

## PANCREAS ALERTS

---

*Eur J Pharmacol* 2012; Feb 21.  
(PMID: 22374261)

### **Platelets regulate P-selectin expression and leukocyte rolling in inflamed venules of the pancreas.**

**Abdulla A, Awla D, Hartman H, Weiber H, Jeppsson B, Regnér S, Thorlacius H.**

*Department of Clinical Sciences, Section for Surgery, Lund University. Malmö, Sweden*

Recent data suggest that platelets regulate inflammatory changes and tissue damage in acute pancreatitis although the role of platelets in leukocyte-endothelium interactions in the pancreatic micro-circulation is not known. The aim of this study was to define the impact of platelet on leukocyte rolling and adhesion in acute pancreatitis. Acute pancreatitis was induced in C57BL/6 mice by caerulein challenge. Mice were treated with an anti-GP1b $\alpha$  (CD42b) antibody, which depletes platelets, or a control antibody before caerulein. Leukocyte rolling and adhesion were determined by the use of intravital fluorescence microscopy 18 h after the last dose of caerulein. In separate experiments, leukocyte-endothelium interactions were determined before and after administration of an anti-P-selectin, anti-PSGL-1 and a control antibody in mice with caerulein pancreatitis. Circulating platelet-neutrophil aggregates and pancreatic P-selectin mRNA were quantified 1 and 6 h respectively after caerulein challenge. Caerulein administration increased leukocyte and platelet interactions in the pancreatic microvasculature, increased tissue damage and expression of P-selectin mRNA in the pancreas as well as platelet-neutrophil complexes in the circulation. Notably, platelet depletion markedly reduced caerulein-provoked leukocyte rolling and adhesion in postcapillary venules. Interestingly, depletion of platelets significantly decreased caerulein-induced gene expression of P-selectin in the pancreas. Moreover, immunoneutralization of P-selectin and PSGL-1 abolished leukocyte rolling in the pancreatic venules triggered by caerulein. These novel findings demonstrate that platelets regulate leukocyte rolling in acute pancreatitis via induction of P-selectin, which was critical in supporting leukocyte rolling in inflamed venules of the pancreas.

---

*Acad Radiol* 2012; Feb 24.  
(PMID: 22366559)

### **Gallbladder patterns in acute pancreatitis: An MRI study.**

**Ji YF, Zhang XM, Li XH, Jing ZL, Huang XH, Yang L, Zhai ZH.**

*Department of Radiology, Sichuan Key Laboratory of Medical Imaging, Affiliated Hospital of North Sichuan Medical College. Nanchong, China*

The aim of this study was to assess the gallbladder patterns on magnetic resonance imaging (MRI) associated with acute pancreatitis (AP). There were 197 patients with AP, all of whom had undergone abdominal MRI. AP was categorized as either edematous or necrotizing according to its findings on MRI and graded as mild (0-3 points), moderate (4-6 points), or severe (7-10 points) according to the magnetic resonance severity index. The changes to the walls and dimensions of the gallbladder and common bile duct, in addition to the presence of biliary stones and pericholecystic fluid, were noted and compared with the severity of AP on the basis of the magnetic resonance severity index. Of the 197 patients with AP, 81% were classified as edematous and 19% as necrotizing on MRI. There were 35%, 59%, and 6% of patients with mild, moderate, and severe AP according to the magnetic resonance severity index, respectively. Seventy-six percent of patients had at least one gallbladder abnormality on MRI, including a thickened gallbladder wall (42%), pericholecystic fluid (38%), gallbladder stones (35%), an enlarged gallbladder (24%), dilatation of the common bile duct (16%), and subserosal edema (15%). Eighty-nine percent of patients (34 of 38) with necrotizing AP had gallbladder abnormalities, which was significantly higher than the 72% of patients (115 of 159) with edematous AP ( $P < 0.05$ ). The prevalence of gallbladder abnormalities was 64% in patients with mild AP, 81% in those with moderate AP, and 91% in those with severe AP ( $P < 0.05$  among the three groups). Most patients with AP have gallbladder abnormalities on MRI, including a thickened gallbladder wall and pericholecystic fluid. The prevalence of gallbladder abnormalities has a positive correlation with the severity of AP on MRI.

