EDITION 4
DRUGS & THE GUT

Gut News You Can Use

What every GP needs to know about drug-related gut injury

MY GUT CARE
EXPERTS IN GUT HEALTH, LIVER AND ENDOSCOPY

Edition 4: Expert Insights for GPs – We are delighted to welcome you to the fourth edition of Gut News You Can Use by My Gut Care.

Welcome to Edition 4 : Drugs & The Gut

Medications are among the most common — and most overlooked — causes of gastrointestinal symptoms. From the proton pump inhibitor your patient has been taking for a decade to the gym supplement they forgot to mention, drugs interact with the gut in ways that are often reversible if caught early. This edition of Gut News You Can Use cuts through the noise of observational data to give you evidence-based, clinically practical guidance across seven key drug-gut topics.

IN THIS EDITION

KEY TAKE-HOME

Most drug related gut complications are reversible when identified promptly. A thorough and systematic medication history — including over-the-counter products and supplements — is your most powerful diagnostic tool.

When in doubt, refer early. Our team at My Gut Care is here to help.

1. Are Proton Pump Inhibitors (PPIs) Safe Long-Term?

PPIs are among the most prescribed medications in general practice. Over the past decade, large observational studies have raised concerns about associations with chronic kidney disease, enteric infections, hypomagnesaemia, dementia, and even gastric malignancy. Understandably, many patients — and clinicians — are asking whether long-term use is justified.

THE EVIDENCE

- Large observational studies suggest associations with infections, kidney disease, and malignancy — but are frequently confounded by indication bias.
- High-quality RCT and meta-analysis data (Moayyedi et al., Vaezi et al., Freedberg et al.) demonstrate PPIs are generally safe when used appropriately.
- Absolute risks, even in observational data, are low — and are outweighed by the risks of undertreating conditions like Barrett's oesophagus, peptic ulcer disease, and severe GORD.
- Unnecessary long-term prescribing without documented indication is the real clinical problem.

VERDICT

✔️ PPIs are safe when clinically indicated
✔️ Avoid unnecessary long-term use without a clear indication
✔️ Reassess PPI necessity at every review
✔️ Step-down or cessation strategies should be trialled where appropriate

Dr Hamarneh's Commentary

PPIs remain one of the most effective and safest medications in gastroenterology. The real issue is ensuring we prescribe with clear intent, review regularly, and don't allow reflexive long-term use without active indication.

KEY REFERENCES: *Moayyedi P et al. Am J Gastroenterol. 2019, Vaezi MF et al. Gastroenterology. 2017, Freedberg DE et al. Gastroenterology. 2017*

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2. Are Statins Safe in Liver Disease?

Statin cessation in patients with abnormal liver function tests or established liver disease is a common occurrence in general practice — but the evidence strongly challenges this practice. Concern about drug-induced hepatotoxicity has led to widespread, unwarranted statin discontinuation, potentially exposing patients to unnecessary cardiovascular risk.

THE EVIDENCE

- Statins do not cause clinically significant hepatotoxicity in the vast majority of patients, including those with pre-existing liver disease.
- They are safe and potentially beneficial in NAFLD (non-alcoholic fatty liver disease) — reducing hepatic inflammation and cardiovascular mortality.
- Safe to use in compensated cirrhosis. Use with caution in decompensated liver disease.
- Athyros et al. (Lancet, 2010) demonstrated that statins can be safely used, and even improve outcomes, in patients with elevated liver enzymes.

VERDICT

✔️ Statins are safe in most liver disease patients
✔️ Do not stop statins based on mildly elevated LFTs alone
✔️ Beneficial in NAFLD — consider as part of management
✔️ Decompensated cirrhosis: seek specialist advice

Dr Adris's Commentary

Statins are often unnecessarily ceased in patients with liver disease, driven by an outdated fear of hepatotoxicity. The cardiovascular benefit is real and the hepatic risk is minimal. When in doubt, a gastroenterology or hepatology opinion can clarify the risk-benefit balance.

