mette Nåmdal Vesterhus
President; Norwegian Gastroenterological Association

Paraguay
Dr. Carolina Miranda
Vice President; Sociedad Paraguaya De Gastroenterología

Peru
Dr. Cecilia Cabrera Cabrejos
Vice President; Sociedad de Gastroenterología del Perú

Poland
Dr. Grażyna Rydzewska
Vice President
Polish Society of Gastroenterology

Portugal
Dr. Marilia Cravo
Vice President; Sociedade Portuguesa de Gastrenterología

Puerto Rico
Dr. Karma Amral
Secretary; Asociación Puertorriqueña de Gastroenterología

Romania
Dr. Mariana Jinga
Secretariat; Romanian Society of Gastroenterology & Hepatology

Serbia
Dr. Aleksandra Pavlovic-Markovic
President; Association of Serbian Gastroenterologists

Serbia
Dr. Milica Stojkovic Lalosevic
Secretary General; Association of Serbian Gastroenterologists

South Africa
Dr. Gill Watermeyer
President; South African Gastroenterological Society

Spain
Dr. Maria Pellisé Urquiz
President; Asociacion Espanola de Gastroenterologia (AEG)

Spain
Dr. Miriam Mañosa Ciria
Secretary; Asociacion Espanola de Gastroenterologia (AEG)

Spain
Dr. Inmaculada Fernández
Vice President; Sociedad Espanola De Patologia Digestiva (SEPD)

Spain
Dr. Carolina Malagelada
Secretary General; Sociedad Espanola De Patologia Digestiva (SEPD)

Sri Lanka
Dr. Jayani Manchanayake
President; Sri Lanka Society of Gastroenterology

Sweden
Dr. Annika Bergquist
Chairman; Swedish Society for Gastroenterology

Tunisia
Dr. Monia Fekih
President; Tunisian Society of Gastroenterology

United Kingdom
Dr. Helen Steed
Secretary; British Society of Gastroenterology

United States of America
Dr. Amy S. Oxentenko
Vice President; American College of Gastroenterology

United States of America
Dr. Barbra Jung
President; American Gastroenterological Association

Uruguay
Dr. Yessica Pontet
Secretary; Sociedad de Gastroenterología Del Uruguay

Venezuela
Dr. María Luisa Clavo
Vice President; Sociedad Venezolana de Gastroenterología

Yemen
Dr. Jameela Al Rabeei
Secretary; Yemen Gastroenterological Association

Zambia
Dr. Violet Kayamba
President; Zambia Association for Gastroenterology & Nutrition (ZAGAN)

Introducing WGO's New Brasília Training Center!

Liliana Sampaio Costa Mendes, MD, PhD

Hepatologista da rede D'or DF, do Hospital de Base do DF
Biocardios e Hospital Sirio-Libanês DF
Brasília, Brazil

We are very happy to be part of the World Gastroenterology Organisation (WGO). The inauguration of the Brasília WGO Training Center for gastroenterology, digestive endoscopy and hepatology was held 15 July, in the capital of Brazil, in a private hospital complex of Rede D'or São Luiz in Brasília.

Applying teaching methodologies properly to improve comprehension has always been a challenge. Sounds, tones and colors used at the right time activate neuronal connections and stimulate learning. Continuing medical education is a necessary tool to bring uniformity of conduct and opportunity to align with the best practices in each region. WGO goes further, seeking to bring the best medical training to the most remote areas of the planet. Their mission is to educate others on best teaching practices and help improve the world of digestive health. WGO's efforts have touched and moved us as a society. It was for these reasons that we wanted to be a part of their global mission.

At the inauguration ceremony we received the honorable presence of Professor Guilherme Macedo, president of WGO, and Professor Susana Lopes, Co-Director of the WGO Training Center in Porto, Portugal. The day after the inauguration, we provided dynamic teaching stations with instructors from the Brasília Training Center in endoscopic procedures, paracentesis and an artificial intelligence station, the station of the future.

The opening ceremony was attended by residents and preceptors of medical residency in gastroenterology, digestive endoscopy and hepatology from all three hospitals linked to medical residency in Brasília. Physicians playing an important role in the formation of gastroenterology in the Federal District and in Brazil were also present.