---

*Br J Cancer* 2012; Feb 28.  
(PMID: 22374460)

### **Multicentre phase II trial of trastuzumab and capecitabine in patients with HER2 overexpressing metastatic pancreatic cancer.**

**Harder J, Ihorst G, Heinemann V, Hofheinz R, Moehler M, Buechler P, et al.**

*Medizinische Klinik II, Hegau-Bodensee Klinikum. Singen, Germany*

New therapeutic options for metastatic pancreatic cancer are urgently needed. In pancreatic cancer, overexpression of the epidermal growth factor receptor 2 (HER2) has been reported in up to 45%. This multicentre phase II study investigated the efficacy and toxicity of the HER2 antibody trastuzumab combined

with capecitabine in the patients with pancreatic cancer and HER2 overexpression. Primary endpoint was progression-free survival (PFS) after 12 weeks. A total of 212 patients were screened for HER2 expression. Immunohistochemical (IHC) HER2 expression was: 83 (40%) grade 0, 71 (34%) grade 1, 31 (15%) grade 2, 22 (11%) grade 3. A total of 17 patients with IHC +3 HER2 expression or gene amplification could be assessed for the treatment response. Grade 3/4 treatment toxicities were: each 7% leucopenia, diarrhoea, nausea and hand-foot syndrome. Progression-free survival after 12 weeks was 23.5%, median overall survival (OS) 6.9 months. This study demonstrates +3 HER2 expression or gene amplification in 11% of patients. Contrary to breast and gastric cancer, only 7 out of 11 (64%) patients with IHC +3 HER2 expression showed gene amplification. Although the therapy was well tolerated, PFS and OS did not perform favourably compared with standard chemotherapy. Together, the authors do not recommend further evaluation of anti-HER2 treatment in patients with metastatic pancreatic cancer.

---

*Endocr J 2012; Feb 25.*  
(PMID: 22374239)

### **Preoperative insulin secretion ability and pancreatic parenchymal thickness as useful parameters for predicting postoperative insulin secretion in patients undergoing pancreaticoduodenectomy.**

**Yoshikawa A, Kozawa J, Okita K, Yoneda S, Okauchi Y, Uno S, et al.**

*Department of Metabolic Medicine, Graduate School of Medicine, Osaka University. Osaka, Japan*

Periampullary malignant neoplasms have been increasing in Japan, mainly in response to an increase in the incidences of pancreatic cancer, and glucose intolerance due to deterioration of insulin secretion is an important problem. The authors investigated preoperative parameters to predict postoperative insulin secretion and the need for insulin therapy in patients undergoing pancreaticoduodenectomy (PD). Thirty-six patients with malignant neoplasms of periampullary lesions were enrolled. Preoperative pancreatic parenchymal thickness was evaluated by computed tomography. Insulin secretion and glucose tolerance were evaluated by a 75 g oral glucose tolerance test and an intravenous glucagon loading test. The relationships between postoperative insulin secretion and preoperative parameters and the cut-off values for predicting the need for postoperative insulin therapy for glycemic control were investigated. Pancreatic parenchymal thickness and other preoperative parameters, including the increment of serum C-peptide ( $\Delta$  C-peptide), fasting plasma C-peptide (F-CPR), insulinogenic index (I.I.) and fasting plasma glucose (FPG), were significantly associated with

postoperative insulin secretion. Multiple regression analyses revealed that preoperative  $\Delta$  C-peptide or F-CPR was the most significant determinant of postoperative insulin secretion, followed by pancreatic parenchymal thickness. In the receiver operating characteristic curve, the best preoperative cut-off values for predicting the need for postoperative insulin therapy were a  $\Delta$  C-peptide of 0.65 ng/mL, a F-CPR of 0.85 ng/mL and a pancreatic parenchymal thickness of 6.0 mm. Both preoperative insulin secretion and pancreatic parenchymal thickness effectively predict postoperative insulin secretion and identify subjects who need postoperative insulin therapy for glycemic control.

