In this issue:

> Acute severe autoimmune hepatitis: steroids or transplant?
> EASL guidelines: drug-induced liver injury
> ECCO review: complementary medicine and psychotherapy in IBD
> Australian guidelines for prevention and control of infection
> TGA – new or extended indications
> TGA – newbiosimilar medicines
> Changes to PPI restriction level
> FDA approves first device for IBS pain in adolescents
> Management of autoimmune pancreatitis
> Bowel cleansing after suboptimal bowel preparation
> Epidemiology of colorectal cancer in average risk young adults
> Portal vein thrombosis in patients with/without cirrhosis
> Conferences, workshops and CPD

**Abbreviations used in this review:**

EASL = European Association for the Study of the Liver
PBAC = Pharmaceutical Benefits Advisory Committee
PBS = Pharmaceutical Benefits Scheme
TGA = Therapeutic Goods Administration

Claim CPD/CME points Click here for more info.

Follow RESEARCH REVIEW Australia on Twitter now @ResearchRevAus
Visit https://twitter.com/ResearchRevAus

Welcome to the 13th issue of Gastroenterology Practice Review.

This Review covers news and issues relevant to clinical practice in gastroenterology. It will bring you the latest updates, both locally and from around the globe, in relation to topics such as new and updated treatment guidelines, changes to medicines reimbursement and licensing, educational, professional body news and more. And finally, on the back cover you will find a summary of upcoming local and international educational opportunities including workshops, webinars and conferences.

We hope you enjoy this new Research Review publication and look forward to hearing your comments and feedback.

Kind Regards,

Dr Janette Tenne
Medical Research Advisor
janette.tenne@researchreview.com.au

**Clinical Practice**

**Acute severe autoimmune hepatitis: corticosteroids or liver transplantation?**

Patients with acute severe autoimmune hepatitis are challenging to treat. As a disease, autoimmune hepatitis has a wide variability in its presentation, and good evidence is lacking to guide diagnosis and treatment. It is vital to consider autoimmune hepatitis as a cause for severe acute liver failure. In the case of drug-induced liver failure, the causative agent should be withdrawn. Current evidence suggests corticosteroid treatment for all patients with suspected autoimmune hepatitis, unless they have high-grade hepatic encephalopathy. A prednisone dose of 0.5-1 mg/kg/day is recommended, but further data are needed to determine the optimal induction protocol (including dose, route, and length of treatment) and the role of other immunosuppressants. In general, corticosteroid treatment does not seem to increase mortality in acute severe autoimmune hepatitis. Evaluation of corticosteroid response should occur early in the treatment course to decide if it should be withdrawn.

Although some patients respond to corticosteroids, it remains difficult to determine at diagnosis which patients will need liver transplant and which will not; therefore, assessment for liver transplant should occur at the same time as corticosteroid initiation so that the decision to proceed to transplant is not delayed by protracted courses of corticosteroids.

Applying the current diagnostic criteria for autoimmune hepatitis in the acute setting is not straightforward, therefore the authors have suggested an algorithm for classification of acute presentation. Improvements in serology and virology testing will probably identify further patients that have been defined as seronegative acute liver failure.

Randomised controlled trials are not feasible due to the rarity of this disease. Rather, multicentre prospective studies may address unanswered questions. There is a need for collaboration of data sets from transplant centres to address the questions of what dose of steroids is appropriate, which patients can be salvaged from liver transplant with corticosteroids, and what are the infectious complications before and after transplantation. The optimal timing of emergency liver transplant also needs to be determined.


**EASL clinical practice guidelines: drug-induced liver injury**

These clinical practice guidelines discuss the available evidence on risk factors, diagnosis, treatment and risk minimization strategies for drug-induced liver injury (DILI). Idiosyncratic (unpredictable) DILI is a challenging liver disorder due to the wide variety of drugs available in clinical practice, herbal and dietary supplements that may cause liver injury, broad clinical and pathological phenotypes associated with the condition and the current absence of specific biomarkers. This makes the diagnosis of DILI an uncertain process, necessitating a high level of awareness of the condition and the exclusion of alternative causes of liver disease. Idiosyncratic DILI can be severe, leading to a particularly serious variety of acute liver failure for which no effective therapy has yet been developed.

