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Inborn errors of metabolism (IEMs) are usually recognized by characteristic neurologic and metabolic manifestations and sometimes by dysmorphism. However, IEMs can present with a wide variety of gastrointestinal manifestations, whether as the primary or a minor clinical symptom. Regardless, gastrointestinal and hepatic manifestations of IEMs are important clinical features that can help identify an underlying defect; these disorders should be taken into consideration as part of a patient's clinical assessment. It is prudent to include metabolic disorders in the differential diagnosis because in some cases, gastrointestinal symptoms may be the only presenting feature in a patient with an underlying IEM.

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This article presents the most common gastrointestinal, hepatic, and pancreatic manifestations of the primary immunodeficiency diseases, including the appropriate laboratory testing, endoscopic evaluation, and recommendations for further management.

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The gut microbiome is fundamental to human health and development. Altered microbiomes have been associated with many diseases. However, variation between individuals, environmental effects, and a lack of standardization across studies makes differentiation between health and disease challenging. Large-scale population cohorts in different countries will be required to match disease subjects with healthy controls, whereas standardized, reproducible pipelines for analysis are required to compare findings between studies. Despite this, several conditions have already demonstrated great promise for developing microbiome-based biomarkers as well as providing a gateway into integrated personalized medicine.

Effective Use of the Laboratory in the Management of Patients with Inflammatory Bowel Diseases

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M. Nedim Ince and David E. Elliott

Inflammatory bowel disease (IBD) comprises a group of chronic, intestinal inflammatory disorders, including ulcerative colitis and Crohn's disease. IBD is characterized by periods of relapse and remission. Long-term progressive intestinal inflammation can result in severe and devastating complications, such as intestinal strictures and/or fistulae. Immune suppressive medications with potent side effects are often used to control inflammation and limit disease activity. Laboratory tests guide various decisions in clinical management of IBD. We discuss tests used to diagnose IBD, assess for relapse or remission, monitor the effectiveness of therapeutic regimen, screen for the maintenance of health, and diagnose or prevent complications.

Laboratory Diagnosis and Monitoring of Viral Hepatitis

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Kunatum Prasadthathsint and Jack T. Stapleton

Many microbes, toxins, autoimmune diseases, and neoplastic diseases may cause liver inflammation; however, 5 viruses whose main pathogenesis is liver disease are referred to as hepatitis A, B, C, D, and E viruses. These viruses cause a significant burden of global illness. With the exception of hepatitis A virus, all may cause chronic infection potentially leading to cirrhosis and hepatocellular carcinoma. Excellent serologic and nucleic acid detection methods are available for determining the precise cause and, in some cases, the duration of infection. Diagnostics are critical for identifying individuals needing treatment and for monitoring the treatment success.

Liver Fibrosis Determination

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Michelle Lai and Nezam H. Afdhal

All chronic liver disease can lead to liver fibrosis. Assessment of the severity of liver fibrosis is central to making treatment and management decisions. Liver biopsy, the gold standard for liver fibrosis assessment, is invasive and carries risks of complications and sampling errors. The use of noninvasive elastography-based radiologic methods of liver fibrosis determination is limited to centers that have the capabilities. Laboratory liver fibrosis determinations, both general clinical scoring systems and combination biomarker panels, are accessible to a wider population of clinicians for identifying patients at low risk of advanced fibrosis who do not need liver biopsies.

IgG4-Related Disease with Emphasis on Its Gastrointestinal Manifestation

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Bijal Vashi and Arezou Khosroshahi

IgG4-related disease is an immune-mediated fibroinflammatory condition with a diverse spectrum of organ involvement, commonly in the pancreas and bile ducts among other organs such as salivary and lacrimal glands. Classic histopathologic findings are the gold standard for confirmation of diagnosis, although diagnosis remains challenging, as biomarkers to date are neither sufficient nor necessary. Glucocorticoids are the most

effective initial treatment, generally having a dramatic response, although limited clinical evidence exists regarding effective maintenance therapy. This review summarizes key GI manifestations of this condition for the practicing gastroenterologist and addresses the pathology, disease mechanism, and current therapeutic recommendations.

Serologic Diagnosis of Celiac Disease: New Biomarkers

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Aaron Lerner, Ajay Ramesh, and Torsten Matthias

Most patients affected by celiac disease (CD) are asymptomatic or hyposymptomatic and undiagnosed, and are at risk of preventable complications. Therefore, early diagnosis is highly recommended. Multiple diagnostic antibodies are available; the most frequently used is IgA to tissue transglutaminase (IgA-tTg). It may yield false results and, alone, does not address IgA deficiency. Recently, a new generation of anti-neo-epitope tTg check (IgG + IgA) has become available. It is highly sensitive and specific, covers IgA-deficient patients with CD, reflects intestinal damage, and has predictive potential in the diagnosis of CD.

Next Generation of Adeno-Associated Virus Vectors for Gene Therapy for Human Liver Diseases

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Kenneth I. Berns and Arun Srivastava

Recombinant vectors based on a nonpathogenic parvovirus, the adeno-associated virus (AAV), have taken center stage in the past decade. The safety of AAV vectors in clinical trials and clinical efficacy in several human diseases are now well documented. Despite these achievements, it is increasingly clear that the full potential of AAV vectors composed of the naturally occurring capsids is unlikely to be realized. This article describes advances that have been made and challenges that remain in the optimal use of AAV vectors in human gene therapy applications.