

PANCREAS ALERTS

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Circulating levels of visfatin, resistin and pro-inflammatory cytokine interleukin-8 in acute pancreatitis.

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Resistin and visfatin, hormones produced by adipose tissue, have pro-inflammatory potential; however, their role in acute pancreatitis (AP) has been investigated only rarely. The study group comprised 32 patients with alcoholic AP and 30 controls. In all cases AP severity was classified according to Balthazar's CT score and according to the Ranson's criteria. The serum level of visfatin, resistin, and interleukin(IL)-8 immunoassays were measured by ELISA on admission and on the third and fifth day of hospitalization. On the admission day serum resistin and IL-8 concentrations in AP patients were significantly higher than in controls and they further increased on the third and fifth day of hospitalization. On the admission day serum visfatin levels in AP patients were significantly higher than in controls and further increased on the third day of hospitalization. On the fifth day the levels decreased; however, they were still higher than on admission. The correlation between visfatin and resistin as well as between C-reactive protein and visfatin, resistin and IL-8 levels has been found. In the course of AP, visfatin and resistin levels increase in parallel with C-reactive protein. The authors speculate that those parameters may provide an additional tool for the prognosis and monitoring of AP.

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Endoscopic retrograde cholangiopancreatography and manometry findings in 1,241 idiopathic pancreatitis patients.

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From ten to 30% of patients with pancreatitis are classified as idiopathic after the initial evaluation. The aim was to assess the diagnostic yield of endoscopic retrograde cholangiopancreatography (ERCP) and

sphincter of Oddi manometry in patients with idiopathic pancreatitis in a tertiary referral center. A single-center, retrospective study analyzing the ERCP and manometry results of 1,241 patients who were classified as having idiopathic pancreatitis based upon their initial evaluation. A single episode of pancreatitis occurred in 20.4%, acute recurrent pancreatitis in 56.3% and chronic pancreatitis in 23.3% of the patients undergoing ERCP. Sphincter of Oddi dysfunction was found in 40.3% and pancreas divisum in 18.8% of the patients. Biliary stone disease was found in 3.0%. Intraductal papillary mucinous neoplasms were identified in 52 patients with increasing frequency in older age groups. The overall diagnostic yield of ERCP and sphincter of Oddi manometry to elucidate a potential cause of pancreatitis was 65.8%. Of these, 91.9% patients had findings amenable to endoscopic therapy. The complication rate was 11.5%. In this large series, ERCP with manometry frequently identified conditions which probably caused or contributed to the idiopathic pancreatitis. Long-term studies are awaited to determine outcomes after correctable factors are addressed.

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A randomized controlled trial of valdecoxib and glyceryl trinitrate for the prevention of post-ERCP pancreatitis.

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Efforts to prevent post-endoscopic retrograde cholangiopancreatography (ERCP) pancreatitis have been largely unsuccessful. Cyclo-oxygenase-2 enzyme-mediated inflammatory pathway has been suggested in the pathophysiology of acute pancreatitis. Glyceryl trinitrate (GTN) might prevent post-ERCP pancreatitis by relaxing the sphincter of Oddi. The authors aimed to evaluate the efficacy of valdecoxib, a cyclo-oxygenase-2 inhibitor, and GTN transdermal patch for the prevention of post-ERCP pancreatitis. Patients undergoing first ERCP procedure from October 2003 to August 2005 were randomized to receive either 20 mg intravenous valdecoxib or GTN patch (10 mg/h) at the start of ERCP, or assigned to control group. The study followed CONSORT guidelines. Primary outcome measure was frequency of post-ERCP pancreatitis in the 3 groups. A total of 380 patients were randomized; 121 patients in valdecoxib (group 1), 124 in GTN (group 2), and 126 in the control arm

(group 3) were analyzed. There was no difference in the frequency of post-ERCP pancreatitis between the groups (12 each in groups 1 and 2, and 13 in group 3; $P=0.986$). None of the patients had severe pancreatitis. The frequency of post-ERCP pain and amylase levels were also similar in the 3 groups ($P=0.769$ and $P=0.947$, respectively). Pancreatic duct cannulation, cholecystectomy, difficult cannulation, and pre-cut were risk factors for pancreatitis on univariate analysis. On multivariate analysis, pancreatic duct cannulation was the only independent risk factor for pancreatitis ($P<0.001$; odds ratio 5.67; 95% confidence interval: 2.76-11.63). Valdecoxib and GTN were not effective for the prevention of post-ERCP pancreatitis.

