^{1}H NMR spectroscopic study of blood serum for the assessment of liver function in liver transplant patients

To the Editor,

We read with interest the paper by Tripathi et al [1] on ^{1}H NMR spectroscopic study of blood serum for the assessment of liver function. This was clearly a small scale, preliminary study, but has raised some interesting issues which we wonder if the authors could or have addressed.

The authors note that pre-operative samples were indistinguishable even though there was a wide age range and very varied disease aetiology, and also both sexes were included in the small data set. Were the authors surprised by this observation?

Protein precipitation in serum samples can be variable, even if the time period permitted for clotting is identical. Did the authors see any variation in protein/lipid content in the serum samples? Did they consider using plasma and/or using NMR techniques to suppress protein signals?

We also note that for quantification purposes α glucose was used in a ratio of 36:64 with β glucose. This however is a dynamic equilibrium which alters and therefore could effect the concentration of α glucose estimated, was this a concern to the authors?

It has been reported in the literature that TSP interacts with albumin thus impacting on the utility of TSP as a concentration marker. Did the authors notice much variation in the integrals they measured for TSP [2,3] in their raw data?

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Reply,

We are thankful to Goldsmith et al for their interest in our paper. We did not observe any marked differences in the pre-operative serum samples of the patients. One of the reasons for this may be that all the patients receiving transplants had reached the same metabolic stage, i.e. end stage liver failure and hence we were not surprised.

We only used serum (not plasma) samples for our analysis. We performed the NMR experiments using the CPMG (Carr-Purcell-Meiboom-Gill) pulse sequence which is used to suppress broad signals of macromolecules such as lipids and proteins. This was necessary for the quantitative estimation of low molecular weight metabolites of interest.

In serum samples, most of the signals of glucose except those for C_1'-protons overlap with signals of other metabolites. The resonances of the β anomer corresponding to C_1'-protons are closer to the presaturated water resonance and therefore they were not used for quantitative purposes. The ratio 36:64 for the α and the β anomers was employed as this is an established fact at the physiological pH [1-3]. Further in a separate experiment, we also checked the results with an 800 MHz NMR spectrometer where the resonances for the C1'-protons corresponding to the β anomer were better separated from the water resonance and which determined the ratio of the α and β anomers. This was found to be the same as reported above within experimental errors.

We are aware of the fact that TSP interacts with albumin hence we did not add TSP to the serum samples. This is explicitly mentioned in the experimental section of the paper. We took the amount of TSP in a sealed co-axial glass capillary and inserted that capillary to the NMR tube and therefore it did not mix with the serum samples [2, 3]. In addition, we gave a repetition time of 20 sec so that resonances from all the metabolites and TSP arose from the fully relaxed nuclei. Since TSP was not added to the serum samples, the question of variation in the integrals in the raw data does not arise.

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The diagnostic yield of gastrointestinal investigations also depends on criteria for iron deficiency anaemia

To the Editor

Although Sidhu et al did not define their criteria for iron deficiency anaemia (IDA), a comparison of the diagnostic yield in patients with overt bleeding (OB) versus patients with IDA [1] might potentially be influenced by the choice of criteria to define patients as being iron deficient for the purpose of enrolment in the study. When IDA is a manifestation of non-inflammatory disorders such as angiodysplasia, it is most likely to be characterised by levels of serum ferritin which are in the unequivocal diagnostic range of 15 mcg/l or less, where the likelihood ratio (LR) of IDA is of the order of 51.85 (95% Confidence Interval, 41.53-62.27) [2]. Conversely, when iron deficiency is a manifestation of chronic blood loss resulting from disorders such as those characterised by tumour cells which produce proinflammatory cytokines, the cytokine-dependent increase in serum ferritin levels [3] might generate a perception that co-existence of IDA is unlikely. An extreme example of the co-existence of carcinomas which typically cause chronic blood loss and high-normal to excessively raised levels of serum ferritin was found in a study where colorectal cancer was associated with serum ferritin levels which, in some instances, ranged from 100 mcg/l to 470 mcg/l [4], notwithstanding the fact serum ferritin levels of the order of 100 mcg/l, generate a LR for IDA amounting to only 0.08 (95% CI 0.07-0.09) [2]. Despite this caveat, in one study a serum ferritin level of 100 mcg/l or more was, in fact, deemed to be appropriate to rule out the need for colonoscopy [5]. In yet another study, "predictors of gastrointestinal lesions on endoscopy in patients without gastrointestinal symptoms" were evaluated only in patients who were defined as being iron deficient on the basis of serum ferritin 20 mcg/l or less for men, and 10 mcg/l or less for women, or on the basis of serum iron concentration of 45 mcg/dl or less with a transferrin saturation of 10% or less [6]. Accordingly, when enrolment criteria are unduly restrictive, there is a potential for some selection bias, hence the need to ascertain the degree of stringency with which IDA was defined in the study [1].