Brazil is a country with more than 203 million inhabitants and is divided into five regions. There are an estimated 2.81 gastroenterologists per 100,000 inhabitants, with a total of 5.997 specialists, with heterogeneous performance scenarios. The Southeast region has 49.2% of specialists and the Central-West region has 8.6% of gastroenterologists. The other Northeast, South and North regions have respectively 21%, 18.1% and 3.1% of specialists.

The Brazilian Federation of Gastroenterology (FBG) is going through a unique moment, with strategic planning linked to Fundação Dom Cabral. Taking the best medical education to the interior areas of the states is one of the priority strategic goals. Receiving support from the FBG at this time is fundamental. In our center, the same teams of gastroenterology, hepatology, and digestive endoscopy work in all four hospitals: DF Star, Hospital Santa Helena, Hospital Santa Luzia and Hospital do Coração.

We manage to perform all the most complex procedures in hepatology, gastroenterology and digestive endoscopy and build multidisciplinary events with interface specialties such as oncology, radio intervention and intensive care in our schedule.

Great projects are never individual projects but bring together several people and institutions surrounding a common goal. We are all stronger together and this training center is to you, for you and for all of us.

World Hepatitis Day (WHD)

World Hepatitis Day (WHD) is celebrated every year on July 28. It is celebrated on the birthday of Dr. Baruch Blumberg who discovered the hepatitis B virus in 1967 and two years later developed the first hepatitis B vaccine. WHD serves as reminder that despite incredible progression in diagnostics and therapeutics, viral hepatitis continues to drive morbidity and mortality around the globe. Yet elimination of viral hepatitis is possible with united efforts. Although many locations remain behind the World Health Organization (WHO) defined targets for elimination, there are several laudable efforts including those in resource-limited settings.

In recognition of WHD, the WGO Hepatology Committee is highlighting these incredible efforts.

Nancy Reau, MD
Chair, WGO Hepatology Committee

Elimination Goals in the Pacific Islands: A Consortium of Pacific Island Physicians Takes the Lead

Alice Lee, MD

Gastroenterologist and Hepatologist
Concord Repatriation General Hospital, University of Sydney
Director, Hepatitis B Free
Sydney, Australia

Thomas Russell, MBBS

PG Dip. Internal Medicine
Specialist Physician
Tungaru Cental Hospital
Tarawa, Kiribati

The Pacific region is broadly classified into three ethnogeographic groupings of Melanesia, Micronesia, and Polynesia. This region is comprised of 22 Pacific Island countries and territories (PICTs), and is home to over 12.7 million people.[1] The region spans over 800,000 square kilometers of land mass with an ocean expanse that is equivalent to 15% of the earth's surface.[2] PICTs vary in land size, geography, and population from the relatively small Pitcairn islands (population 50) to the larger volcanic islands of Papua New Guinea (population 9.3 million), Fiji (population 901,603), and Solomon Islands (population 744,407).[1] In order of decreasing population size, Vanuatu, French Polynesia, New Caledonia, Samoa, Guam, Kiribati, the Federated States of Micronesia, Tonga, American Samoa, Northern Marianas, Marshall Islands, Palau, Cook Islands, Nauru, Wallis and Futuna, Tuvalu, Niue, and Tokelau round up and complete the group.

All are classified as low to middle income and face similar challenges in health care delivery. Funding support for health systems is sought offshore through donor partners and non-government organizations to meet the essential service requirements. The addition of new health programs generally requires close scrutinization and rationalization. Some of the highest prevalence rates of hepatitis B are seen in PICTs with variation within the region. In response to the elimina-

tion goals, and with the support of increased awareness (World Hepatitis Day), advocacy for hepatitis B needs have been met with great success in some of the islands. Hepatitis B treatment guidelines have been endorsed, tenofovir added to the essential medicines list, patients screened and treated in Kiribati, Vanuatu, Solomon Islands, Tonga, and Papua New Guinea. Despite the interruption from COVID pandemic, the programs have persisted and are now being reinvigorated. Challenges in introducing such programs have been met with a resolve from the local team to find locally appropriate solutions to ensure optimal care whilst considering inclusivity (with a test and treat approach where needed) and funding/resource restrictions. Niue has completed an entire country screening for hepatitis B and C, and all the eight identified hepatitis B patients have been linked to care.[3] Kiribati has screened over 20,000 patients including screening in the remote outer islands with rates of 15% consistently seen.[4] Further high rates of co-infection with hepatitis D have not been addressed.[5] Papa New Guinea is now ready to start the third site for treatment roll out (prevalence of 15% or more are also reported).