---

*Ann Oncol 2012; Feb 28.*  
(PMID: 22373539)

### **European cancer mortality predictions for the year 2012.**

**Malvezzi M, Bertuccio P, Levi F, La Vecchia C, Negri E.**

*Department of Epidemiology, Istituto di Ricerche Farmacologiche 'Mario Negri'. Milan, Italy*

Estimating current cancer mortality figures is important for defining priorities for prevention and treatment. Using logarithmic Poisson count data joinpoint models on mortality and population data from the World Health Organization database, the authors estimated numbers of deaths and age-standardized rates in 2012 from all cancers and selected cancer sites for the whole European Union (EU) and its six more populated countries. Cancer deaths in the EU in 2012 are estimated to be 1,283,101 (717,398 men and 565,703 women) corresponding to standardized overall cancer death rates of 139/100,000 men and 85/100,000 women. The fall from 2007 was 10% in men and 7% in women. In men, declines are predicted for stomach (-20%), leukemias (-11%), lung and prostate (-10%) and colorectal (-7%) cancers, and for stomach (-23%), leukemias (-12%), uterus and colorectum (-11%) and breast (-9%) in women. Almost stable rates are expected for pancreatic cancer (+2-3%) and increases for female lung cancer (+7%). Younger women show the greatest falls in breast cancer mortality rates in the EU (-17%), and declines are expected in all individual countries, except Poland. Apart for lung cancer in women and pancreatic cancer, continuing falls are expected in mortality from major cancers in the EU.

---

*J Gastroenterol 2012; Feb 17.*  
(PMID: 22350698)

### **Analysis of lymph node metastasis in pancreatic neuroendocrine tumors (PNETs) based on the tumor size and hormonal production.**

**Tsutsumi K, Ohtsuka T, Mori Y, Fujino M, Yasui T, Aishima S, et al.**

*Department of Surgery and Oncology, Graduate School of Medical Sciences, Kyushu University. Fukuoka, Japan*

Because of the rarity and variety of pancreatic neuroendocrine tumors (PNETs), there have been few reports regarding the indication for lymph node dissection in patients with these tumors. This study aimed to evaluate the risk of lymph node metastasis of PNETs based on the tumor size and hormonal production. Data for a total of 66 patients who had PNETs resected between 1987 and 2010 were retrospectively studied. The clinicopathological features, including the disease-specific survival rate, were assessed based on the status of lymph node metastasis at the time of initial surgical resection. Then the cut-off point of tumor size to predict lymph node metastasis was estimated. There were 12 patients (18%) with lymph node metastasis. The frequency of lymph node metastasis tended to be higher in gastrinomas than that in other tumors (43 vs. 15%;  $P=0.08$ ). The size of PNETs with lymph node metastasis was significantly larger than that of the PNETs without metastasis ( $P=0.04$ ). The postoperative survival rate in the PNET patients with lymph node metastasis was significantly lower than that in the patients without metastasis ( $P<0.0001$ ). Only 2 (8%) of 26 PNETs with a tumor size of  $<15$  mm had lymph node metastasis, and both of these were gastrinomas. On the other hand, 10 (25%) of the remaining 40 PNETs with a tumor size of  $\geq 15$  mm had lymph node metastasis. Notably, there were no PNETs with lymph node metastasis in 22 non-gastrinomas with a tumor size of  $<15$  mm. Non-gastrinomas with a tumor size of  $\geq 15$  mm and all gastrinomas would be an indication for pancreatectomy with lymph node dissection.

---

*Ann Surg Oncol 2012; Feb 14.*  
(PMID: 22350605)

### **Incidental detection of pancreatic neuroendocrine tumors: An analysis of incidence and outcomes.**

**Cheema A, Weber J, Strosberg JR.**

*Department of Gastrointestinal Oncology, H. Lee Moffitt Cancer Center and Research Institute. Tampa, FL, USA*