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Brown colon (melanosis coli) harbouring pale tumors (adenocarcinoma and an adenomatous polyp)

To the Editor,

A 72-year man was admitted to our hospital because of anemia and chronic constipation. For the latter condition he had been taking antraquinone laxatives for many years. The colonoscopy showed diffuse brown pigmentation throughout the colon and in the descending one an ulcerated neoplasm with a substenosis of the lumen.

The pathological examination of the tissue biopsy

revealed an adenocarcinoma and subsequently a left hemicolectomy was performed. On examination (Fig. 1) the mucosa appeared diffusely dark brownish (left panel) and in the lower half a 2.5 cm neoplasm was found by stretching the intestinal wall (right lower panel). The neoplasm appeared pale, lacking pigment, as well as a little polyp (right upper panel).

On microscopic examination (Fig. 2) the samples from the intestinal wall showed pigment-laden macrophages in the lamina propria and in the submucosa, a finding consistent with melanosis coli. The presence of melanosis pigment was observed in some pericolonic lymph nodes too.

The histology of the neoplasm showed a poorly differentiated infiltrating adenocarcinoma, with slight invasion beyond the border of the muscularis propria (pathologic stage T3bN2).

The polyp was a tubular adenoma with low-grade dysplasia.

Melanosis coli refers to abnormal brown or black pigmentation of the colonic mucosa. It is a relatively frequent finding in colonic biopsies and resection specimens. The pigment storage is a consequence of colonic epithelial cells apoptosis: the deposits of apoptotic cells are ingested by macrophages, which migrate in the lamina propria, where the conversion into lipofuscin pigment occurs by lysosomal enzymes [1]. Since the granules are composed of lipofuscin and not melanin, it has been suggested that this entity might be more precisely labeled "nigrosis" coli, "lipofuscinosis" or "pseudomelanosis" [2] instead of melanosis.

Although previous studies have linked the presence of pseudomelanosis coli to chronic laxative use, especially antraquinones [3] more recently it has been indicated that laxatives are only one and not the exclusive cause of pseudomelanosis [4]. In fact patients affected by inflammatory bowel diseases, diarrhea unrelated to inflammatory bowel diseases, constipation and patients taking non-steroidal anti-inflammatory medication may have colonic pigmentation, in the absence of laxative use [2, 4, 5].

In spite of the relatively common occurrence of peudomelanosis coli, the pigment has been reported infrequently to involve pericolonic lymph nodes [6].

Most of the hyperplastic polyps, adenomas and carcinomas of the colon lack pigment and appear pale endoscopically after formaldehyde fixation as well as on microscopic slides [2, 4, 7]. An explanation for this interesting finding has been provided by showing in colonic adenomas an impaired transition of apoptotic bodies derived from the epithelium into the lamina propria [2]. No definitive associations have been found with the use of laxatives, pseudomelanosis coli and colorectal cancer [4, 6, 8].