Treatment guidelines have been contextualized for locally available resources, models of care delivery have been established (including testing and treatment for patients in areas of high prevalence whereby they are counselled and offered treatment based on a positive HBsAg only) and healthcare worker training rolled out. Monitoring and evaluation has been a challenge with significant limitations identified. Program support through telehealth has ensured that local teams are well supported.

Small numbers of patients, limited resources, small orders for supplies including drugs and health care personnel have meant that a collaborative Pacific wide approach is being explored to improve efficiency and outcomes. Pooled procurement, training, sharing experiences, and learning from the challenges will be recorded as part of implementation research. A consortium of local physicians will implement prevention of mother to child transmission (PMTCT) program in a systematic manner throughout the countries where tenofovir is available.

As we celebrate another World Hepatitis Day, we look forward to welcoming the Pacific group and partnering with them towards the common goal of elimination. This will only be possible with the support of the global community.

1. The Pacific Community (SPC). *Pacific Community Results Report 2021.* 2022. (Accessed online 19 July 2023). https://www.spc.int/about-us
2. The World Bank. *The World Bank in Pacific Islands. 2023.* (Accessed online 19 July 2023). https://www.worldbank.org/en/country/pacificislands/overview
3. World Health Organization (WHO). *Harnessing the Covid-19 pandemic to eliminate viral hepatitis in Niue.* 2023. (Accessed online 19 July 2023). https://www.who.int/niue/news/feature-stories/detail/harnessing-the-covid-19-pandemic-to-eliminate-viral-hepatitis-in-niue
4. National Hepatitis Program. *Hepatitis program Zero Survey outreach report 2018 – 2022.* 2023. Ministry of Health & Medical Services (MHMS), Kiribati.
5. Jackson K, Tekoaua R, Holgate T, Edwards R, Yuen L, Lee A, Nicholson S, Littlejohn M, Locarnini S, Tuneti K. *Hepatitis B and D in the Pacific Islands of Kiribati*. J Clin Virol. 2020 Aug; 129:104527. doi: 10.1016/j.jcv.2020.104527. Epub 2020 Jun 29. PMID: 32645613.

A Successful Midwest Metabolic Clinical Symposium

Dr. Jacobs, the Dean of the School of Medicine at Saint Louis University, opened the Symposium.

Dr. Brent Tetri, Professor of Internal Medicine for the Division of Gastroenterology and Hepatology at Saint Louis University.

The first annual Midwest Metabolic Clinical Symposium was organized and chaired by Dr. Wing-KinSyn, the GI Division Director at Saint Louis University. The sessions at the symposium focused on current and emerging best practices for the management of obesity, diabetes, non-alcoholic fatty liver disease, and cardiovascular disease. More specifically, these sessions highlighted the rising incidence and prevalence of obesity and T2DM, the parallel increase in prevalence of NAFLD (up to 40% of the US population affected), as well as introducing current and new treatment strategies to address these multiple overlapping disorders (with common pathogenic mechanisms). These conditions are seen by all physicians and are often not captured or under-diagnosed. Our aim is to bring attention to these common disorders and the need for early identification of those at highest risk.

This was a state-of-the-art international meeting, with 120 registrants with many coming from outside our state of Missouri. Attendees came from California, Connecticut, Illinois, Louisiana, Michigan, Minnesota, New Jersey, New York, Ohio, and South Carolina as well as from the United Kingdom, Austria, and Germany. They represent professionals from various backgrounds including MDs (General Internal Medicine, GI, Hepatology, Endocrine, Geriatrics, Renal, Hematology, Primary Care, Cardiology, Critical Care, Psychiatry), RNs, APPs, Psychologists, PharmDs, as well as students in training and some industry representatives.