Pancreatic neuroendocrine tumors (NETs) are increasingly discovered incidentally during radiologic or endoscopic examinations. The frequency of incidental detection is unknown. It is also unclear whether patients with incidentally discovered, early-stage, asymptomatic tumors should be treated similarly to patients who present with tumor-related symptoms. Patients with nonmetastatic pancreatic NETs treated at the H. Lee Moffitt Cancer Center between 1999 and 2010 were assigned a stage (I-III) on the basis of the new American Joint Committee on Cancer

classification. The frequency of incidentally diagnosed tumors was evaluated and stratified by stage. Progression-free survival was measured by log rank testing to compare patients with incidentally detected versus symptomatic tumors. Multivariate analysis was performed controlling for other prognostic factors including tumor stage, grade, and location, and patient age. Among 143 patients with nonmetastatic pancreatic NETs, 56 patients (40%) had tumors that were discovered incidentally. Most stage I tumors (55%) were incidental. The 5-year progression-free survival rate was 86% for incidentally diagnosed tumors, versus 59% for symptomatic tumors ( $P=0.007$ ). On multivariate analysis, incidental detection of tumors was the strongest prognostic factor for progression. A sizable fraction of patients with early-stage pancreatic NETs are diagnosed incidentally during evaluations for other conditions or unrelated symptoms. This study highlights the necessity of developing guidelines for management of patients with incidentally discovered early-stage tumors.

---

*Ann Surg Oncol 2012; Feb 16.*  
(PMID: 22350603)

### **Association of type O Blood with pancreatic neuroendocrine tumors in von Hippel-Lindau syndrome.**

**Weisbrod AB, Liewehr DJ, Steinberg SM, Patterson EE, Libutti SK, Marston Linehan W, et al.**

*Endocrine Oncology Section, Surgery Branch, National Cancer Institute, National Institutes of Health. Bethesda, MD, USA*

ABO blood type antigens are expressed not only on human red blood cells, but also throughout the gastrointestinal tract and in normal pancreatic tissue. Previous studies have identified an association between ABO blood type and various malignancies. The authors analyzed the association of ABO blood type with pancreatic neuroendocrine tumors (PNETs) in a high-risk cohort of patients with von Hippel-Lindau (VHL) syndrome. A retrospective review was performed of 798 patients with VHL syndrome. Blood type was confirmed for 181 patients. Fisher's exact test and Mehta's modification to Fisher's exact test were used to test for an association between ABO blood type and manifestations of VHL syndrome. The authors found a strong trend for association between O blood type and pancreatic disease manifestation in patients with VHL syndrome ( $P=0.047$ ). More importantly, there was a significant association of O blood type with solid pancreatic lesions consistent with PNETs ( $P=0.0084$ ). Patients with solid pancreatic lesions who met criteria for surgical resection at the National Institutes of Health also had a higher rate of O blood type than those who did not require surgery ( $P=0.051$ ). These findings suggest an association between O blood type

and pancreatic manifestation of disease in patients with VHL syndrome, especially for PNETs. Screening and surveillance approaches for pancreatic lesions in patients with VHL syndrome should also consider patient blood type. The possibility of A, B, H misexpression in PNETs should also be explored to determine whether the serologic association with disease translates into a relationship with tissue pathology.

---

*J Med Imaging Radiat Oncol* 2012; 56(1):40-7.  
(PMID: 22339744)

### **High management impact of Ga-68 DOTATATE (GaTate) PET/CT for imaging neuroendocrine and other somatostatin expressing tumours.**

**Hofman MS, Kong G, Neels OC, Eu P, Hong E, Hicks RJ.**

*Centre for Cancer Imaging, Peter MacCallum Cancer Centre  
Departments of Medicine and Radiology, University of  
Melbourne. Melbourne, Australia*