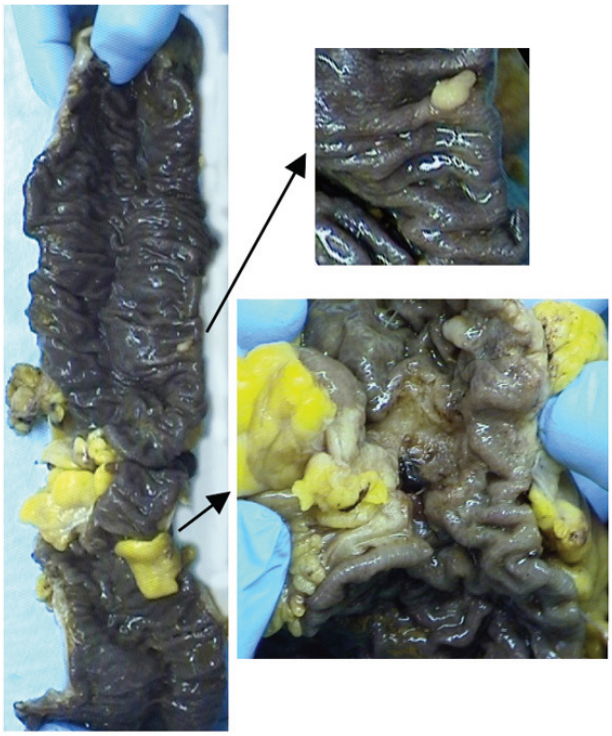

Fig 1. Macroscopic examination of the left hemicolectomy showing the diffuse dark brownish mucosa pigmentation (left) from a little polyp (right upper panel) and an ulcerated neoplasm (right lower panel).

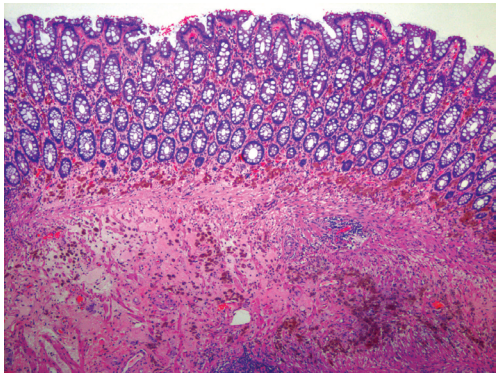

Fig 2. Melanosis with numerous pigment-laden macrophages in non-neoplastic colonic mucosa and submucosa.

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Splenic marginal zone lymphoma in a patient with chronic hepatitis B

To the Editor,

A 38-year-old man was evaluated for a 6-month history of abdominal discomfort, weight loss of 20 kg, and increasing fatigue. He had also noted intermittent low grade fever for two months prior to admission. Past history was remarkable for chronic hepatitis B virus (HBV) infection diagnosed 20 years back; he had received no medication. Physical examination showed hepatomegaly and huge splenomegaly. Significant laboratory data on admission were: haemoglobin 10 g/l, platelet count 20,000 cells/mm^3, lactate dehydrogenase 1,810 IU/l (normal range, 225-450), aspartate aminotransferase 46 IU/l (10-35), alanine aminotransferase 56 IU/l (10-35), and beta-2-microglobulin 7,214 μg/l (700-3,400); HBV DNA levels were increased (2x10^5 copies/ml). No abnormal cells were seen on peripheral blood smear; haemoglobin electrophoresis did not detect thalassaemia. Infection with malaria parasite or leishmania was excluded; hepatitis C virus (HCV) serology, including PCR, was negative. Abdominal and chest tomography confirmed physical findings; liver and spleen parenchyma had normal density without focal lesions and no lymphadenopathy was seen.

Bone marrow biopsy revealed intrasinusoidal small lymphoid cells, a highly characteristic feature of splenic marginal zone lymphoma (SMZL). Lymphoma cells expressed CD20 (Fig. 1) but typically lacked CD5, CD10, bcl6, CD23, CD43, and cyclin D1. The patient was initially given cyclophosphamide and prednizone, which induced tumor lysis syndrome with a dramatic decrease of spleen size, and an improvement of his clinical condition. Splenectomy was eventually performed followed by adjuvant cyclophosphamide, vincristine, doxorubicin, and prednisone administration. Post-chemotherapy histopathological assessment of spleen sections showed no neoplastic cells. Lamivudine 100 mg/d was started prior to chemotherapy administration and 6 months later HBV DNA was undetectable. A relapse occurred 3 years later with generalized lymphadenopathy and liver lesions in association with a viral breakthrough. A complete remission was attained with fludarabine, rituximab, and cyclophosphamide and the patient remains well on adefovir after two years of follow up.

SMZL is an indolent splenic B-cell lymphoproliferative disorder, which accounts for less than 1% of non-Hodgkin lymphomas and affects primarily elderly people [1]. Most patients present with moderate-to-massive splenomegaly without lymphadenopathy. Lymphocytosis may be absent while severe thrombocytopenia occurs only rarely. Bone marrow biopsies can be diagnostic, obviating the need for spleen histology. Treatment includes splenectomy with or without chemotherapy [1].