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Surgical decompression for abdominal compartment syndrome in severe acute pancreatitis.

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In patients with severe acute pancreatitis and abdominal compartment syndrome, establishment of the indications and optimal time for surgical decompression may avoid exacerbation of multiple-organ dysfunction syndrome. In this retrospective study carried out in a tertiary care university teaching hospital were enrolled twenty-six consecutive patients with severe acute pancreatitis and abdominal compartment syndrome treated by surgical decompression. Surgical decompression of the abdomen was carried out and morbidity, mortality, and organ dysfunction before and after surgical decompression were evaluated. At the time of surgical decompression, the median sequential organ failure assessment score among patients was 12 (interquartile range, 10-15), and the median intra-abdominal pressure was 31.5 (interquartile range, 27-35) mmHg. After surgical decompression, renal or respiratory function was improved in 14 patients (54%). The overall hospital mortality was 46%, but mortality was 18% among 17 patients in whom surgical decompression was performed within the first 4 days after disease onset. Patients with severe acute pancreatitis and abdominal compartment syndrome managed by surgical decompression had severe multiple-organ dysfunction syndrome and high mortality. Surgical decompression may improve renal or respiratory function. Early surgical decompression is associated with reduced mortality in patients with severe acute pancreatitis, early multiple-organ dysfunction syndrome, and abdominal compartment syndrome.

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***Helicobacter pylori* in autoimmune pancreatitis and pancreatic carcinoma.**

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Helicobacter pylori has been suggested to be involved in pancreatic diseases, namely autoimmune pancreatitis and pancreatic carcinoma. The authors investigated the presence of conserved sequences of *Helicobacter* in pancreatic tissue and pancreatic juice from patients with chronic nonautoimmune and autoimmune pancreatitis as well as pancreatic ductal adenocarcinoma (PDAC). Thirty-five pancreatic juices collected during routine endoscopic retrograde cholangiopancreatography and 30 pancreatic tissues were studied. Nested PCR was used to detect *H. pylori* in the isolated DNA samples. In order to exclude a methodological bias, the samples were analyzed blindly in 2 different laboratories using either conventional or LightCycler PCR for *H. pylori* urease A and 16S ribosomal DNA. In the pancreas of 11 patients with autoimmune pancreatitis, no *H. pylori* DNA could be detected. Further, in none of the other tissue samples of chronic pancreatitis or PDAC the authors could detect any *Helicobacter* sequences. Out of the pancreatic juice samples, none demonstrated either of the 2 *Helicobacter* gene sequences investigated. Despite good scientific reasoning for an involvement of *Helicobacter* in pancreatic diseases, a direct infection of the microbial agent seems unlikely. Rather, the pathomechanism must involve molecular mimicry in autoimmune pancreatitis, or the transformation of nitric food constituents to nitrosamines in pancreatic cancer.

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Body mass index reflects islet isolation outcome in islet autotransplantation for patients with chronic pancreatitis.