KEY REFERENCES: AASLD Practice Guidance 2018, Kim G et al. Hepatology. 2017, Athyros VG et al. Lancet. 2010

3. GLP-1 Agonists & The Gut

GLP-1 receptor agonists (semaglutide, liraglutide, dulaglutide) have transformed the management of type 2 diabetes and obesity. Their gastrointestinal side effect profile, however, is significant and increasingly being referred to gastroenterologists as the patient population grows rapidly.

THE EVIDENCE

- GLP-1 agonists cause delayed gastric emptying — a desired metabolic effect that can tip susceptible patients into symptomatic gastroparesis.
- Most common GI side effects: nausea (up to 44%), constipation, bloating, and early satiety — particularly on dose escalation.
- Can worsen pre-existing reflux and exacerbate symptoms in patients with undiagnosed gastroparesis.
- Generally safe in IBD and NAFLD — and may offer metabolic benefits in NAFLD/MASH populations.
- Nauck MA et al. (Diabetes Care, 2021) provides the most comprehensive review of GI effects.

VERDICT

✔️ Can cause gastroparesis-like symptoms — screen before initiating
✔️ Safe in IBD and NAFLD
✔️ Pre-treatment gastric emptying assessment in high-risk patients
✔️ Refer if symptoms persist beyond dose titration