**Risk factors**

Risk factors for DILI include increasing age, female gender, certain ethnicities, regular alcohol intake, components of metabolic syndrome, chronic hepatitis B and C, and drugs with predominant hepatic metabolism by cytochrome P450 enzymes.

**Diagnosis**

Most cases of DILI present acutely, with elevations of liver enzymes with or without non-specific symptoms, the development of jaundice, or sometimes acute liver failure (ALF). However, some cases of DILI have no distinct clinical, imaging or histopathological features, for example acute fatty liver, acute veno-occlusive syndromes, secondary sclerosing cholangitis or drug-induced autoimmune hepatitis.

Because there are no specific biomarkers for DILI, diagnosis is made on interpretation of serum liver biochemistry and other routine laboratory and imaging tests to rule out alternative causes of liver disease. An abdominal ultrasound should be undertaken in all patients suspected of DILI. The use of additional imaging studies relies on the clinical context. Liver biopsy may be considered during the investigation of selected patients suspected of suffering from DILI.
Any adverse reactions to chlorhexidine should be reported to the TGA. Including the use of surveillance systems to record their presence. Chlorhexidine use is recommended. The guidelines provide updated information and evidence on multi-resistant organism management, personal protective equipment, has been updated to reflect new national and international evidence. Guidance on basic infection prevention and control practices, such as hand hygiene and use of personal protective equipment, has been updated to reflect new national and international evidence. Healthcare workers should be immunised as recommended in the Australian Immunisation Handbook. Patients with ALF should be hospitalised. Regular liver tests are necessary for patients taking drugs that may cause DILI.

European Crohn's and Colitis Organisation review on complementary medicine and psychotherapy in inflammatory bowel disease

This is a review of complementary and alternative interventions in the treatment of IBD. It is estimated that up to half of all patients with IBD use various forms of complementary and alternative medicine during some point in their disease course. While cannabis use may be associated with a reduction of some symptoms in IBD, there is no good evidence to show that has a benefit on the disease course. Curcumin in combination with 5-aminosalicylic acid may be effective in inducing remission in mild-to-moderately active ulcerative colitis. Curcumin, psyllium, and a preparation consisting of myrrh, chamomile and coffee charcoal may be effective as complementary maintenance therapy in ulcerative colitis. Omega-3 fatty acids may be effective in maintaining remission in Crohn's disease. However, study quality and the heterogeneity of trials limit these findings. There is no evidence to support the use of probiotics or prebiotics in Crohn's disease. Escherichia coli Nissle 1917 may be effective in inducing and maintaining remission in ulcerative colitis. A multi-strain probiotic containing a combination of lactis acid bacteria, streptococcus and bifidobacteria may be effective in inducing and maintaining remission in ulcerative colitis. There is insufficient evidence to support the use of vitamins and minerals, or diet supplements or specific diets to induce or maintain remission in Crohn's disease and ulcerative colitis.

Mind–body medicine and psychotherapeutic interventions

Cognitive behavioural therapy improves quality of life in IBD patients over the short term. Evidence for the efficacy of hypnotherapy to reduce IBD symptoms is limited, but the efficacy of hypnotherapy in functional gut disorders suggest future studies in IBD. Psychodynamic therapy and sleep management may decrease symptoms of depression and anxiety, but not IBD severity. Solution-focused therapy may benefit patients with fatigue. Mediation and relaxation may improve quality of life and potentially reduce IBD inflammatory activity. Evidence for mindfulness-based interventions and yoga in IBD management is limited, but yoga may improve quality of life.