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Total pancreatectomy with autologous islet cell transplantation (TP with AIT) is an effective treatment for chronic pancreatitis patients with severe abdominal pain. Body mass index (BMI) of the pancreatic donor is proven to be a useful predictor for islet isolation and transplantation outcomes in allogenic islet transplantation. However, the association between BMI and

islet isolation outcome and/or metabolism after AIT was previously unclear. Twelve patients who received TP with AIT were included in this study. All pancreata were preserved with both pancreatic ductal injection and oxygen-charged static two-layer method using ET-Kyoto solution. The cohort was divided into two groups; low-BMI group (BMI<23 kg/m², n=5) and high-BMI group (BMI≥23, n=7). High-BMI group had a significantly higher islet yield per gram than low-BMI group both in pancreas post-digestion and in final product (Post-digestion: 7,330±539 vs. 3,509±563 IE/g; P<0.001, Final product: 6,555±585 vs. 3,476±546 IE/g; P=0.004). For islet yield in final product per patient body weight, high BMI group had also significantly higher islet yield than low-BMI group (7,997±779 IE/kg vs. 4,175±750, P=0.007). Insulin independence rate in high-BMI group (71%) was also higher than low-BMI group (40%), but it did not reach statistical significance. Pancreata from patients with higher BMI could obtain higher islet yield in the setting of autologous islet cell transplantation for chronic pancreatitis.

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Extracorporeal shock wave lithotripsy and endotherapy for pancreatic calculi: a large single center experience.

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Large pancreatic ductal calculi and pain are a feature of chronic calcific pancreatitis (CCP) in the tropics. This large single center study evaluates the role of extracorporeal shock wave lithotripsy (ESWL) in fragmentation of large pancreatic stones and relief of pain in patients with CCP. Patients with CCP presenting with pain and large pancreatic duct (PD) calculi (>5 mm diameter) not amenable to extraction at routine endoscopic retrograde cholangiopancreatography (ERCP) were taken up for ESWL using a 3rd generation lithotripter. Stones in the head and body of pancreas were targeted at ESWL; 5,000 shocks were given per session. The calculi were fragmented to <3 mm size and then cleared by endotherapy. Pancreatic duct stents were deployed when indicated. A total of 1,006 patients underwent ESWL. Complete clearance was achieved in 762 (76%), partial clearance in 173 (17%) and unsuccessful in the rest. More than 962 (90%) of patients needed less than three sessions of ESWL. At 6 months, 711 (84%) of 846 patients who returned for follow-up had significant relief of pain with a decrease in analgesic use. Complications were mild and minimal. ESWL is an effective and safe modality for fragmentation of large PD calculi in patients with CCP.

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Are genetic variants in the platelet-derived growth factor beta gene associated with chronic pancreatitis?

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Platelet-derived growth factor beta (PDGF-beta) is a major signal in proliferation and matrix synthesis through activated pancreatic stellate cells, leading to fibrosis of the pancreas. Recurrent acute pancreatitis (RAP) seems to predispose to chronic pancreatitis (CP) in some patients but not others. The authors tested the hypothesis that 2 known PDGF-beta polymorphisms are associated with progression from RAP to CP. The authors also tested the hypothesis that PDGF-beta polymorphisms in combination with environmental risk factors such as alcohol and smoking are associated with CP. Three hundred eighty-two patients with CP (n=176) and RAP (n=206) and 251 controls were evaluated. Platelet-derived growth factor beta polymorphisms +286 A/G (rs#1800818) seen in 5'-UTR and +1135 A/C (rs#1800817) in first intron were genotyped using single-nucleotide polymorphism polymerase chain reaction approach and confirmed by DNA sequencing. The genotypic frequencies for PDGF-beta polymorphisms in positions +286 and +1135 were found to be similar in controls and patients with RAP and CP. There was no difference in genotypic frequencies among RAP, CP, and controls in subjects in the alcohol and smoking subgroups. Known variations in the PDGF-beta gene do not have a significant effect on promoting or preventing fibrogenesis in pancreatitis. Further evaluation of this important pathway is warranted.

Electrophoresis 2010 Aug 19.
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Multi-parameter detection of diabetes mellitus on multichannel poly(dimethylsiloxane) analytical chips coupled with nanoband microelectrode arrays.