KEY REFERENCES

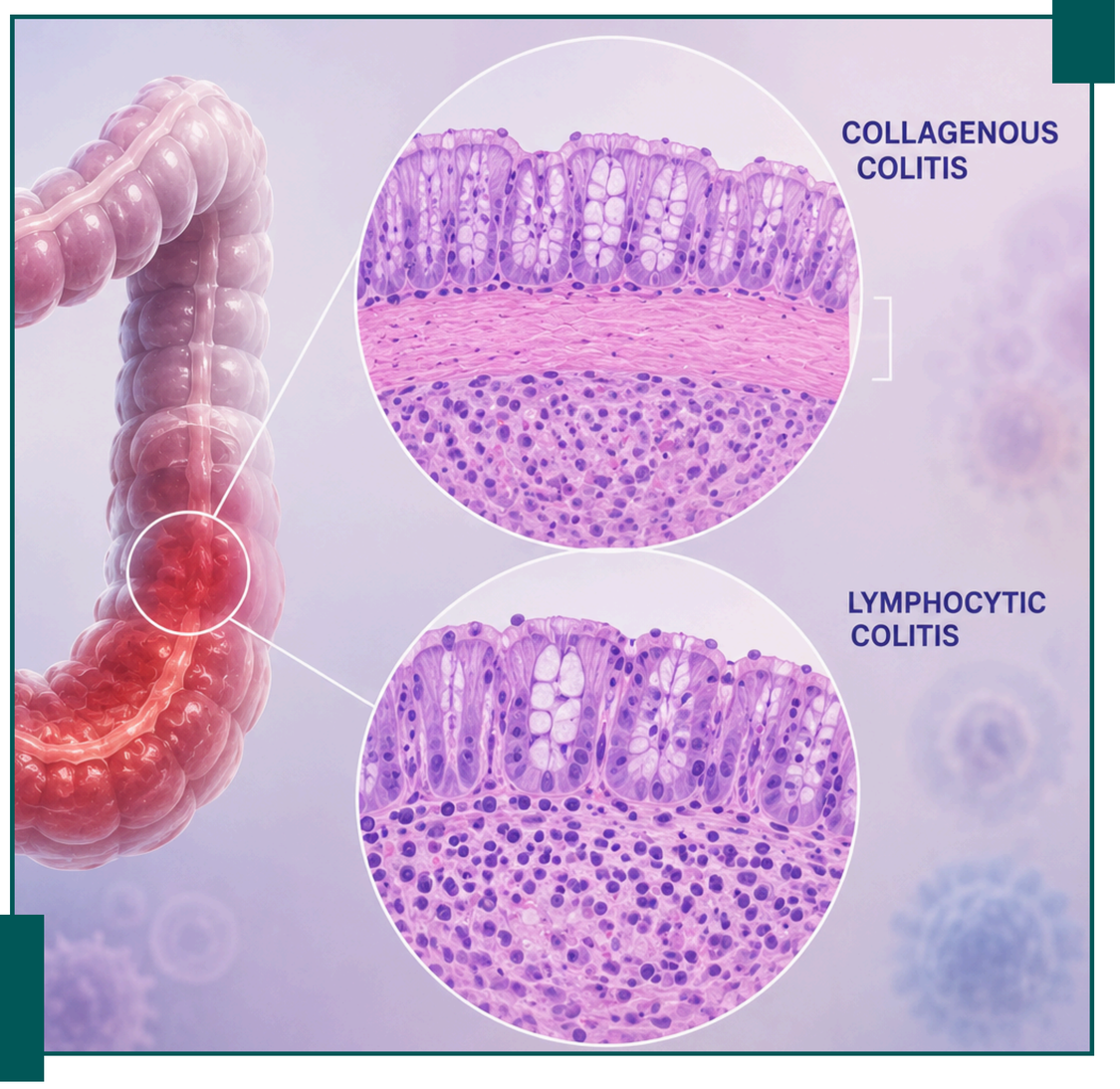
- Nauck MA et al. Diabetes Care. 2021

Dr Kia's Commentary

We are seeing a rising tide of GLP-1-related gastroparesis referrals. A brief symptom screen before initiation and careful dose titration can prevent many of these presentations. Patients with pre-existing dysmotility symptoms should be flagged early.

4. Drugs & Microscopic Colitis

Microscopic colitis is an increasingly recognised cause of chronic, watery, non-bloody diarrhoea — particularly in middle-aged to older women. Its aetiology is multifactorial, but medications are a key and reversible trigger that must be reviewed in every patient with this presentation.



THE EVIDENCE

- Strong associations with SSRIs, NSAIDs, and PPIs — particularly lansoprazole.
- The mechanism is thought to involve altered colonic immune response and epithelial permeability.
- Diagnosis requires colonoscopy with biopsies — macroscopic appearance is normal.
- Cessation of the offending drug leads to complete remission in many cases, avoiding the need for budesonide or bismuth therapy.

VERDICT

✔️ Always review medications in chronic watery diarrhoea
✔️ Cessation of the offending drug is often curative
✔️ Colonoscopy with biopsies is required for diagnosis
✔️ Refer if symptoms persist after drug withdrawal
✔️ Don't Forget Metformin, It doesn't cause Microscopic colitis but Diarrhea

KEY REFERENCES

- Münch A et al. Gut. 2012
- Cotter TG et al. Clin Gastroenterol Hepatol. 2017

5. GLP-1 Medications and the Pancreas: What GPs Need to Know

The widespread use of GLP-1 receptor agonists — including semaglutide, liraglutide, dulaglutide and tirzepatide — has rapidly changed the landscape of obesity and type 2 diabetes management.

As use increases, so do questions regarding pancreatic safety. Patients are increasingly presenting to GPs and emergency departments with abdominal symptoms while on these medications, raising concerns regarding pancreatitis, pancreatic cancer, and delayed gastric emptying.

Do GLP-1 Medications Cause Pancreatitis?

This remains one of the most discussed concerns surrounding GLP-1 therapy.

Early post-marketing reports suggested a possible association with acute pancreatitis. However, subsequent large, randomised trials, cardiovascular outcome studies, and meta-analyses have been largely reassuring.

Current evidence suggests:

- No convincing increase in pancreatitis risk has been demonstrated
- If a risk exists, the absolute risk appears to be very low
- Rates of pancreatitis in major studies are typically around 0.1–0.3%

Importantly, patients with obesity and diabetes already have a higher baseline risk of pancreatitis independent of medication exposure.