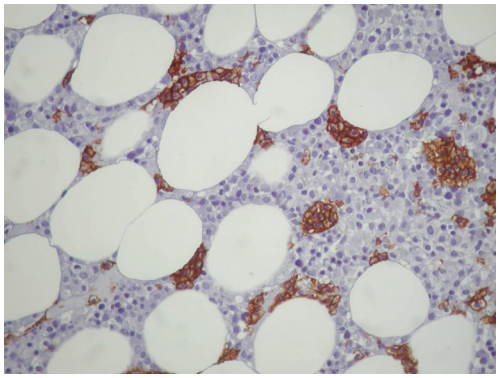

Fig 1. Intrasinusoidal bone marrow infiltration characteristic of splenic marginal zone lymphoma with CD20 positive lymphoma cells (immunostaining, magnification X 250)

The histogenesis of SMZL is obscure. Recently, an association with HCV has been suggested [2]. Chronic HBV infection has been involved in the pathogenesis of B-cell non-Hodgkin lymphomas [3], including two cases of SMZL [4, 5]. HBV gene products have been identified in nodal and bone marrow lymphocytes, spleen, and endothelial cells of tumor tissues of leukemia and lymphoma patients [6, 7]. HBV has been suggested to stimulate expression, production, and release of haematopoietic tumor growth factors, eventually leading to lymph cell proliferation [6]. Suppression of lymphocytic p53 function by HBV-encoded proteins [8] and chronic antigenic stimulation could also promote an abnormal B-cell proliferation [3].

In **conclusion**, we report the third case of SMZL occurring in the course of chronic HBV infection. Though a direct association of HBV with SMZL cannot be asserted at present, its potential pathogenetical role warrants further investigation.

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Acute pancreatitis during pegylated interferon therapy in a patient with chronic hepatitis B

To the Editor,

Acute pancreatitis (AP) as a side effect during Interferon (IFN) therapy is well established by recurrence cases after the restarting of the therapy [1, 2]. However, its responsibility in the occurrence of AP in chronic hepatitis patients is rarely reported in the literature [2-7]. If human immunodeficiency virus (HIV) co-infection is excluded, there are 49 cases of AP attributed to the use of standard IFN in chronic hepatitis C patients [2, 3] and only 5 cases associated to the use of Pegylated (PEG) IFNα-2b and ribavirin [2, 4-7]. To our knowledge, we describe the first case of AP occurring after six months of PEG IFNα-2a therapy in a patient affected by chronic hepatitis B.

A 47-year-old man was followed for chronic hepatitis B mutant pre-core. He had no concomitant medical disorders, no drug usage or alcohol history. His aminotransferase (ALT, AST) serum levels were elevated (ALT = 69 U/L, AST = 58 U/L), HBV DNA was 177,000 copies/mL by PCR and abdominal ultrasonography was normal. The histological study of the liver biopsy concluded at the A2 F2 Metavir score. PEG IFNα-2a (Pegasys®) was started subcutaneously 180 µg/week, the monthly monitoring showed a normalization of aminotransferases and a negative viremia at the third month. The patient developed at the sixth month of the antiviral therapy, severe epigastric pain radiating to his back with nausea and food vomiting. Clinical examination was normal. Laboratory testing showed high levels of serum lipase 2,255 U/L (N: 114 - 286 U/L), amylase 583 U/L (N: 25 - 115 U/L) and C-reactive protein (CRP) 57 mg/L (N: 0.5 - 3.0 mg/L). Blood cells count, AST, ALT, alkaline phosphatase, total bilirubin, calcium, cholesterol and triglycerides were within normal limits. Abdominal ultrasonography was normal: normal gallbladder and common bile duct, no gallstones were noted and the pancreas was normal. Abdominal computed tomography (CT) scan showed a normal pancreas, stage A of Balthazar. Magnetic resonance cholangiopancreatography (MRCP) was also normal. Diagnosis of moderate AP induced by Pegasys® was suggested. Pegasys® was stopped and the patient underwent supportive care. The outcome one week after cessation of the antiviral therapy was favourable with clinical and biological improvement. Pancreatic and biliary ultrasound endoscopy performed four weeks later was normal. Patient refused to continue IFN therapy and did not develop any recurrence of AP and no virological relapse during eight months of follow-up.