Manipulative and body-based interventions

There is minimal evidence on the efficacy of chiropractic and osteopathy in the management of active Crohn's disease. There are no published studies of chiropractic and osteopathy in patients with ulcerative colitis or IBD. There is not enough evidence to support the use of motrinaxol and acupuncture for the treatment of active ulcerative colitis or Crohn's disease. Exercise can benefit overall health, physical well-being, stress and quality of life of IBD patients. There is promising but limited evidence for the role of exercise in preventing IBD development and in disease management.

Australian guidelines for the prevention and control of infection in healthcare

The National Health and Medical Research Council and the Australian Commission on Safety and Quality in Health Care have published updated guidelines for the prevention and control of infection in healthcare. Key changes in the 2019 version are discussed below. Guidance on basic infection prevention and control practices, such as hand hygiene and use of personal protective equipment, has been updated to reflect new national and international evidence.

Healthcare workers should be immunised as recommended in the Australian Immunisation Handbook. A structured system for clinical handover is advised, including documented policies and protocols. The guidelines provide updated information and evidence on multi-resistant organism management, including the use of surveillance systems to record their presence. Chlorhexidine use is recommended only when clinically indicated, to aid in preventing adverse reactions and chlorhexidine resistance. Any adverse reactions to chlorhexidine should be reported to the TGA.

Regarding emerging disinfection methods, there is not enough high-quality evidence to support the routine use of hydrogen peroxide vapour, ultra-violet light or antimicrobial surfaces. Hydrogen peroxide vapour and ultra-violet light may be used in high-risk settings when standard disinfectants have been ineffective. Replacement of peripheral intravenous catheters should be based on a formal risk assessment. In adults, such catheters may be replaced every 72 hours or as clinically indicated. Peripheral intravenous catheters should not be routinely replaced in neonates and children.

In case of norovirus, grouping of similarly symptomatic patients in bays may be more efficient for outbreak control than closing an entire ward. Such an approach should be implemented within three days of the first patient becoming ill. For disinfection of hard surfaces, TGA-listed hospital-grade disinfectants with specific indications for hard surface disinfection in healthcare facilities are recommended. This change is based on reduced regulation for hard surface disinfectants implemented by the TGA which has resulted in changes to terminology and requirements of entry. Finally, the guidelines have an increased focus on involving patients and caregivers in infection prevention and control.

Media release.

Guidelines.

TGA – new or extended indications

Tofacitinib (Xeljanz®) is now also indicated for the treatment of adult patients with moderately to severely active ulcerative colitis who have had an inadequate response, lost response, or were intolerant to either conventional therapy or a biological therapy. Read more here.

TGA – new biosimilar medicines

An adalimumab biosimilar (Hyrimoz®) is indicated for a number of gastroenterology indications including:

• Treatment of moderate to severe Crohn's disease in adults and children (≥6 years), to reduce the signs and symptoms of the disease and to induce and maintain clinical remission in patients; who have had an inadequate response to conventional therapies or who, have lost response to or are intolerant to infliximab.

• Treatment of moderate to severe ulcerative colitis in adult patients who have had an inadequate response to conventional therapy or who are intolerant to or have medical contraindications for such therapies.

Hyrimoz® has also been approved for the treatment of rheumatoid arthritis, polyarticular juvenile idiopathic arthritis, enthesis-related arthritis, anklyosing spondylitis, psoriatic arthritis, plaque psoriasis, hidradenitis suppurativa and uveitis.

A trastuzumab biosimilar (Ontruzant®) is indicated in combination with cisplatin and either capcitabine or S-FU for the treatment of patients with HER2-positive advanced adenocarcinoma of the stomach or gastro-oesophageal junction who have not received prior anti-cancer treatment. Ontruzant® has also been approved for the treatment of breast cancer. Read more here.

Changes to proton pump inhibitor restriction level

The July 2018 PBAC recommendations included restriction level changes for the following PBS-listed medicines from 1 May 2019:

• Esomeprazole 40mg with one repeat will change from Restricted Benefit to Authority Required (Telephone).

