Immuno-Reactive Trypsine and external pancreatic status in cystic fibrosis children

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Background: The aim of our study was to evaluate the significance of the Immuno-
Reactive Trypsine (IRT) as a marker for exocrine pancreatic insufficiency, assessed
on fecal elastase, in pancreatic sufficient and insufficient cystic fibrosis (CF)
children.

Patients and Methods: From August 2006 to January 2008, fifty-six children
followed-up in CF Centre, Department of Pediatrics, Angers (France), were studied.
From their fecal elastase concentration they were divided into 2 groups: pancreatic
sufficient or insufficient (>200 mg/g of stool or ×100 mg/g of stool). For every
patient, IRT concentration was assessed on a dried blood sample.

Results: The fifty pancreatic sufficient patients all had IRT concentrations upper
than 9.5 ng/mL whatever their age. Thirty-four of the 41 pancreatic insufficient
patients had IRT concentrations lower than 9.5 ng/mL whatever their age, and 33 of
the 35 pancreatic insufficient patients over than 4 years-old had IRT concentrations
lower than 9.5 ng/mL. IRT concentration lower than 9.5 ng/mL measured in a more
than 4 years-old CF child permit to affirm that he has pancreatic insufficiency,
with sensibility of 94%, specificity of 100%, positive predictive value of 100% and
negative predictive value of 83%.

Conclusion: From the age of 4 in cystic fibrosis children, IRT concentration is
correlated with external pancreatic status. This could be used as a marker for exocrine
pancreatic insufficiency when difficulties to obtain stools in consultation.

Clinical outcome in cystic fibrosis patients with or without meconium ileus

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Aims: Meconium ileus (MI) is the presenting symptom in 20% of patients with
cystic fibrosis (CF). The aims of the present study were to assess the clinical
outcomes in cohorts of CF patients with MI at 5, 10 and 15 years in comparison to
patients without MI.

Methods: Clinical records of CF patients with and without MI admitted to a tertiary
referral centre were examined. In patients with MI, data on birth weight, genotype,
type and extent of surgery, duration of parenteral nutrition were recorded. In both
groups clinical status at 5, 10, and 15 years were accessed from annual review
records.

Results: Eighteen patients (7 F) (with MI) and 16 controls (5 F) (without MI)
were reviewed. Of the patients, 8 were homozygous for δF508, 4 were simple
MI and 11 patients received parenteral nutrition for a median of 24 days (10–
120 days). Compared with controls, the median weight, height, FEV1, FVC,
Shwachman score, at 5 years, were 16.9 kg (13.6–23) [20 kg (14.5–27.8)*], 105 cm
(102–120) [109.8 cm (100.1–121.0)*], 82% [36–121] [86% (83–94)*], 82% (36–121)
[92% (85–107)*], and 93 (83–113) [96 (75–92)]; at 10 years were 30.4 kg (25–39)
[32.4 kg (22.9–46.8)*], 134 cm (127–140) [138 cm (126–149)*], 76% (66–72) [83%
(64–102)*], 76% (42–98) [93% (83–113)*] and 85 (65–87) [84 (59–94)]; and at
15 years, 52 kg (28–65) [42.6 kg (34.7–59.8)*], 161 cm (135–170) [156.7 cm (140–
185)*], 77% (63–104) [86% (49–119)*], 80% (77–99) [90% (63–118)*], and 71
(57–79) [71.5 (62–81)].

Abnormal findings on ultrasound scan (USS) of the liver were seen 36% (45), 70%
(35)*, and 85% (60)* of patients at 5, 10 and 15 years. *p < 0.05.

Conclusion: The study has shown that patients without MI have better growth
and lung function parameters throughout childhood. Abnormal USS of liver is
significantly higher in patients with both simple and complicated MI.

Pancreatic status in cystic fibrosis patients depending upon phenotype-genotype correlations

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The influence of genetic and epigenetic factors on functional status of pancreas
in patients with cystic fibrosis and on course of the disease in general has been analysed.

96 cases of CF were verified at Lviv regional CF centre and 89 CF patients were
under observation in terms from 2 month to 12 years. Among them 13 (13.4%)
died – 9 (69.2%) girls and 4 (30.8%) boys. The studied group of patients was
divided on the genotype differences and disease manifestation severity and the
obtained results of glucose-toleration test, sonographical investigation data and
facial elastase-1 level were compared. It was determined that CFTR genotype influences on exocrine pancreatic insuffi-
ciency manifestation. “Major” CFTR mutations associates with severe exocrine pan-
creatic insufficiency phenotype. “Minor” changes of alleles dominate on “severe”
and could result sufficient exocrine function of pancreas. Both negative (for the
F508del mutation) and positive (for the 3849+10kbC→T, R334W, 3272−11A>G
mutations) correlations between genotype and the degree of exocrine pancreatic
insufficiency have been revealed.

CF patient genotype and the degree of exocrine pancreatic insufficiency don’t
seem to determine his endocrine status and dynamics of progression of fibrinotic
and atrophic changes in pancreas. It is established that older age of cystic fibrosis
patients, progression of fibrinotic and atrophic changes in pancreas as well as severe
pulmonary insufficiency, all are predictors of deterioration in endocrine function of
pancreas.

Intestinal inflammation is present in young infants with cystic fibrosis

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Background: It has been documented that intestinal inflammation is one of the
major features of cystic fibrosis (CF). However, the age of its onset is not well
known. Therefore, we have aimed to assess whether intestinal inflammation is
present in young CF infants at diagnosis.

Material and Methods: The study comprised 10 infants detected in CF neonatal
screening programme. The age of infants at the assessment was in range from 6 to
10 weeks. Intestinal inflammation was assessed by the measurement of fecal
calprotectin concentrations (Immundiagnostik AG, Bensheim, Deutschland). Three
children were pancreatic sufficient at the assessment (fecal elastase-1 concentra-
tions: 200, 350 and 680 mcg/g of stool), the remaining seven were pancreatic
insufficient (fecal elastase-1 concentrations from 6 to 33 mcg/g of stool).

Results: The range of fecal calprotectin concentrations was from 7.5 to 400 mg/L
(median 81.2; mean±SEM: 42.5±37.3). In 8 (80%) infants abnormal calprotectin
results were obtained. The highest value, significantly different than in the other
subjects, was observed in an infant who was operated due to meconium ileus.
However, the second child who experienced meconium ileus and was treated in
a conservative mode presented with normal calprotectin concentration (7.5 mg/L).

No differences between pancreatic sufficient and insufficient patients were detected.
However, all pancreatic sufficient subjects presented with abnormal calprotectin
results.

Conclusions: Intestinal inflammation is already present in young CF infants.