IFN-induced AP is rarely reported in the literature. This complication occurred within two hours and eight months in patients treated with IFN and the resolution period of symptoms was less than three months [2, 3]. It occurred within one and seven weeks in patients treated with PEG IFNα-2b; the pancreas was edematous at CT scan in four cases [2, 4, 6, 7] and normal in one case [5]. The resolution period of symptoms was rapid in these patients. Our patient had no alcohol history and no potential cause of AP; he developed AP at the sixth month of PEG IFNα-2a therapy with a favourable outcome after stopping the therapy, suggesting a probable drug-induced pancreatitis [8].

In **conclusion**, AP during PEG IFN therapy in chronic hepatitis C or B patients is a rare complication, but can occur at any time of the IFN therapy. So, we underline the importance of clinical and biological monitoring in these patients for an early diagnosis of AP.

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A tough case to swallow: esophageal intramural pseudodiverticulosis

To the Editor,

Esophageal intramural pseudodiverticulosis (EIPD) is a benign and rare condition often associated with a significant impact on the quality of life. The diagnosis is often delayed because of failure to recognize its stigmata during endoscopy. We present a case of recurrent dysphagia and food impaction due to EIPD.

A 76-year old man presented with a 3-year history of intermittent dysphagia, esophageal food impaction, recurrent Candida esophagitis and weight loss of 29 kg in the past years. His medical history consisted of type 2 diabetes and hypertension. Physical examination was unremarkable with a BMI of 31.2 kg/m2. Upper endoscopy three years ago revealed a benign stricture in the proximal esophagus, successfully treated with endoscopic dilatation. Subsequently, several upper endoscopy series were performed in the following years due to persistent dysphagia. These frequently showed a Candida esophagitis and reflux disease despite repeated medical treatment for both conditions. Recurrent esophageal stricture could not be detected. In order to rule out a small Zenker's diverticulum, a barium esophagogram was performed showing typical signs of EIPD (Fig. 1).

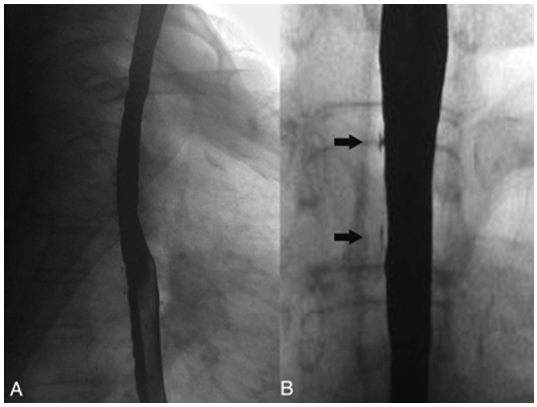

Fig 1. Barium swallow showing multiple small esophageal outpouchings (arrows).

A short time later the patient presented with acute dysphagia due to food impaction. The ensuing upper endoscopy revealed a circular mucosal erosion, located exactly at the previously reported stricture. A large food bezoar was located in the stomach and had probably spontaneously passed and dilated the esophageal stricture. Additionally, multiple small esophageal diverticula, about 1-2 mm in diameter, which could have been easily overlooked, were located mainly in the proximal half of the esophagus (Fig. 2). Extensive signs of peptic esophagitis were present in the distal esophagus. Stomach and duodenum were normal. Our patient has remained asymptomatic for 16 months since the last upper endoscopy.

Esophageal intramural pseudodiverticulosis was first described by Mendl et al in 1960 [1]. Since then about 250 cases of EIPD have been reported in literature but the true incidence remains unclear. There appears to be a slight male predominance (male: female ratio 1.4:1) with over half of the patients being in their 7th and 8th decade of life [2]. Diabetics, patients with chronic GERD and alcohol abusers may be affected more frequently. Esophageal intramural pseudodiverticulosis is a rare, benign cause of dysphagia associated with multiple small diverticula, (proximal) esophageal strictures (70-90%) and persistent Candida esophagitis (50%) [3]. While speculation continues regarding the etiology, chronic inflammation due to either reflux or (Candida) infection might be a causative factor [4]. A barium esophagogram is the modality of choice since the small orifices of the diverticula are often missed during endoscopy, as in this case. The ostia of the pseudodiverticuli are only seen in about 20% of cases [3,5]. Treatment is symptomatic, i.e. acid suppression, antimycotics or endoscopic dilatation in case of strictures. Despite these treatment options, patients will often experience recurrence of symptoms but may remain asymptomatic for many months in between. In conclusion, EIPD is an unusual cause of dysphagia, easily missed by endoscopy. Typical signs can be seen on a barium esophagogram.

