Highlights from this issue

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Luminal GI

Helicobacter pylori eradication and MALT lymphoma in Japan

H pylori infection plays a causative role in the development of gastric MALT lymphoma and its eradication leads to a complete remission of disease in the majority of subjects. However, large-scale long-term follow-up outcome after the eradication therapy is still limited, particularly with regard to relapse or progression and survival. In this issue of *Gut*, Nakamura *et al* conducted one of the largest studies with the longest follow-up in Japan. Four hundred twenty patients with gastric low-grade MALT lymphoma who had undergone successful *H pylori* eradication and been followed up for at least 3 years were registered from 21 participating institutes. Three hundred twenty-three patients (77%) responded to *H pylori* eradication. The excellent long-term clinical outcome of gastric MALT lymphoma after *H pylori* eradication was confirmed by the follow-up study ranging from 3.0 to 14.6 years (mean 6.5 years, median 6.04 years); the probabilities of freedom from treatment failure, overall survival and event-free survival after 10 years were 90%, 95% and 86%, respectively (see figure 1). A logistic regression analysis showed that absence of *H pylori*, submucosal invasion determined by endoscopic ultrasonography and t(11;18)/API2-MALT1 were independent predictors of resistance to *H pylori* eradication (see page 507).

Figure 1 Kaplan–Meier curves of 420 patients with gastric MALT lymphoma after *Helicobacter pylori* eradication showing event-free survival.

Are variations in oral microbiota relevant to pancreatic disease?

Pancreatic cancer carries a dismal prognosis and represents a disease that is in dire need of new hypotheses. Recent data suggest an association between pancreatic cancer and oral disease, particularly periodontitis. Chronic pancreatitis is also known to increase the risk of pancreatic cancer and as such, a role for microbial agents is worth exploring. In this issue of *Gut*, Farrell *et al* present the first study showing that variation of oral microbiota diversity is associated with pancreatic cancer. They looked at the oral microbiota in patients with resectable pancreatic cancer, those with chronic pancreatitis and healthy controls. They carried out microbial profiling using the Human Oral Microbe Identification Microarray and identified and verified bacterial candidates by real-time quantitative PCR. They also validated these bacterial candidates by real-time quantitative PCR on an independent cohort of 28 resectable pancreatic cancer, 28 matched healthy control and 27 chronic pancreatitis samples. Their results suggest a fascinating difference in bacterial diversity between health and disease, for example the combination of two bacterial biomarkers (*N elongata* and *S mitis*) yielded a receiver operating characteristic plot area under the curve value of 0.90 (95% CI 0.78 to 0.96, $p < 0.0001$) with a 96.4% sensitivity and 82.1% specificity in distinguishing patients with pancreatic cancer from healthy subjects. Naturally, this work does not clarify whether the association is causative or reactive but nonetheless, we hope that this study will act as a catalyst for researchers to consider a microbial aetiology in the pathogenesis of pancreatic cancer (see page 582).

A better understanding of cancers that are not detected by FOBT

The performance of guaiac faecal occult blood testing (GFOBT) has been assessed in a demonstration pilot programme of biennial GFOBT screening carried out in Scotland between 2000–2007 and that has consisted of three rounds of GFOBT testing. Steele and his colleagues have assessed the cancers that were not detected by GFOBT (“interval cancers”) and report their findings in this issue. They found that of the cancers diagnosed in the screened population, interval cancers comprised 31.2% in the first round, 47.7% in the second and 58.9% in the third. This percentage increase was due to a decline in the numbers of GFOBT detected cancers rather than an increase in interval cancers. Interestingly, they found interval cancer patients had both overall and cancer specific survival that were better compared with cancers arising in the non-screened population. They also found that the percentage of cancers arising in females was significantly higher in the interval cancer group (50.2%) compared with either the screen-detected group (35.3%, $p < 0.001$) or the non-screened group (40.6%, $p < 0.001$) (see table 1). These findings suggest changes in the program are needed to optimise GFOBT colon cancer screening.