The Metabolic Symposium was well received, and attendees gained new knowledge with many state-of-the-art presentations. Planning for next year's symposium is already in the works! Our GI Division Administrative Team, who helped organize the successful inaugural event, is below.

Dr. Ali Canbay, President of the German Association for the Study of the Liver (GASL), was one of the invited speakers.

From left to right: Donna Crowder (Administrative Assistant), Dzana Turan (Liver Center and GI Division Research Manager, Myron Minner (Business Manager), Laura Robinson (Residency Program Specialist), LaDonna Willis (Administrative Assistant), Dr. Wing-Kin Syn (GI Division Director)

Indonesian Digestive Disease Week (IDDW) 2023 Report

Dadang Makmun, MD, PhD, FACG

President, Indonesian Society of Gastroenterology (ISG)
Head Department of Internal Medicine, Faculty of Medicine Universitas Indonesia, Cipto Mangunkusumo National General Hospital
Jakarta, Indonesia

The Indonesian Society of Gastroenterology (ISG) in collaboration with the Indonesian Society for Digestive Endoscopy (ISDE) and Division of Gastroenterology, Pancreatobiliary and Digestive Endoscopy, Department of Internal Medicine, Faculty of Medicine Universitas Indonesia/ Cipto Mangunkusumo National General Hospital Jakarta, has once again successfully organized "Indonesian Digestive Disease Week (IDDW) 2023" from 16-20 May 2023.

Due to the increasing challenges posed by gastrointestinal diseases in Indonesia, as well as the advancements in new tools and techniques in digestive endoscopy, we have specifically arranged this event as a platform to exchange the latest knowledge and skills in the field of gastroenterology and digestive endoscopy.

The scientific agendas comprised in IDDW 2023 included "Hands on Endoscopy Workshop" that was held on the first two days (16 - 17 May 2023) at Auditorium of IMERI Building, Faculty of Medicine, Universitas Indonesia, Jakarta, followed by the IDDW 2023 Symposium. The

Hands-on Endoscopy Workshop was divided into four sessions covering the topics of EUS, ERCP, Intragastric Balloon Placement, PEG, and Cold Snare Polypectomy.

All sessions were presented by facilitators/faculties who are competent in the field of Digestive Endoscopy, including; Prof. Roy M Soetikno, MD, MS, MSM (USA), Prof. Thawee Ratanachu-ek, MD, PhD (Thailand), Prof. Mark Anthony de Lusong, MD (Philippines), and Prof. Kanokpoj Chanpiwat, MD (Thailand). There were many national faculties as well including; Prof. Dadang Makmun,

MD, PhD, FACG, Prof. Marcellus Simadibrata, MD, PhD, FACG, FASGE, Prof. Murdani Abdullah, MD, PhD, FACG, FASGE, Prof. Ari Fahrial Syam, MD, PhD, MMB, FACP, FACG, Achmad Fauzi, MD, Kaka Renaldi, MD, Hasan Maulahela, MD, Amanda Pitarini Utari, MD, Saskia Aziza Nursyirwan, MD. Each faculty member shared their valuable experiences to improve knowledge and skills of all participants in the field of digestive endoscopy.

The IDDW 2023 Symposium was held on 18 – 20 May 2023 in Hotel Shangri-la, Jakarta. There were three plenary lectures, six symposiums, 18 satellite symposiums, and a poster session that aimed to provide the latest information and knowledge in the field of gastroenterology and digestive endoscopy.