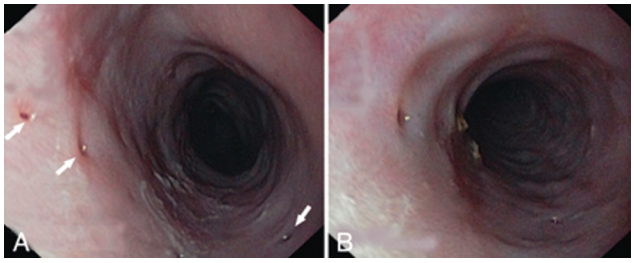

Fig 2. Upper endoscopy showing multiple small ostia of the pseudodiverticuli (arrows).

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Helicobacter pylori infection and correlation with upper gastrointestinal pathologies: an eleven-year trend

To the Editor,

Helicobacter pylori (HP) infection is associated with significant gastrointestinal (GI) pathologies and eradication has been widely recommended and practiced [1-3]. This study assessed the HP infection trend and its correlation with upper GI pathologies seen in a developing Southeast Asian nation over an 11 year period.

All upper digestive endoscopies (EDGs) (17,159) performed between 1994 and 2004 were retrospectively reviewed. Procedures with the testing of HP (CLO Test®, Kimberly-Clarke, Australia) for the first time (8,323, 48.5%) were used to assess the prevalence of HP infection. Data on gastric and esophageal cancer were obtained from the National Cancer Registry. The incidences were then age standardized to the world population and presented as Age Standardized Rate (ASR). Data were coded and entered into the SPSS (Version 10.0, Chicago, IL, USA) program for analysis. The Student's *t*-test and the Chi-squared test were used for analysis. Level of significance was considered when $p<0.05$.

There was a significant decline in the prevalence of HP infection from 53.5% (1994) to 25.6% (2004, $p<0.05$ for trend).

Overall, there was a marked decline in the overall incidence of duodenal ulcer from 22.2/100 EGD (1994) to 12.5/100 EGD (2004) but only a minor decline for gastric ulcer (10.9/100 to 9.2/100 EGD) (Fig. 1). More importantly, there was a significant decline in the prevalence of HP positive peptic ulcer disease from 71.6% (1994) to 21.3% (2004) ($p<0.001$ for trend)

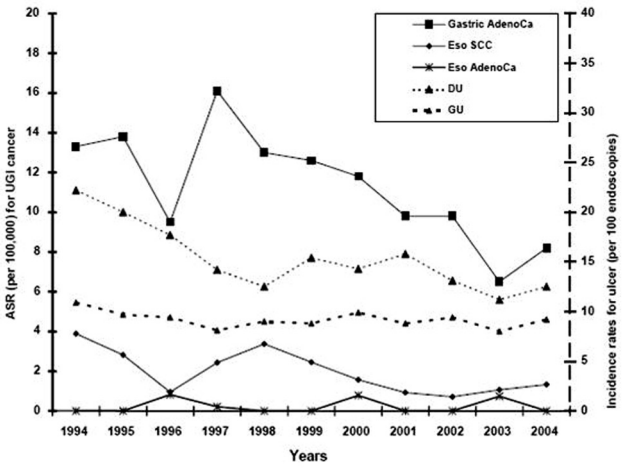

Fig 1. Prevalence of duodenal and gastric ulcers (per 100 EGDs) and the ASR incidence of gastric adenocarcinoma, esophageal adenocarcinoma and SCC (per 100,000 population).

The overall ASR incidence for gastric adenocarcinoma was 11.3/100,000 population, declining from 13.3/100,000 population (1994) to 8.2/100,000 (2004). The overall ASR incidence for esophageal adenocarcinoma remained low (0.23/100,000) without any obvious trend. The overall ASR for esophageal squamous cell carcinoma (SCC) was 1.95/100,000, declining from 3.89/100,000 (1994) to 1.33/100,000 (2004).

Overall, our study showed a decline in the prevalence of HP infection over the 11 year period. Other studies have shown similar findings but most had been completed in developed nations where standards of living and health care provision are good [4, 5]. The only study from a developing nation reporting such a decline was from Turkey [6].

There are several reasons that may account for this trend. Eradication of HP has been widely practiced for quite sometime and widespread use of antibiotics for minor infections may be important. However, the continuous improvement in health care provisions and living standards is probably the most important factor.