Practical GP Considerations

While routine pancreatic monitoring is not recommended, clinicians should remain vigilant for symptoms suggestive of pancreatitis.

Symptoms warranting assessment include:

- persistent severe epigastric pain
- pain radiating to the back
- persistent vomiting
- inability to tolerate oral intake

If pancreatitis is suspected:

- cease the GLP-1 medication
- investigate appropriately (lipase, LFTs ± imaging)
- avoid re-challenge if pancreatitis is confirmed and no alternative cause is identified

Should Lipase Be Monitored?

Routine lipase monitoring is not recommended.

Mild asymptomatic lipase elevation is relatively common with GLP-1 therapy and does not reliably predict pancreatitis. In practice, isolated enzyme elevation without compatible symptoms is usually not clinically meaningful.

This is an important distinction, as incidental lipase elevation can create unnecessary anxiety and downstream investigations.

Which Patients Warrant More Caution?

A cautious approach is reasonable in:

- patients with previous idiopathic pancreatitis
- patients with recurrent unexplained pancreatic-type pain
- patients with established severe gastroparesis

In contrast, GLP-1 therapy may still be reasonable in patients with a clear prior pancreatitis trigger (for example gallstone pancreatitis following cholecystectomy), provided the benefits outweigh risks.

What Gastroenterologists Are Seeing More Often

In day-to-day gastroenterology practice, the far more common issue is not pancreatitis — but gastrointestinal side effects and altered gastric motility.

Common presentations include:

- nausea
- reflux
- bloating
- constipation
- delayed gastric emptying
- early satiety
- vomiting

These symptoms are often dose-related and may improve with:

- slower dose escalation
- smaller meal sizes
- reduced dietary fat intake
- temporary dose reduction

GLP-1 medications should also be considered in patients presenting with otherwise unexplained nausea or symptoms suggestive of gastroparesis.

What About Pancreatic Cancer?

This remains an area of ongoing research and public attention.

Reassuringly, current evidence does not demonstrate a convincing increase in pancreatic cancer risk associated with GLP-1 therapy.

Longer-term data are still evolving, but large population studies to date have not identified a clear signal for pancreatic malignancy.

Specialist Perspective

“Pancreatic safety concerns understandably receive significant attention with GLP-1 therapy, however clinically significant pancreatic complications remain uncommon in practice. Far more frequently, we are seeing medication-related gastrointestinal symptoms and delayed gastric emptying. The key is recognising which patients require investigation versus reassurance and supportive management.”

— Dr Zaki Hamarneh

Dr. Zaki Hamarneh (MD, FRACP)
Gastroenterologist & Interventional Endoscopist
Greenslopes Private Hospital

Key Takeaways for GPs

- Current evidence does not demonstrate a strong causal link between GLP-1 therapy and pancreatic cancer
- Acute pancreatitis appears uncommon, but remains an important clinical consideration
- Routine lipase monitoring is not recommended
- Mild asymptomatic lipase elevation is relatively common and usually not clinically significant
- Consider caution in patients with prior idiopathic pancreatitis or severe gastroparesis
- Gastrointestinal side effects and delayed gastric emptying are much more commonly encountered in routine practice

