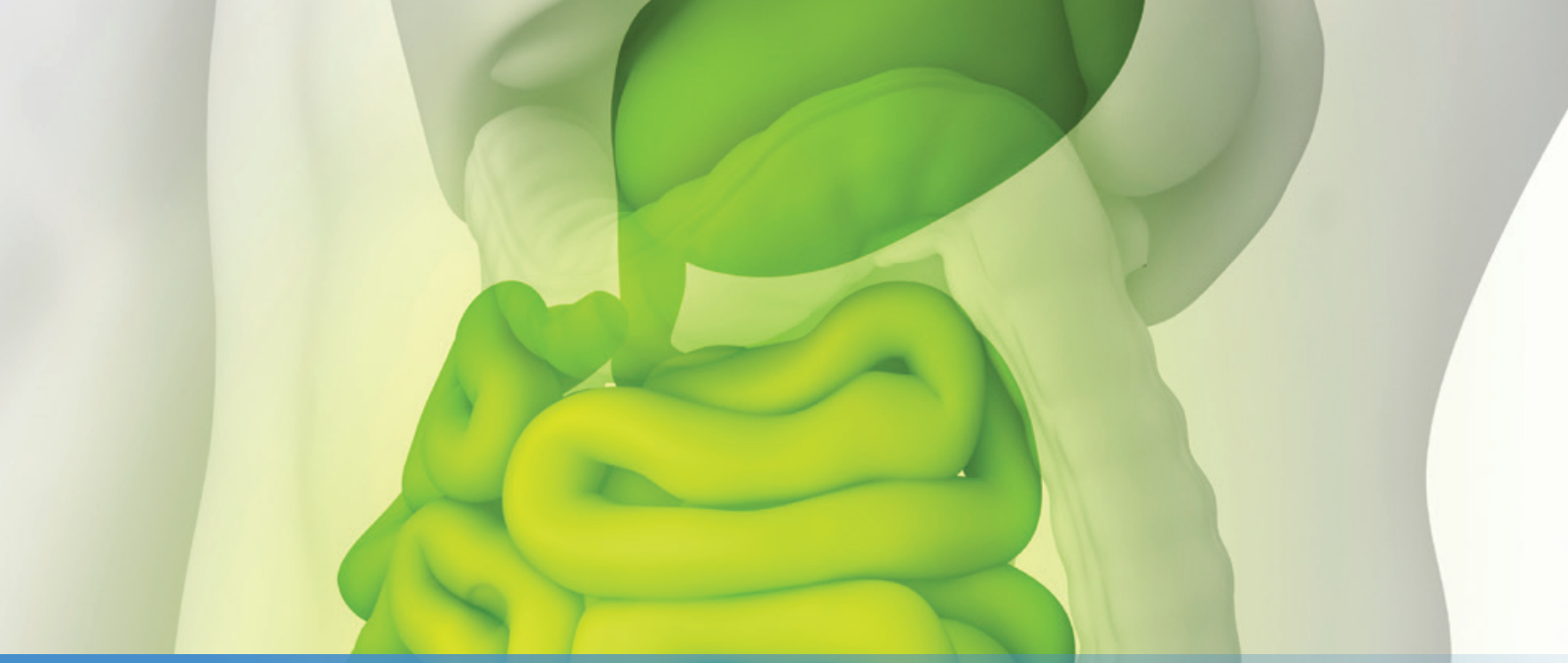

GUT FEELING GASTROLAB NEWS FOR GPs AUTUMN 2016

THIS ISSUE Non-alcoholic fatty liver disease

NON-ALCOHOLIC FATTY LIVER DISEASE

Non-alcoholic fatty liver disease (NAFLD) is the spectrum of liver diseases that is the hepatic manifestation of obesity or the metabolic syndrome, from simple hepatic steatosis (fatty infiltration), through to non-alcoholic steato-hepatitis (NASH), which can progress to cirrhosis, liver cancer and liver failure.

The global prevalence of NAFLD is > 25%[1]. Other population studies from Western countries estimate the prevalence is higher and sits between 30 - 40% of all adults[2]. With the growth of obesity in the population, NAFLD is becoming increasingly common and is expected to become the leading cause of liver transplantation in the future. However we do not have accurate predictors to determine which patients with NAFLD will progress to cirrhosis or liver-related death, and we have neither accurate population screening techniques nor evidence-based therapy.