The declining infection in our local setting correlated with the decline in the prevalence of PUD, especially duodenal ulcer. The less marked decline of gastric ulcer may be due to the increasing prevalence of non steroidal anti-inflammatory drugs associated or idiopathic PUD [7]. A declining trend was also observed in the incidence of gastric cancer. The incidence of esophageal adenocarcinoma has been reported to be increasing along with a decline in esophageal SCC. [8] In our study, only a declining trend for esophageal SCC was seen. However, the overall incidence of esophageal adenocarcinoma was low.

In **conclusion**, our study showed a declining prevalence of HP infections in a developing Southeast Asian nation. This correlated with the decline in HP associated pathologies.

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Giant malignant gastrointestinal stromal tumor presenting as an intraabdominal abscess

To the Editor,

A 74 year-old diabetic woman presented with epigastric pain and weight loss for two months. She had a fever of 38.5^{0}C and a slight tenderness on the epigastrium. She had anemia, a WBC of 28,700/mm^3 and moderately elevated LDH and bilirubin. External compression and an intraabdominal mass with central necrosis were demonstrated by upper gastrointestinal endoscopy and CT, respectively (Fig. 1). Under IV antibiotics, en block excision of a 20x15x16 cm mass with wedge resection of the stomach, splenectomy and distal pancreatectomy was performed without any complication. Cultures from the abscess within the mass revealed *Enterococcus* spp. and *P. aureginosa*.

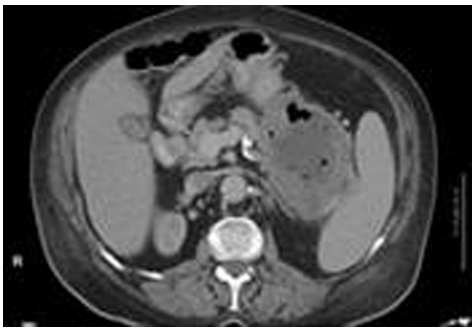

Fig 1. Enhanced CT scan of the abdomen with a large mass lesion originating from the stomach wall and extending to the spleen and pancreas; air and fluid levels are seen suggesting central necrosis.

Histopathologic examination demonstrated a GIST with spindle cells infiltrating the stomach wall. Mitotic and Ki-67 (MIB-1) indexes were >5/50 high power fields (HPF) and >10 %, respectively (Fig. 2). Immunohistochemical staining with CD117, vimentin, CD34, and actin antibodies were positive. Imatinib was started in the third postoperative month for newly detected liver metastases .

GIST is seen most commonly in the stomach (50-70%). Tumor size >10 cm, mitotic index>5/50 HPF, tumor necrosis and MIB-1 index≥10% are predictors of the worse prognosis. Function-sparing resection en block with involved organs avoiding tumor rupture is the mainstay

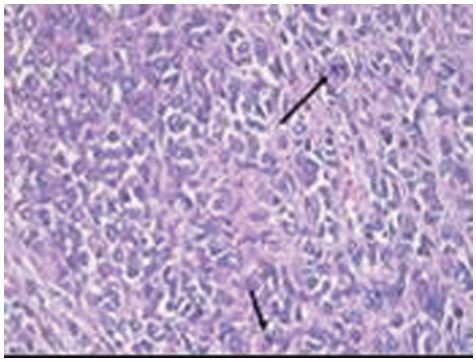

Fig 2. Gross appearance of a gastrointestinal stromal tumor with central necrotic and haemorrhagic area within multiple septa (arrow in the tumor); spleen is attached to the tumor (arrow on the lower corner). Atypic spindle cells with widespread mitoss. Arrows: mitosis (x400, H&E) (B).

treatment for malignant GISTs. Imatinib has been used in metastatic or unresectable GISTs and recently as an adjuvant therapy in high risk tumors [1].

Gastric abscess may rarely present as a prolonged illness with minimal or no signs of infection as was the case in our patient [2]. We thought that the presence of diabetes mellitus and intratumoral necrosis and focal hemorrhage which predominate in large tumors contributed to the abscess development [2-4].