6. ARBs & Drug-Induced Enteropathy

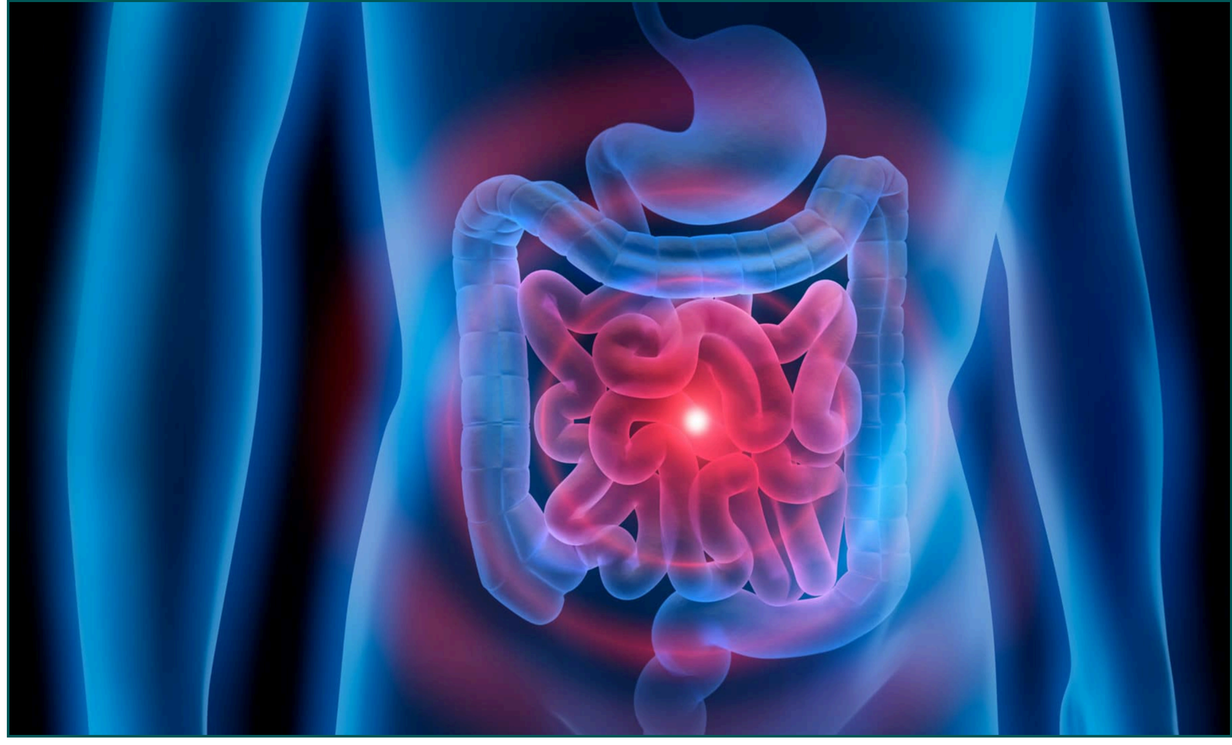
Angiotensin II receptor blockers (ARBs) — particularly olmesartan — are an important and underrecognised cause of severe enteropathy. This condition can closely mimic coeliac disease, and missing it leads to unnecessary dietary restriction, ongoing investigations, and patient harm.

THE EVIDENCE

- ARBs can cause villous atrophy and a clinical-histological picture indistinguishable from coeliac disease.
- Patients present with diarrhoea, weight loss, and malabsorption — serology for coeliac disease is negative (seronegative enteropathy).
- Olmesartan is most frequently implicated, but other ARBs have been reported.
- Dr Shahzad has published on this condition in the Medical Journal of Australia, highlighting its relevance in Australian clinical practice.
- Drug cessation leads to complete mucosal recovery — often within months.

VERDICT

✔️Consider in all cases of seronegative villous atrophy
✔️Always take a thorough ARB medication history
✔️Cessation of the ARB is diagnostic and therapeutic
✔️Refer for gastroscopy and duodenal biopsy if suspected



Dr Shahzad's Commentary

This is a diagnosis we continue to see missed. Any patient with a seronegative villous atrophy who is on an ARB should have the medication ceased before committing to a diagnosis of refractory coeliac disease. The response to drug withdrawal is often dramatic.

KEY REFERENCES

- *Rubio-Tapia A et al. Mayo Clin Proc. 2012*
- *Shahzad A et al. Medical Journal of Australia*

7. ADHD Medications & Gastritis

With ADHD diagnoses increasing across all age groups, methylphenidate and amphetamine-based medications are now prescribed with greater frequency. Gastrointestinal side effects — particularly upper GI symptoms — are among the most common adverse effects, yet are often not attributed to the medication.

