Table 1 Allele frequency of the Val26 mutation in German cohorts of ICP patients and controls

	n	26V allele frequency	OR	95% CI	p Value
Controls	100	0.48	0.718	0.45 to 1.15	0.147
Patients	64	0.398			

CI, confidence interval; ICP, idiopathic chronic pancreatitis; OR, odds ratio.

Table 2 Allele frequencies of Val26 mutations in individual ethnic groups

Population	Ethnic origin	(n)	pG (Val26)
CEPH	Mixed white	92	0.320
Pooled_CEPH	White	94	0.323
HapMap-CEU	European	55	0.355
SC_95_C	White	45	0.367
HapMap-YRI	Sub-Saharan African	52	0.394
TSC_42_C	White	41	0.430
JBIC-allele	Japanese	732	0.493
HapMap-JPT	Asian	44	0.523
HapMap-HCB	Asian	43	0.547
Total		1198	0.452 ± 0.042

see refSNP ID: rs12338 at http://www.ncbi.nlm.nih.gov/SNP/snp_ref.cgi?rs=12338.

Table 2 shows wide variation in frequency (0.32 to 0.547), with Val26 being the commonest allele in two of the cohorts. The mean Val26 frequency of 0.452 (n = 1198; 95% confidence interval, 0.410 to 0.494) approaches that of our German control subjects (0.48) and is not different from our pancreatitis patients.

We conclude that a high frequency of Val26 in a given cohort merely represents a polymorphic allele variation and not a susceptibility factor for idiopathic chronic pancreatitis. While this is likely to be the case in most ethnic groups it does not explain the findings of Mahurkar and coworkers,⁴ who found significantly fewer Val26 alleles in two Indian control cohorts. Their findings may either indicate subtle differences in the ethnic background of their patients and controls or they could be explained by a specific role for cathepsin B in tropical rather than idiopathic chronic pancreatitis. Further investigations addressing the role of cathepsin B in more common varieties of pancreatitis and in different ethnic groups are still urgently needed.

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F U Weiss, C-O Behn, P Simon, M Ruthenbrger
Department of Medicine A, Ernst-Moritz-Arndt
Universitt, Friedrich-Loefflerstr 23A, 17475
Greifswald, Germany

W Halangk

Department of Experimental Surgery, Otto-von-Guericke Universitt, 39120 Magdeburg, Germany

M M Lerch

Department of Medicine A, Ernst-Moritz-Arndt
Universitt, Friedrich-Loefflerstr 23A, 17475
Greifswald, Germany

Correspondence to: F U Weiss, Department of Medicine
A, Ernst-Moritz-Arndt Universitt, Friedrich-Loefflerstr
23A, 17475 Greifswald, Germany;
ulrich.weiss@uni-greifswald.de

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References

- 1 **Lerch MM, Halangk W.** Human pancreatitis and the role of cathepsin B. *Gut* 2006;**55**:1228–30.
- 2 **Halangk W, Lerch MM, Brandt-Nedelev B, et al.** Role of cathepsin B in intracellular trypsinogen activation and the onset of acute pancreatitis. *J Clin Invest* 2000;**106**:773–81.
- 3 **Kukor Z, Mayerle J, Krger B, et al.** Presence of cathepsin B in the human pancreatic secretory pathway and its role in trypsinogen activation during hereditary pancreatitis. *J Biol Chem* 2002;**277**:21389–96.
- 4 **Mahurkar S, Idris MM, Reddy DN, et al.** Association of cathepsin B gene polymorphisms with tropical calcific pancreatitis. *Gut* 2006;**55**:1270–5.
- 5 **Rossi L, Pfutzer RH, Parvin S, et al.** SPINK1/PSTI mutations are associated with tropical pancreatitis in Bangladesh. A preliminary report. *Pancreatol* 2001;**1**:242–5.
- 6 **Weiss FU, Simon P, Bogdanova N, et al.** Complete cystic fibrosis transmembrane conductance regulator gene sequencing in patients with idiopathic chronic pancreatitis and controls. *Gut* 2005;**54**:1456–60.