Risk factors, pathogenesis & natural history

NAFLD commonly co-exists with features of the metabolic syndrome, a clustering of cardiovascular risk factors related to reduced insulin sensitivity. Insulin resistance underpins the pathogenesis of NAFLD and disease progression, and this association is independent of BMI or glucose tolerance. Other features of the metabolic syndrome include central obesity, hypertriglyceridaemia, low HDL, and hypertension, with each additional component exponentially increasing the NAFLD risk.

The exact pathogenesis and triggers of NAFLD progression are not understood in detail at present. The current multiple hit hypothesis considers multiple insults acting together on genetically predisposed subjects to induce NAFLD. Such hits include insulin resistance, hormones secreted from the adipose tissue, gut microbiota, and dietary and lifestyle factors.

NAFLD is asymptomatic unless advanced liver disease is present, when patients present with jaundice, ascites, oedema, encephalopathy, gastrointestinal bleeding, fatigue and muscle wasting. Simple steatosis appears to be a relatively benign condition, although it may progress to NASH over time. Comorbid diabetes increases the likelihood of progression to NASH as well as cirrhosis, malignancy and liver related death. Importantly, diabetes also increases the risk of progression to cardiovascular death which is the number one cause of mortality in patients with NAFLD.

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Diagnosis in general practice

Diagnosis of NAFLD requires evidence of fatty infiltration (from either imaging or biopsy), exclusion of significant alcohol consumption, and exclusion of other causes of hepatic steatosis (e.g. blood tests, medications, surgery). NAFLD should be considered in all metabolic syndrome patients and in any patient with abnormal LFTs, hepatomegaly or ultrasound features of steatosis not attributable to hepatitis C, alcohol or other causes.

Liver enzyme tests are not predictive of NAFLD or its severity[3]. The entire histological spectrum of NAFLD can be seen with normal ALT. However it is often elevated liver enzymes (persistently raised ALT or AST, and elevations in GGT and ALP) in those with metabolic syndrome that makes one suspicious of underlying NAFLD. Indeed, NAFLD is the most common cause of an elevated ALT in general practice[4]. It is therefore useful to include LFTs as part of routine blood tests that include CRP, fasting BSL, fasting insulin, cholesterol, HDL, LDL, and triglycerides. However there are several other important causes of raised ALT that may need to be excluded:

CONSIDERATION	TEST
Viral hepatitis	Hepatitis B (HBsAg, anti-HBs, anti-HBc) Hepatitis C (Hepatitis C antibody)
Autoimmune hepatitis	Anti-nuclear Ab (ANA) Anti-smooth-muscle Ab (ASMA) Anti-mitochondrial Ab (AMA) Anti-liver kidney microsomal Ab (LKM)
Haemochromatosis	Iron Studies
Thyroid disease	Thyroid function tests
Coeliac disease	Coeliac serology (IgG deamidated gliadin peptide Ab, IgA tissue transglutaminase Ab)

Biopsy is the traditional gold standard diagnostic test for NAFLD, however it is not part of routine clinical practice. Liver biopsy may be considered where cirrhosis is suspected or where an alternative diagnosis is considered. Confirming hepatic fatty infiltration using a variety of imaging techniques is important, but there is no accessible gold standard. Ultrasound tends to be used most often because it is accessible, has no radiation exposure and is relatively inexpensive. Transient elastography (FibroScan®) is a safe, accurate and non-invasive means of measuring liver stiffness as a surrogate marker of fibrosis.

Management

There are no prescriptive therapies for NAFLD. Management focusses on achieving weight loss, lifestyle modification (diet and exercise), and modifying the comorbid cardiovascular risk factors of obesity, diabetes, dyslipidaemia and hypertension. A diet with less processed carbohydrates / sugars and more vegetables has been shown to be most effective, although any diet that results in a modest weight loss (7-10%) should result in clinical improvement in NAFLD[5]. Pharmaceutical companies are beginning to focus on the treatment of this disease. Clinical trials using new pharmaceutical interventions are being conducted at some or our tertiary hospitals.

Conclusion

NAFLD is increasingly prevalent and represents a growing challenge in terms of prevention and treatment. Despite its high prevalence, only a small minority of affected patients develops inflammation and subsequently cirrhosis and chronic liver disease. In the absence of a full understanding of the mechanisms underlying the development of NAFLD and NASH, like many things in life, "an ounce of prevention is worth a pound of cure".

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