THE EVIDENCE

- Stimulant medications (methylphenidate, lisdexamfetamine, dexamfetamine) can cause gastric irritation, nausea, epigastric pain, and appetite suppression.
- Reduced appetite and altered gut motility may contribute to nausea and early satiety.
- Upper GI symptoms are a common cause of non-adherence in adolescent and adult patients.
- In some patients, these symptoms may present as unexplained gastritis on endoscopy.

VERDICT

✔️ Consider ADHD medications in unexplained gastritis
✔️ Review timing of medication relative to meals
✔️ Dose adjustment or formulation change may resolve symptoms
✔️ Refer if symptoms persist or if alarm features are present

KEY REFERENCES

- Storebø OJ et al. Cochrane Database. 2015

8. Gym Supplements & Gut Injury

Patients rarely volunteer information about over-the-counter supplements and protein powders — and clinicians rarely ask. Yet gym supplements represent a significant and growing source of drug-related gut injury, particularly among young and middle-aged patients who may otherwise appear 'healthy'.

THE EVIDENCE

- High-dose caffeine supplements are directly linked to gastritis, peptic ulceration, and in severe cases, gastrointestinal bleeding.
- Pre-workout formulas often contain multiple stimulants, unregulated herbal extracts, and artificial sweeteners that can cause osmotic diarrhoea.
- Creatine, protein powders, and mass-gainers are generally well tolerated but can cause bloating and loose stools at high doses.
- Supplement contamination and mislabelling are documented problems — regulatory oversight is limited.

VERDICT

✔️ Always ask about supplements in your drug history
✔️ Cessation is often diagnostic and therapeutic
✔️ High caffeine supplements are a significant ulcerogenic risk
✔️ Refer if symptoms persist or complications arise

KEY REFERENCES

- Nawrot P et al. Food Addit Contam. 2003
- Cohen PA et al. JAMA. 2014

Dr Shahzad's Commentary

I routinely ask patients about supplements and protein shakes as part of the standard drug history. The number of times this reveals the cause of an otherwise unexplained gastritis or diarrhoeal illness is striking. It is a simple question with significant diagnostic yield.

Final Take Home Messages

✔️ Most drug-related gut complications are reversible if recognised early
✔️ A detailed and systematic medication history — including supplements — is your most powerful diagnostic tool
✔️ SSRIs, NSAIDs, PPIs, ARBs, and stimulants are all potential gut offenders
✔️ Never stop statins based on mildly elevated LFTs without specialist input
✔️ Consider GLP-1 gastroparesis in patients on semaglutide with dysmotility symptoms
✔️ When uncertain, refer to My Gut Care — early referral prevents delayed diagnoses

For complex or refractory drug-related gut presentations, or any gastroenterology concern, our team is ready to help. We offer timely, expert assessment with a strong focus on GP communication and patient outcomes.

MY GUT CARE

Join us in **welcoming Dr. Terry Holt** to My Gut Care. Dr. Holt's medical expertise is backed by a foundational career as an analytical chemist and a Ph.D. in the metabolic consequences of chronic disease from the University of Queensland. An accomplished researcher, he has published over two dozen papers and collaborated with institutions like Cambridge University and the WHO. For the past 22 years, he has been proudly serving the Ipswich community, providing dedicated, high-quality specialist care.

Dr Terry Holt

B.AppSc, MBBS, FRACP, Ph.D
Gastroenterologist and Hepatologist

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OUR LOCATIONS

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- Greenslopes Private Hospital
- QGOS, Suite 110, 1808 Logan Road, Upper Mount Gravatt.
- Suite 2, 18 Limestone Street, Ipswich.
- St Andrew's War Memorial Hospital, Specialist Suites.
- Mater Health Centre Redland

Procedures

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- Ipswich Day Hospital
- Sunnybank Private Hospital
- St Andrew's War Memorial Hospital Brisbane
- Canossa Private Hospital Oxley
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