Ga-68 DOTATATE (Ga-octreotate, GaTate) positron emission tomography (PET)/CT has multiple advantages compared with conventional and In-111 octreotide imaging for neuroendocrine tumours and other somatostatin-receptor expressing tumours. This study assesses the management impact of incremental diagnostic information obtained from this technique compared with conventional staging. Fifty-nine GaTate PET/CT studies were performed over an 18-month period (52 proven or suspected gastro-entero-pancreatic or bronchial neuroendocrine tumours and seven neural crest/mesenchymal tumours). A retrospective blinded review was performed on the number of abnormalities (1, 2-5 or >5) within defined regions with comparison to conventional imaging to assess incremental diagnostic information. Subsequent management impact (high, moderate or low) was determined by clinical review and follow up to assess pre-PET stage, treatment intent and post-PET management change. Eighty-eight percent of GaTate studies were abnormal. Compared with conventional and In-111 octreotide imaging, additional information was provided by GaTate PET/CT in 68% and 83% of patients, respectively. Management impact was high (inter-modality change) in 47%, moderate (intra-modality change) in 10% and low in 41% (not assessable in 2%). High management impact included directing patients to curative surgery by identifying a primary site and directing patients with multiple metastases to systemic therapy. GaTate PET/CT imaging provides additional diagnostic information in a high proportion of patients with consequent high management impact. GaTate PET/CT could replace (1) In-111 octreotide scintigraphy at centres where it is available given its superior accuracy, faster acquisition and lower radiation exposure. Rapid implementation could be achieved by allowing substitutional funding in the Medicare Benefit Schedule.

---

*Gut Liver* 2012; 6(1):10-20.  
(PMID: 22375166)

### **Gut Hormones and appetite control: A focus on PYY and GLP-1 as therapeutic targets in obesity.**

**De Silva A, Bloom SR.**

*Department of Diabetes, Endocrinology and Metabolism,  
Hammersmith Campus, Imperial College London. London,  
UK*

The global obesity epidemic has resulted in significant morbidity and mortality. However, the medical treatment of obesity is limited. Gastric bypass is an effective surgical treatment but carries significant perioperative risks. The gut hormones, peptide tyrosine tyrosine (PYY) and glucagon-like peptide 1 (GLP-1), are elevated following gastric bypass and have been shown to reduce food intake. They may provide new therapeutic targets. This review article provides an overview of the central control of food intake and the role of PYY and GLP-1 in appetite control. Key translational animal and human studies are reviewed.

---

*World J Diabetes* 2012; 3(2):29-34.  
(PMID: 22375163)

### **Diabetes patients and non-diabetic patients intensive care unit and hospital mortality risks associated with sepsis.**

**Tayek CJ, Tayek JA.**

*Chandler J Tayek, Palos Verdes Peninsula High School,  
Rolling Hills Estates, CA, USA*

The authors compared mortality risks associated with known diabetic patients to hyperglycemic non-diabetic patients. PubMed data base was searched for patients with sepsis, bacteremia, mortality and diabetes. Articles that also identified new onset hyperglycemia (NOH) (fasting blood glucose >125 mg/dL or random blood glucose >199 mg/dL) were identified and reviewed. Nine studies were evaluated with regards to hyperglycemia and hospital mortality and five of the nine were summarized with regards to intensive care unit (ICU) mortality. Historically, hyperglycemia has been believed to be equally harmful in known diabetic patients and non-diabetics patients admitted to the hospital. Unexpectedly, having a history of diabetes when admitted to the hospital was associated with a reduced risk of hospital mortality. Approximately 17% of patients admitted to hospital have NOH and 24% have diabetes mellitus. Hospital mortality was significantly increased in all nine studies of patients with NOH as compared to known diabetic patients (26.7±3.4% vs. 12.5±3.4%, P<0.05; analysis of variance). Unadjusted ICU mortality was evaluated in five studies and was more than doubled for those

patients with NOH as compared to known diabetic patients (25.3±3.3% vs. 12.8±2.6%, P<0.05) despite having similar blood glucose concentrations. Most importantly, having NOH was associated with an increased ICU and a 2.7-fold increase in hospital mortality when compared to hyperglycemic diabetic patients. The mortality benefit of being diabetic is unclear but may have to do with adaptation to hyperglycemia over time. Having a history of diabetes

mellitus and prior episodes of hyperglycemia may provide time for the immune system to adapt to hyperglycemia and result in a reduced mortality risk. Understanding why diabetic patients have a lower than expected hospital mortality rate even with bacteremia or acute respiratory distress syndrome needs further study. Having hyperglycemia without a history of previous diabetes mellitus is a major independent risk factor for ICU and hospital mortality.

---