Deranged metabolism in colon cancer may provide opportunity for new form of treatment

Cell metabolism can be roughly divided into anaerobic glycolytic metabolism and aerobic oxidative metabolism. It is well known that cancer cells have increased

Table 1 Site and gender distribution of screen-detected, interval and non-screened cancers in all three rounds

Site	Screen-detected, % (n)		Interval, % (n)		Non-screened, % (n)	
	Male	Female	Male	Female	Male	Female
Right colon	17.7 (74)	27.7 (62)	27.3 (85)	37.2 (116)	21.4 (855)	31.8 (849)
Left colon	53.8 (225)	52.2 (117)	40.2 (125)	31.1 (97)	44.3 (1764)	42.6 (1161)
Rectum	28.5 (119)	20.1 (45)	32.5 (101)	31.7 (99)	34.3 (1364)	26.2 (713)

Male versus female in screen-detected: $\chi^2 = 10.95$, $p = 0.009$.

Male versus female in interval: $\chi^2 = 8.3$, $p = 0.016$.

Male versus female in non-screened: $\chi^2 = 85.18$, $p < 0.001$.

glycolytic metabolism, which causes the accumulation of glucose (a reducing sugar) and methionine (an amino acid). Of importance, the reaction between reducing sugars and amino acids can produce lactic acid and carcinogenetic materials such as acrylamide and hydrogen sulphide. Yamagishi and colleagues have studied the metabolites produced by cancer cells in more detail and have found that methionine or its metabolites accumulate in cancer cells, which produces gaseous sulphur-containing compounds such as methanethiol and hydrogen sulphide. They have found that the amount of methanethiol in flatus from colon cancer patients is significantly higher than that from healthy individuals and that preventing the diffusion of sulphur-containing gases inhibited tumour growth (see figure 2). Their results suggest that these metabolites might be used for cancer diagnosis and therapy (see page 554).

Figure 2 Comparison of methanethiol (Rh-CSH component) content in flatus for colon cancer, healthy and silky egg groups. Data for cancer group are plotted on basis of tumour progression (Dukes' classification).

Hepatology

Think of Hepatitis E upon paediatric liver transplantation

Hepatitis E virus (HEV) has been associated with acute and mostly self-limiting hepatitis in developing countries. Recently, HEV hepatitis and even liver failure were observed in pregnancy and following organ transplantation, respectively. This important study from Quebec suggests that HEV is rather common following paediatric liver transplantation. Moreover, HEV may be the cause of abnormal liver function tests in such patients (see figure 3). Since HEV has been found in farm animals and even in cultured strawberries, updated nutritional recommendations and HEV awareness in general should be considered for children

Figure 3 Liver disease activity and hepatitis E virus (HEV) infection. Course of HEV infection and markers of liver disease activity in patient 11 between 2 months and 16.2 years after orthotopic liver transplantation (OLT).

following liver transplantation (see page 597).

A novel approach to treat portal hypertension

Portal hypertension causes dangerous complications of cirrhosis such as variceal bleeding and ascites. Therefore, effective tools to reduce portal hypertension are of great clinical importance. β blockers, vasopressin analogues and TIPS are widely used but are not suitable for every patient. This interesting study from Belgium

proposes a novel approach: electrical vagal nerve stimulation. In a rat model of cirrhosis electrical stimulation decreased portal pressure by lowering intrahepatic resistance via release of vasoactive intestinal peptide (see figure 4). Since vagal pacing has been introduced in the treatment of patients with neuropsychiatric disorders a clinical application for patients with cirrhosis may be feasible. However, as acknowledged by the authors, long-term effects remain to be investigated (see page 604).

Figure 4 Electrical vagus nerve stimulation decreases portal pressure (PP). Both normal (NL) and cirrhotic (TAA) rats were subjected to either hepatic branch vagotomy (HV) or sham-operation (Sham). In cirrhotic rats, 10 Hz stimulation (D) caused a significant decrease in portal pressure.