**The size of the spleen by MRI in patients with CF with and without diabetes**

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**Background:** There is currently no information about the size of the spleen in CF patients.

**Patients and Methods:** We studied 51 adult volunteers: 28 pancreatic insufficient CF patients (13 with CF related diabetes (CFRD) and 15 non-diabetic) and 23 male non-CF patients (12 with type 1 diabetes mellitus (T1DM) and 11 controls). Patients with liver disease were excluded. Spleen size was measured by magnetic resonance imaging (MRI). For comparison of spleen size in the 4 study groups, only male CF patients were included.

For CF patients, spleen size was correlated with FEV1, body mass index (BMI), number of days of intravenous (IV) antibiotic treatment in the year previous to study, circulating white blood cell count, glycosylated haemoglobin A1c (HbA1c) level and pancreatic exocrine function, as assessed by daily requirement of oral lipase.

**Results:** Amongst the 4 study groups, spleen size was greatest in male non-diabetic CF patients (P = 0.01). For CF patients, spleen size was greatest in male compared to female (P = 0.012). For patients with CFRD, there was an inverse correlation between the spleen size and HbA1c (r = −0.59 P = 0.04) and the daily intake of lipase (r = −0.63 P = 0.02).

Spleen size in CFRD patients, but not in CF patients without CFRD, inversely correlated with the number of days of IV antibiotic treatment (r = −0.67 P = 0.012). There was no correlation between spleen size and FEV1, BMI and white blood cell counts in any group.

**Conclusions:** By MRI, the spleen was greatest in male non-diabetic CF patients in comparison with other groups. Spleen size in CFRD patients was smaller when diabetes was poorly controlled, when exocrine pancreatic function was greatly impaired and in those with a greater need for IV antibiotics in the year prior to the study.

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**Detection of bile acids in sputum as a screening method for assessment of aspiration of duodenogastric contents in patients with cystic fibrosis**

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Up to 80% of patients with cystic fibrosis (CF) may have increased gastrooesophageal reflux. Aspiration of duodenogastric contents during a reflux event might be harmful in CF patients.

The aim of our study was to identify the presence of aspiration in CF patients, by measuring duodenogastric components in sputum.

**Methods:** In 42 CF patients [25 men; 24 (11–43) years] sputum was obtained after inhalation of hypertonic saline. Sputum was separated from saliva, supernatant was collected and tested for bile acids (BA) (enzymatic assay). Concentrations of IL-8 (rt-PCR) and neutrophil elastase (enzymatic assay) were measured in sputum. Lung function and BMI were assessed on the day of sputum collection.

**Results:** 26/42 patients had BA in sputum [2.2 (1.7–2.9) μmol/L]. In patients with detectable BA, we found a neg correlation between BA concentrations and FEV1/forced expiratory volume in 1 second (FEV1)/forced vital capacity (FVC) (r = −0.4, p = 0.04). Patients with BA in sputum had a higher concentration of neutrophil elastase compared to patients without [139.4 ± 14.09 vs. 87.0 ± 13.52 pg/mL, p = 0.01]. BA concentrations were similar in patients with genotypes DF508 homozygote, DF508 heterozygote and others [2.4 (1.8–2.8), 2.1 (1.6–2.5), 2.2 (1.6–2.9) μmol/L] and were unrelated with BMI and age.

**Conclusion:** BA can be found in the sputum of half of CF patients, suggesting aspiration of duodenogastric contents into the lungs. Aspiration of BA was associated with increased airway inflammation. In patients with BA aspiration, BA levels were associated with lung function impairment. BA determination in sputum can be used as a screening method for assessment of aspiration in CF patients.

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**Gallbladder dysfunction contributes to impaired bile salt homeostasis in cystic fibrosis**

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The aim of the study was to elucidate mechanisms whereby CFTR defect alters bile salt (BS) homeostasis.

**Methods:** Cftr−/− (Cftrtm1Unc) mice and their normal Cftr+/+ littermates were maintained under PEG and investigated at 14 weeks of age. Bile secretion was tested in serum and bile were analyzed by LC-MS. Duodenal and bile pH was measured with a microprobe. Gene expressions by hepatobiliary scintigraphy. BS in serum and bile were analyzed by LC-MS. Duodenal and bile pH was measured with a microprobe. Gene expressions were determined by RT-QPCR.

**Results:** Cftr−/− weighed significantly less than Cftr+/+. While no liver damage was detected, gallbladder (GB) volumes were significantly increased in cftr−/− mice. Scintigraphy showed delayed GB emptying with a 120-min ejection fraction of 35.4% vs 93.1% in cftr+/+ (p < 0.009), whereas emptying in response to cholecystokinin was normal. While no significant difference in total concentrations of BS was found, secondary BS were almost completely lacking in bile and serum from cftr−/−. pH was significantly lower in GB bile and in the duodenum. The transcript levels of VIP in the duodenum were 3.5-fold higher in cftr−/− mice (LF-0.004). Those of SHP, I-BABP and ASBP in the ileum were 4.3 (p < 0.01), 6.7 (p < 10−5), and 1.8-fold lower (p < 0.01) respectively.

In conclusion, CFTR defect causes a severe impairment of gallbladder emptying; it can be attributed to increased production of the relaxant factor VIP by duodenum, as a result of increased acidity. Impaired release of factor VIP into the intestine is attested by the decrease in SHP and I-BABP ileal expressions, and by the lack of secondary BS. While these mechanisms may participate to a poor nutritional status in CF, they may also provide protection against liver damage in this disease.

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**Gastro-oesophageal reflux and gastric emptying in children with cystic fibrosis**

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**Aim:** Increased gastro-oesophageal reflux (GOR) and abnormal gastric emptying (GE) are common in children with cystic fibrosis (CF).

**Methods:** Nineteen CF children (11 boys, mean age 5 years range 1–17 years) with gastrointestinal and/or respiratory symptoms suggestive for GOR were studied. They underwent an impedance-pH monitoring for detection of GOR. Acid reflux parameters were regarded as increased if the total oesophageal acid exposure was above the 95 th percentile of normal data obtained in healthy subjects (Vandenplas et al 1991). A 13C-acetate breath test to measure GE of solids was performed. GE parameters were considered as increased if the gastric half emptying time was above the 95 th percentile of normal data obtained in healthy subjects (Hauser et al, unpublished data).

**Results:** Ten of the 19 children (52.6%) had increased acid GOR with a mean total acid exposure of 7.2% (range 0.9–22.1%) for the whole group. Nine of the 19 children (47.4%) had delayed GE with a mean gastric half emptying time of 101 minutes (range 79–138 minutes) for liquids for the whole group and 197 minutes (range 110–388 minutes) for solids for the whole group. Four patients had increased GOR and delayed GE (21.1%), 6 patients had increased GOR and normal GE (31.6%), 5 patients had normal GOR and delayed GE (26.3%), and 4 patients had normal GOR and normal GE (21.1%).

**Conclusions:** Increased acid GOR and delayed GE are prevalent in CF children, but delayed GE is present in about half of the children with increased GOR but also in about half of the children with normal GOR.