External compression seen in upper gastrointestinal series and thickened gastric wall in US, CT, and MR are helpful in the diagnosis of gastric abscess. Air-fluid levels and mass lesions might also be detected by imaging techniques. A gastric abscess is seen as a submucosal mass with antral thickening and reddened folds in endoscopy. Endo-ultrasonographic drainage might be considered although there are scarce reports. Endoscopic drainage in cases with a fistulous opening formed either spontaneously or due to endoscopic biopsy, might be a definitive treatment in gastric abscesses and a bridge to surgery in mass lesions with abscess [2-6]. Although percutaneous biopsy has been used successfully in the diagnosis of GISTs, the risk of tumor implantation which was considered due to a recent report of a tract metastasis after a laparoscopic biopsy of a GIST, and the presumed low chances of success due to the multiple septa in the lesion, precluded percutaneous or laparoscopic drainage in our case [7, 8].

This rare case of an abscess in a GIST is unique because the abscess occurred spontaneously; however, it was not spontaneously drained into the stomach although it was larger than in the previously reported three cases [3-5]. This made the diagnosis even harder since the presentation is usually vague. We recommend function-sparing resection of the lesion including the abscess and involved organs after a short period of systemic antibiotics and optimization of the general condition of the patient.

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Underweight in adult celiac patients in the community; is screening program necessary in low weight individuals?

To the Editor,

Recently we studied celiac disease (CD) in patients with gastrointestinal (GI) symptoms in an Iranian community [1]. According to our findings and similar studies, related malabsorptive symptoms, such as diarrhea/steatorrhea and abdominal distension may not be observed in many cases necessarily [1, 2] but growth failure in terms of length (or height) or weight may be the earliest sign of the disease [3].

We studied the body mass index (BMI) in celiac patients diagnosed in a population-based study, using a well-matched case-control analysis in order to obtain updated information regarding the underweight in celiac patients [1, 4, 5]. From a total of 670 individuals with GI symptoms, 25 individuals were positive for anti-transglutaminase antibodies tTGA [1]. Seventy healthy people were selected from the same database [5]. These healthy people were selected from the population in which CD patients were drawn up but without any GI symptoms. They matched according to demographic factors (sex and age) with CD patients in order to compare height, weight and body mass index. The study was approved by the Ethics Committee of RCGLD.

A positive tTGA test was found in 22 out of the 670 investigated subjects (17 women, 5 men), and a positive tTGG test was found in 3 of 8 IgA deficient and matched with 70 healthy subjects (44 women, 22 men) entered to this case control study.

The mean ± SD for body mass index in the tTG positive patients and in healthy subjects were 23.7±2.38 and 26.8±4.3, respectively (P<0.001). Twenty two patients were observed with a BMI<25, three patients in the overweight group (BMI: 25-30) and no patient in the obese group (BMI>30), in contrast to the control group where 26 subjects were observed with BMI<25, 26 subjects were overweight and 18 were obese (P<0.001). Table I shows the anthropometric measurements including weight, height and BMI according to sex, indicating that all anthropometric measurements were significantly lower in CD patients as compared to healthy controls in both men and women.

Table I. The mean ±sd of anthropometric measurements for 22 CD patients and 70 sex- and age-matched healthy control subjects

	Women			Men		
	Patients	Control subjects	P-Value	Patients	Control subjects	P-Value
Weight (kg)	55.0 ± 5.5	76.8 ± 13.3	<0.001	62.0 ± 8.2	68.5 ± 11.1	0.03
Height (cm)	162.0 ± 5.9	173.1 ± 17.9	0.04	163.2 ± 5.5	158.4 ± 8.5	0.02
BMI (kg/cm2)	20.9 ± 0.7	25.8 ± 4.1	<0.001	23.2 ± 2.4	27.4 ± 4.4	<0.001

In contrast with the Dickey and Kearney study [6], which states that few celiac patients are underweight at diagnosis time our results indicated that a large group of CD patients in our community were underweight and there were differences in anthropometric measurements between CD patients and healthy controls. Other studies reported at least up to 33% of CD patients being underweight [7, 8].

Given the fact that all patients who entered in this study were diagnosed for the first time and most of them were adults, it can be concluded that the low weight and height in adult CD patients in our community are associated with a lower total daily energy intake because of misdiagnosed disease. We did not consider dietary components and life stress. This is a potential limitation of this study.

On the other hand, the high number of underweight individuals must draw the attention of physicians, during clinical practice, to consider celiac disease at the top of list of causes of low body weight and there is a real necessity for providing clinical practice and screening program for early diagnosis of celiac disease in the community and for starting a gluten-free diet.

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