• All standard dose PPIs (esomeprazole 20mg, lansoprazole 30mg, omeprazole 20mg, pantoprazole 40mg, rabeprazole 20mg) will change from Restricted Benefit to Authority Required (STREAMLINED).

Find out more here.
'ENTYVIO is indicated for the treatment of adult patients with moderate to severe ulcerative colitis or Crohn’s disease who have had an inadequate response with, lost response to, or are intolerant to either conventional therapy or a TNFα antagonist.'

PBS Information: Section 100 (S100) Highly Specialised Drugs Program. Authority required. Refer to PBS for full details.

FDA permits marketing of first medical device for relief of pain associated with irritable bowel syndrome in patients 11-18 years of age

The US Food and Drug Administration (FDA) has permitted marketing of the first medical device to decrease functional abdominal pain in patients aged 11-18 years with irritable bowel syndrome (IBS) when combined with other therapies for IBS. The prescription-only IB-Stim device is comprised of a small single-use mild electrical nerve stimulator that is placed behind the patient’s ear. It's battery-powered chip emits low-frequency electrical pulses to stimulate certain cranial nerves continuously for five days, at which time it is replaced. Stimulating these nerves is thought to provide pain relief. The device can be used for up to three consecutive weeks to reduce functional abdominal pain associated with IBS.

Approval was granted based on a study of 50 patients aged 11-18 years with IBS - 27 patients used the IB-Stim device and 23 patients used a placebo device. Patients were permitted medication to treat chronic abdominal pain. Worst baseline pain was similar between the treatment and placebo arms.

The Iβ-Stim group had a greater change (improvement) in worst pain from baseline to week 1, 2, and 3 than the placebo group. Greater change was also seen in composite Pain Frequency Severity Duration scores from baseline to week 3 in the Iβ-Stim group compared to the placebo group. At least a 30% decrease in worst pain was seen in 59% and 26%, respectively. During the study, six patients had mild ear discomfort and three patients had adhesive allergy at the site of application.

It is suggested readers review the full trial data before forming a final conclusion on its merits.

Diagnosis, development, and treatment of portal vein thrombosis in patients with and without cirrhosis

This review addresses portal vein thrombosis in patients with and without cirrhosis, including the controversial topic about treatment in patients with cirrhosis. Early diagnosis and management of acute symptomatic portal vein thrombosis are important. Failure to detect and treat thromboses can lead to mesenteric ischaemia, chronic cavernous transformation, and complications of portal hypertension. There are data to support treatment of specific cirrhosis patients with anticoagulation agents.

Conferences, Workshops, and CPD

Please click on the links below for upcoming local and international gastroenterology meetings, workshops, and CPD.

- AGGIS - Events
- EASL - coming events
- AGIS ASM 21-23 August 2019
- TheConferenceWebsite - gastroenterology conferences
- World Gastroenterology Organisation - meetings & events
- COMS - conferences and meetings on gastroenterology

Research Review Publications

- Biologics Research Review with Associate Professor Paul Bird
  https://tinyurl.com/yhik66gt
- Gastroenterology Research Review with Dr Kate Nagiah and Dr Ian Fok
  https://tinyurl.com/yb66wexk3
- Hepatitis Research Review with Professor Stephen Riordan
  https://tinyurl.com/y4o48fby
- IBD Research Review with Dr Alissa Walsh, Dr Brit Christensen and Dr Jake Begun
  https://tinyurl.com/je679dp
- Speaker Series – RMH-WeHI Gastrointestinal Mucosal Immunology Translational Symposium
  https://tinyurl.com/y4o48fby
- DDW 2019 Conference Review
  https://tinyurl.com/y3is5d7a
- ECCO (IBD) 2019 Conference Review
  https://tinyurl.com/v2j4k6n
- EASL 2019 Conference Review
  https://tinyurl.com/y656jhy

RESEARCH REVIEW™
Australia’s Leader in Special Publications

Australian Research Review subscribers can claim CPD/CME points for time spent reading our reviews from a wide range of local medical and nursing colleges. Find out more on our CPD page.