Familial association of benign pancreatic hyperenzymaemia and pancreatic cancer

Benign pancreatic hyperenzymaemia (BPH) is a syndrome characterised by a chronic increase in serum pancreatic enzymes in the absence of pancreatic disease.^{1–5} In March 2000 we saw a woman who had this form of hyperenzymaemia, whose mother had died of pancreatic cancer. Prompted by this observation, we undertook a prospective study to determine whether there is a familial association between BPH and pancreatic cancer. Between June 2000 and October 2006, we saw 68 subjects with BPH (42 male, 26 female; age range 8 to 72 years, mean age 45.7 years). They were questioned about the presence of pancreatic cancer in members of their families. The subjects who had relatives with pancreatic cancer and their immediate family members were included in

the study. In addition to serum pancreatic enzymes, all underwent magnetic resonance imaging (MRI) with secretin stimulation and endoscopic ultrasound for detailed study of the Wirsung duct and pancreatic parenchyma.

Among the 68 subjects who had BPH, six had relatives who had died of pancreatic cancer. The demographic and clinical characteristics of these six subjects are shown in table 1. MRI was normal in all six, while endoscopic ultrasonography was normal in five; in the sixth (subject 6), parenchymal abnormalities (lobularity and hyperechoic strands) were present in the head of the pancreas. Two of the 10 relatives of these six subjects had pancreatic hyperenzymaemia; in both these subjects, MRI and endoscopic ultrasonography results were normal (table 1). Among the six study subjects there were nine relatives who had died of pancreatic ductal cancer (table 1). Four of the six had only one relative; one (subject 2), had two family members with pancreatic cancer, and another (subject 6) had three relatives with pancreatic cancer. The diagnosis of pancreatic cancer was based on histology in seven of the nine subjects, and on clinical and imaging findings in the other two.

Our findings show that there may be a familial association between BPH and pancreatic cancer. The significance of this association is not clear. BPH probably results from a defect in the passage of enzymes from acinar cells into the blood which results in greater than normal quantities in the circulation.⁴ The anomaly is benign, generally being discovered during a routine blood analysis which includes amylase determination. At this point it is not known whether the occurrence of BPH in a family member or a relative of someone who has pancreatic cancer is incidental or the result of an underlying connection between the two conditions.

In order to see whether there were pancreatic lesions in subjects included in the study, they underwent MRI with secretin stimulation as well as endoscopic ultrasonography, which are generally sensitive for the detection of even small pancreatic lesions.⁶ MRI was normal in all six subjects, while endoscopic ultrasonography was normal in all but one; this subject had three family members who had died of pancreatic cancer. The parenchymal abnormalities were lobularity and hyperechoic strands in the pancreatic head—lesions that have been seen by other investigators^{7–9} in relatives of patients with pancreatic cancer, primarily subjects who had two or more relatives with the tumour. These changes, together with others,^{7–9} have been shown to be associated with pancreatic dysplasia, a precursor lesion of pancreatic cancer.¹⁰ Our study subject who had pancreatic abnormalities on endoscopic ultrasonography will be carefully followed, both clinically and ultrasonographically.

In conclusion, our study shows that persistent pancreatic hyperenzymaemia may be encountered in family members of patients with pancreatic cancer. The significance of this association is not clear, but it is possible that these individuals could be at increased risk of pancreatic cancer.