All sessions were delivered by remarkable international faculties, including; Prof. Raja Affendi Raja Ali, MB BCh, MMed.Sc,MRCPI, MD, FRCP, AM (Malaysia), Prof. Nonthalee Pausawasdi, MD (Thailand), Prof. Christopher Khor, MD, MBBS, FRCP, FAMS, FASGE (Singapore), Prof. Eiji Umegaki, MD, PhD (Japan), Prof. Jong H Moon, MD, PhD, FASGE, FJGES (Korea), Prof. Pradermchai Kongkam, MD, PhD (Thailand), Prof. Sutep Gonlachanvit, MD, PhD (Thailand), Prof. Sundeep Lakhtakia, MD, MNAMS, DM, FASGE (India), Prof. Mohan Ramchandani, MD, DM (India), and also experts from Indonesia. Throughout the event, we were pleased to welcome over 700 participants.

Looking ahead, the Indonesian Society of Gastroenterology (ISG) will be hosting the "Asian Pacific Digestive Week (APDW) 2024" in Bali, Indonesia. We eagerly anticipate another successful meeting and extend a warm invitation to participants from all Asian-Pacific countries and worldwide.

Newly Updated Probiotics and Prebiotics Published in Mandarin and Portuguese

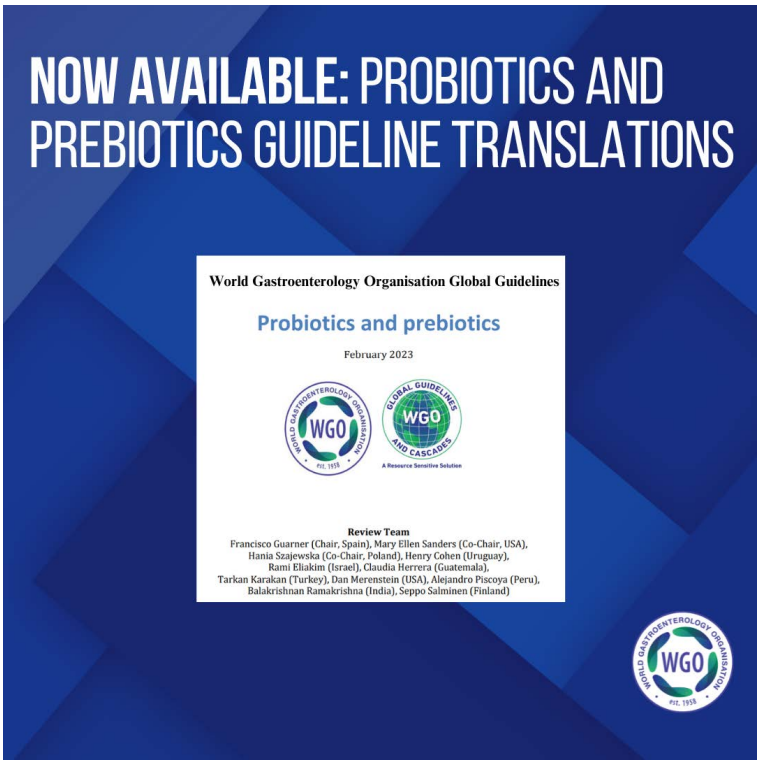
WGO is pleased to announce that the updated Probiotics and Prebiotics Guideline is now available in Mandarin and Portuguese language translations under the titles "益生菌和益生元" and "Probióticos e Prebióticos." These are in addition to the English and Spanish versions made available earlier in the year. The updated WGO Probiotics and Prebiotics Guideline will also soon be available in French and Russian. It can be viewed at https://www.worldgastroenterology.org/guidelines/probiotics-and-prebiotics.

This guideline is chaired by Dr. Francisco Guarner (Spain) and co-chaired by Dr. Mary Ellen Sanders (USA) and Dr. Hania Szajewska (Poland). The guideline was created through the global view of many Guideline Review Team experts including Profs. Alejandro Piscoya (Peru), Henry Cohen (Uruguay), Rami Eliakim (Israel), Claudia Herrera (Guatemala), Tarkan Karakan (Turkey), Dan Merenstein (USA), Balakrishnan Ramakrishna (India) and Seppo Salminen (Finland). This updated version revises one that dated to 2017.

Probiotics are live microorganisms that, when administered in adequate amounts, confer a health benefit on the host. Lactobacilli, along with species of *Bifidobacterium*, have historically been common probiotics. In 2020, the genus *Lactobacillus* underwent a major restructuring to address the wide diversity of microbes assigned to this genus. 23 new genera have been defined, including some with well-studied probiotic species.

