Smoking promotes the development of alcoholic pancreatitis

Alcohol consumption is known to be the principal cause of pancreatitis. Although smoking has also been implicated as a risk factor, its effects on the development of the disease have not been widely investigated.

Maisonneuve *et al.* conducted a retrospective, multicenter US and European cohort study in 934 patients of known smoking status with chronic alcoholic pancreatitis. The aim was to evaluate the impact of smoking on the age at diagnosis of pancreatitis, and on the development of pancreatic calcification (as diagnosed by abdominal radiography) and diabetes (defined as raised fasting blood glucose level or an abnormal glucose tolerance result). The analyses were adjusted for gender, age, center and alcohol consumption.

Mean age at diagnosis of pancreatitis was 4.7 years lower in smokers compared with non-smokers. At the time of diagnosis of pancreatitis, calcification was observed in 40% of males and 34% of females overall and was more prevalent in smokers than non-smokers. The presence of diabetes at diagnosis was noted in 21% of males and 20% of females and showed no association with smoking; however, development of diabetes after diagnosis occurred in a greater proportion of smokers than non-smokers. The degree of tobacco consumption (<1 pack/day or >1 pack/day) had no significant effect on the correlation between smoking and calcification or diabetes.

The authors conclude that smoking is an independent risk factor for earlier diagnosis of chronic alcoholic pancreatitis and the development of calcification and diabetes.

Original article Maisonneuve P *et al.* (2005) Cigarette smoking accelerates progression of alcoholic chronic pancreatitis. *Gut* **54:** 510–514

Similarities in familial and sporadic gastrointestinal stromal tumors

Recently there has been considerable interest in molecular-targeted therapies for gastrointestinal stromal tumors (GISTs). To understand more about this hereditary syndrome, Li *et al*. evaluated GISTs with a germline *KIT* oncogene mutation in a kindred of six family members over four consecutive generations. Members of the kindred underwent physical examination, imaging studies and germline *KIT* analysis.

Multiple GISTs, lentigines, malignant melanoma and angioleiomyoma were identified from members of the kindred. Molecular studies showed a germline *KIT* exon 11 (T→C) mutation resulting in a V559A substitution within the juxtamembrane domain in three family members. A recurrent gastric GIST was excised from the proband and studied using microarray, karyotypic, immunohistochemical and immunoblotting techniques. A heterozygous V559A mutation was found to be present. Fifteen metaphase cells were also analyzed from the proband's GIST and all were found to have a similar cytogenetic profile to those found in sporadic GISTs. Immunoblotting demonstrated a profile of phosphorylated protein kinase B (AKT) and mitogen-activated protein kinase (MAPK), but not signal transducer and activator of transcription 5B (STAT5), which is phosphorylated after *KIT* activation. This finding is also comparable with sporadic GISTs.

The authors conclude that this investigation provides the first evidence that the genetic mechanisms are similar in sporadic and familial GISTs. Further studies are needed to learn more about the epidemiology and environmental risk factors leading to the development of these tumors.

Original article Li FP *et al.* (2005) Familial gastrointestinal stromal tumor syndrome: phenotypic and molecular features in a kindred. *J Clin Oncol* **23:** 2735–2743

Expression of *CXCR4* in colorectal cancer

Results of a recent study involving patients with different stages of colorectal cancer (CRC) suggest that the chemokine receptor gene *CXCR4* has the potential to become a prognostic marker of CRC disease outcome.

Kim *et al.* carried out microarray screening of CRC cell lines and tumor specimens collected from 125 patients with various stages of CRC, and assessed expression of the *CXCR4* gene in both malignant and benign specimens using a realtime quantitative reverse transcription–polymerase chain reaction. They then correlated their findings with incidences of