L Gullo, M Migliori

Institute of Internal Medicine, Sant'Orsola Hospital,
University of Bologna, Bologna, Italy

P Fusaroli, G Caletti

Unit of Gastroenterology and Digestive Endoscopy,
Castel San Pietro Terme, University of Bologna,
Bologna, Italy

Table 1 Demographic and clinical data of the members of the six families included in the study

Study subject and involved relatives	Age A* (years)	Age B* (years)	Pan-iso IU/l (nv, <53 IU/l)	Lipase IU/l (nv, <60 IU/L)	MRI	EU	Loc	Age at death (years)
Subject 1 (male)	45	51	210	54	Normal	Normal	–	–
Father	–	–	–	–	–	–	Body	84
Subject 2 (female)	58	65	102	156	Normal	Normal	–	–
Brother	–	–	–	–	–	–	Head	71
Mother	–	–	–	–	–	–	Head	80
Subject 3 (female)	51	54	111	387	Normal	Normal	–	–
Father	–	–	–	–	–	–	Head	61
Subject 4 (male)	43	50	104	127	Normal	Normal	–	–
Father	–	–	–	–	–	–	Tail	76
Subject 5 (male)	24	33	178	238	Normal	Normal	–	–
Father†	62	66	206	273	Normal	Normal	–	–
Paternal aunt	–	–	–	–	–	–	Head	55
Subject 6 (male)	48	51	88	107	Normal	Pathological	–	–
Father†	70	85	115	150	Normal	Normal	–	–
Paternal aunt	–	–	–	–	–	–	Head	76
Paternal uncle	–	–	–	–	–	–	Head	80
Paternal great aunt	–	–	–	–	–	–	Head	82
Mean	44.8‡	50.6‡	139.2	186.5				73.8
Median	47.0‡	52.0‡	141.0	182.5				65.5

*Age A, age at the first discovery of hyperenzymaemia; Age B, age at the time of this study.

†Relatives with pancreatic hyperenzymaemia but no evidence of cancer.

‡The ages of the fathers of subjects 5 and 6 are not included.

EU, endoscopic ultrasonography; Loc, location of pancreatic cancer; MRI, magnetic resonance imaging; nv, normal value; Pan-iso, pancreatic isoamylase.

Correspondence to: Professor Lucio Gullo, Institute of Internal Medicine – PAD 11, Sant' Orsola Hospital, Via Massarenti 9, 40138 Bologna, Italy; lucio.gullo@unibo.it

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References

- Gullo L. Chronic nonpathological hyperamylasemia of pancreatic origin. *Gastroenterology* 1996;**110**:1905–8.
- Gullo L. Familial pancreatic hyperenzymemia. *Pancreas* 2000;**20**:158–60.
- Gullo L, Ventrucci M, Barakat B, et al. Effect of secretin on serum pancreatic enzymes and on the Wirsung duct in chronic nonpathological pancreatic hyperenzymemia. *Pancreatol* 2003;**3**:191–4.
- Gullo L. Day-to-day variations of serum pancreatic enzymes in benign pancreatic hyperenzymemia. *Clin Gastroenterol Hepatol* 2007;**5**:70–4.
- Gullo L, Migliori M. Benign pancreatic hyperenzymemia in children. *Eur J Pediatr* 2007;**166**:125–9.
- Sahai AV. EUS and chronic pancreatitis. *Gastrointest Endosc* 2002;**56**(suppl):S76–81.
- Brentnall TA, Bronner MP, Byrd DR, et al. Early diagnosis and treatment of pancreatic dysplasia in patients with a family history of pancreatic cancer. *Ann Intern Med* 1999;**131**:247–55.
- Kimmy MB, Bronner MP, Byrd DR, et al. Screening and surveillance for hereditary pancreatic cancer. *Gastrointest Endosc* 2002;**56**:S82–6.
- Canto MI, Goggins M, Hruban RH, et al. Screening for early pancreatic neoplasia in high-risk individuals: a prospective controlled study. *Clin Gastroenterol Hepatol* 2006;**4**:766–81.
- Hruban RH, Goggins M, Parsons J, et al. Progression model for pancreatic cancer. *Clin Cancer Res* 2000;**6**:2969–72.