The prebiotic concept is a more recent concept than probiotics. First proposed by Gibson and Roberfroid in 1995, the key aspects of a prebiotic are that it is nondigestible by the host and that it leads to health benefits for the consumer through positive influence on the resident beneficial microbes.

The administration and use of prebiotics or probiotics is intended to influence the gut environment, which is inhabited by trillions of microbes, for the benefit of human health. Both probiotics and prebiotics have shown to have beneficial effects that extend beyond the gut, but this WGO Guideline focuses on gut effects.



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/meetings-and-events-calendar

WGO RELATED EVENTS

Women in GI: Women in Leadership Webinar
When: September 21, 2023
Location: Online webinar
Organizer: WGO
Website: https://www.worldgastroenterology.org/education-and-training/webinars/women-in-g

CALENDAR OF EVENTS

Annual Meeting SGG-SGVC-SASL and SVEP 2023
When: September 14, 2023 - September 15, 2023
Location: CongressCentre Kursaal
Address: Interlaken, Switzerland
Organizer: Swiss Society of Gastroenterology
Website: www.sgg-sgvc-congress.ch

EUS ENDO International Live Course 2023
When: September 28, 2023 - September 30, 2023
Location: Marseille
Country: France
Organizer: Dr. Marc Giovannini, Course Director
Website: https://eus-endo.org/

Semana Panamericana de las Enfermedades Digestivas 2023
When: October 8, 2023 - October 11, 2023
Location: Santiago
Country: Chile
Organizers: Organización Panamericana de Gastroenterología and Sociedad Interamerican de Endoscopia Digestiva
Website: https://www.opge.org/sitio/

UEG Week 2023
When: October 14, 2023 - October 17, 2023
Location: Bella Center
Address: Copenhagen, Denmark
Organizer: United European Gastroenterology
Website: https://ueg.eu/week

ACG 2023 Annual Scientific Meeting & Postgraduate Course
When: October 20, 2023 - October 25, 2023
Location: Vancouver Convention Centre
Address: Vancouver, British Columbia, Canada
Organizer: American College of Gastroenterology
Website: http://www.gi.org

CONGRESO ACADI
When: November 2, 2023 - November 4, 2023
Location: Medellin
Country: Colombia
Organizer: Asociación Colombiana de Gastroenterología
Website: http://www.gastrocol.com

JDDW 2023 - Japan Digestive Disease Week 2023
When: November 2, 2023 - November 5, 2023
Location: Kobe, Japan
Organizer: Organization of JDDW
Website: https://www.jddw.jp/jddw2023/en/index.html

The Liver Meeting 2023
When: November 10, 2023 - November 14, 2023
Location: Hynes Convention Center
Address: Boston, Massachusetts, USA
Organizer: AASLD
Website: https://www.aasld.org/the-liver-meeting

KDDW 2023
When: November 16, 2023 - November 18, 2023
Location: Seoul
Country: Korea
Organizer: The Korean Society of Gastroenterology
Email: kddw2023@medioffice.or.kr
Website: www.kddw.org

Semana Nacional de Gastroenterologia 2023
When: November 17, 2023 - November 21, 2023
Location: Cancun
Country: Mexico
Organizer: Asociación Mexicana de Gastroenterología
Website: https://www.gastro.org.mx/

43rd Panhellenic Gastroenterology Congress
When: November 23, 2023 - November 26, 2023
Location: Thessaloniki
Country: Greece
Organizer: Hellenic Society of Gastroenterology
Website: www.hsgcongress2023.gr

HSI World Series Webinar on Stomach Health and Disease - Americas

When: November 30, 2023
Location: Online webinar
Country: Americas
Organizer: Healthy Stomach Initiative (HSI)
Website: https://us02web.zoom.us/webinar/register/WN_ginmtBOKSY-CEufHpsHAL-g
WGO-Endorsed Event

Lebanese Society of Gastroenterology Annual Meeting 2023

When: December 1, 2023 - December 2, 2023
Location: Phoenicia Hotel
Country: Lebanon
Organizer: The Lebanese Society of Gastroenterology
Website: www.lsge.org