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This article demonstrates a novel method for multi-parameter detection of diabetes mellitus. The authors propose an approach for fabrication of a 3-D metal

films array with gold and copper using electroless deposition technique on PDMS substrate. The obtained PDMS slices containing metal films were superimposed layer by layer as a sandwich structure to form 3-D metal films array. The cross-sections of the array could be used as nanoband array electrochemical detectors, which are further integrated with a multichannel microchip for simultaneously detecting multi-parameter of diabetes mellitus, including glucose and metabonomics of diabetes containing aldehyde compounds (glyoxal and methylglyoxal) and short organic acids (lactate, urate and 2-hydroxybutyrate). Under optimized separation and detection conditions, glucose, aldehyde compounds and short organic acids respond linearly in the concentration range of 10-2,000, 1-500 and 5-600 μ M, with the LODs of 4, 0.5 and 3 μ M for glucose, aldehyde compounds and short organic acids, respectively. This system is successfully employed to detect these compounds in serum. This study reveals that the electrochemical array detectors with different materials integrated with multichannel microchip provide a flexible and inexpensive approach for routine, simultaneous and direct detection of some metabolites in metabonomics.

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Improved glycemic control with colessevelam treatment in patients with type 2 diabetes is not directly associated with changes in bile acid metabolism.

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Bile acids (BAs) are essential for fat absorption and appear to modulate glucose and energy metabolism. Colesevelam, a BA sequestrant, improves glycemic control in type 2 diabetes mellitus (T2DM). The authors aimed to characterize the alterations in BA metabolism associated with T2DM and colessevelam treatment and to establish whether metabolic consequences of T2DM and colessevelam are related to changes in BA metabolism. Male subjects with T2DM (n=16) and controls (n=12) were matched for age and body mass index. BA pool sizes and synthesis/input rates were determined before and after 2 and 8 weeks of colessevelam treatment. T2DM subjects had higher cholic acid (CA) synthesis rate, higher deoxycholic acid (DCA) input rate, and enlarged DCA pool size. Colesevelam resulted in a preferential increase in CA synthesis in both groups. CA pool size was increased

whereas chenodeoxycholic acid and DCA pool sizes were decreased upon treatment. Fasting and postprandial fibroblast growth factor 19 (FGF19) levels did not differ between controls and diabetics, but were decreased by treatment in both groups. Colesevelam treatment reduced hemoglobin A1C by 0.7% ($P<0.01$) in diabetics. Yet, no relationships between BA kinetic parameters and changes in glucose metabolism were found in T2DM or with colessevelam treatment. In conclusion, these results reveal significant changes in BA metabolism in T2DM, particularly affecting CA and DCA. Colesevelam treatment reduced FGF19 signaling associated with increased BA synthesis, particularly of CA, and resulted in a more hydrophilic BA pool without altering total BA pool size. However, these changes could not be related to the improved glycemic control in T2DM.

Eye Contact Lens 2010 Aug 10.
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Repeatability of measuring corneal subbasal nerve fiber length in individuals with type 2 diabetes.

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The authors analyze the repeatability of measuring nerve fiber length (NFL) from images of the human corneal subbasal nerve plexus using semiautomated software. Images were captured from the corneas of 50 subjects with type 2 diabetes mellitus who showed varying severity of neuropathy, using the Heidelberg Retina Tomograph 3 with Rostock Corneal Module. Semiautomated nerve analysis software was independently used by two observers to determine NFL from images of the subbasal nerve plexus. This procedure was undertaken on two occasions, 3 days apart. The intraclass correlation coefficient values were 0.95 (95% confidence interval: 0.92-0.97) for individual subjects and 0.95 (95% confidence interval: 0.74-1.00) for observer. Bland-Altman plots of the NFL values indicated a reduced spread of data with lower NFL values. The overall spread of data was less for (a) the observer who was more experienced at analyzing nerve fiber images and (b) the second measurement occasion. Semiautomated measurement of NFL in the subbasal nerve fiber layer is highly repeatable. Repeatability can be enhanced by using more experienced observers. It may be possible to markedly improve repeatability when measuring this anatomic structure using fully automated image analysis software.

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