Safe endoscopic polypectomy of jejunal polyps with a detachable snare during double balloon enteroscopy

We read with interest the article by Yen *et al* (*Gut* 2007;**56**:12) on a patient with obscure gastrointestinal bleeding in whom a juvenile polyp 1 cm in size, with a shallow ulcerated

surface, was found in the jejunum on double balloon enteroscopy (DBE). Because the patient was receiving regular dialysis and because of the hypervascular nature of the polyp, it was resected surgically. In such cases, however, we believe that endoscopic polypectomy can safely be undertaken with the use of a detachable snare.

Major complications of endoscopic polypectomy are bleeding and perforation, which are most commonly associated with the removal of large polyps with thick stalks.¹ For safer removal of large polyps, a detachable snare is designed for endoscopic ligation instead of a surgical suture.¹ The snare is composed of an attached nylon loop and an operating part,^{1,2} 2300 mm in working length, which makes the snare available for DBE. After the snare is placed at the base of the stalk, tightened around the stalk, and left in place to ensure haemostasis, endoscopic polypectomy is done near the head of the polyp.^{1,2} Endoscopic polypectomy of large pedunculated polyps with a detachable snare is reported to be safer than conventional polypectomy without the snare.^{1,2} In our case series with the use of the snare, neither immediate nor delayed bleeding occurred in any patient with a bleeding tendency.¹

Juvenile polyps have been considered to be benign hamartomas or inflammatory growths with little or no malignant potential.² They are common in children under the age of 10 years, and are generally located in the colon. Because juvenile polyps often manifest initially with bleeding and are usually pedunculated, endoscopic polypectomy is often indicated.² We reported a one year old girl with a large juvenile polyp in the descending colon, in whom endoscopic polypectomy with a detachable snare was successfully carried out without complications.² The resected pedunculated polyp with an eroded surface was 2 cm in size, and several arteries were present in the thick stalk.

Before the recent advance of DBE, our routine approach for small bowel diseases was transenterotomy panenteroscopy, assisted by laparoscopy with mini-laparotomy, which can investigate the entire small bowel with a standard endoscope.³ DBE is a novel technique for visualising the entire small bowel, either by

a peroral or a peranal approach, and provides high diagnostic yields and therapeutic capabilities such as polypectomy.⁴ During DBE, successful endoscopic polypectomy was reported in patients with Peutz–Jeghers syndrome.⁴ All 18 polyps, 1–6 cm in size, in the small bowel were resected without bleeding or perforation. We therefore believe that endoscopic polypectomy of jejunal polyps with a detachable snare during double balloon enteroscopy can be an effective and safe alternative.

M Matsushita, M Shimatani, K Uchida, K Okazaki

Third Department of Internal Medicine, Kansai Medical University, Osaka, Japan

Correspondence to: Dr M Matsushita, Third Department of Internal Medicine, Kansai Medical University, 2-3-1 Shinmachi, Hirakata, Osaka 573-1191, Japan; matsu-mit@hirakata.kmu.ac.jp

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References

- Matsushita M, Hajiro K, Takakuwa H, et al. Ineffective use of a detachable snare for colonoscopic polypectomy of large polyps. *Gastrointest Endosc* 1998;**47**:496–9.
- Matsushita M, Hajiro K, Okazaki K, et al. A large juvenile polyp in a 1-year-old child safely removed by colonoscopic polypectomy with a detachable snare. *Gastrointest Endosc* 2000;**52**:118–20.
- Matsushita M, Hajiro K, Takakuwa H, et al. Laparoscopically assisted panenteroscopy for small bowel diseases: trans-enterotomy versus peroral approach. *Gastrointest Endosc* 2000;**51**:771–2.
- Ohmiya N, Taguchi A, Shirai K, et al. Endoscopic resection of Peutz–Jeghers polyps throughout the small intestine at double-balloon enteroscopy without laparotomy. *Gastrointest Endosc* 2005;**61**:140–7.

Author's reply

We agreed with Dr Matsushita's opinion that snare polypectomy could be a therapeutic option in addition to surgical resection in our reported case. With the advent of double balloon enteroscopy, endoscopists are now