APDW 2023

When: December 6, 2023 - December 9, 2023
Location: Bangkok
Country: Thailand
Organizer: Asian Pacific Digestive Week
Website: https://www.apdwcongress.org/

Annual Scientific Meeting 2023

When: December 6, 2023 - December 8, 2023
Location: Rotorua
Country: New Zealand
Organizer: New Zealand Society of Gastroenterology
Website: https://www.gastroconference.co.nz/

Egypt Gastro Hep 2023

When: December 7, 2023 - December 9, 2023
Country: Egypt
Email: training@roeyaegypt.com
Website: roeyaegypt.com

64th Annual Meeting of Indian Society of Gastroenterology (ISGCON) to be held at Bengaluru

When: December 21, 2023 – December 24, 2023
Location: Bengaluru
Country: India
Organizer: Indian Society of Gastroenterology (ISG)
Website: http://www.isg.org.in/

Annual Meeting of the Norwegian Gastroenterology Association 2024

When: February 8, 2024 - February 10, 2024
Location: Lilliehammer
Country: Norway
Organizer: Norwegian Gastroenterology Association
Website: http://legeforeningen.no/fagmed/norsk-gastroenterologisk-forening/

APASL 2024

When: March 27, 2024 - March 31, 2024
Location: ICC Kyoto
Address: Kyoto, Japan
Organizer: Asian Pacific Association for the Study of the Liver
Website: www.apasl2024kyoto.org

DDW 2024

When: May 18, 2024 - May 21, 2024
Location: Washington, DC
Country: United States
Organizers: AASLD, AGA, ASGE and SSAT
Website: https://ddw.org/attendee-planning/ddw-2024/

EASL Congress 2024

When: June 5, 2024 - June 8, 2024
Location: Milan
Country: Italy
Organizer: EASL
Website: https://easl.eu/event/easl-congress-2024/

JDDW 2024 - Japan Digestive Disease Week 2024

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

WGO Member Societies Submit Your Event

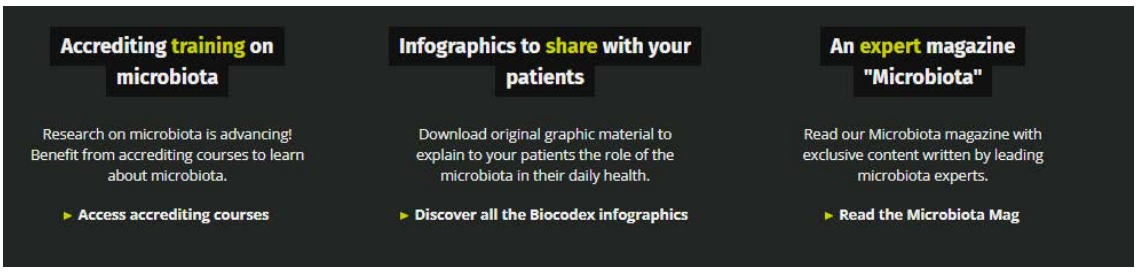
Are you a WGO Member Society wanting to share your event with WGO readers? Visit https://www.worldgastroenterology.org/forms/submit-event.php to submit your event for publication in WGO's website conference calendar as well as the quarterly *e-WGN* calendar of events!

www.biocodexmicrobiotainstitute.com/pro:
an international hub of knowledge dedicated to microbiota!

Biocodex Microbiota Institute is an international scientific institution that aims to foster health through spreading knowledge about the human microbiota. To do so, the Institute addresses both healthcare professionals and the general public to raise their awareness about the central role of this still little-known organ of the body.

It is designed to provide you with reliable, updated, and adapted content. It is also designed to reflect the dynamism and innovation of the human microbiota.

Available in 7 languages (English, French, Spanish, Russian, Polish, Turkish, and Portuguese), this online international hub provides Healthcare Professional with the latest scientific news and data about microbiota including the Institute's exclusive content such as Microbiota magazine, thematic folders, continuing medical education (CME) courses and interviews with experts. Check them out!



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