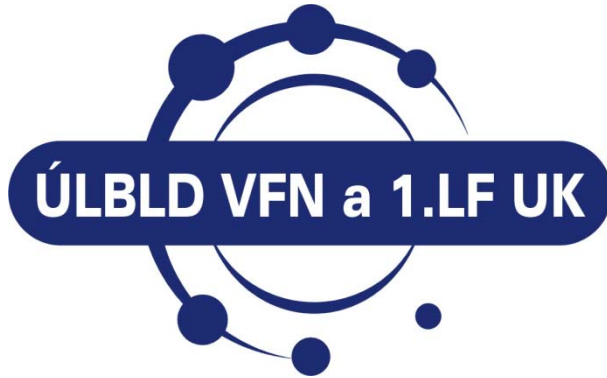


**CLINICAL,  
THERAPEUTICAL AND  
ECONOMICAL BENEFIT  
OF EXOCRINE  
PANCREATIC  
FUNCTION TESTS**



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# SUMMARY

**Introduction.** Follow-up of patients with exocrine pancreatic insufficiency can be easily performed with non-invasive test of exocrine pancreatic function -  $^{13}\text{C}$ -mixed triglycerides breath test ( $^{13}\text{C}$ -MTG) and fecal elastase-1 (FELA).

**Aims & Methods.** 56 patients (25/31 female/male; mean age 51 years) with diagnosed or suspected chronic pancreatitis (CHP) or after severe acute pancreatitis (AP) treated with enzyme substitution were included.  $^{13}\text{C}$ -MTG test was performed with 250mg Glyceryl-1,3-dioctadecanoate-2-octanoate-1- $^{13}\text{C}$ , standardized test procedure and calculated using BMR (Basal Metabolic Rate). Fecal elastase 1 (FELA) were determined using ELISA with monoclonal antibody (ScheboTech, Germany).

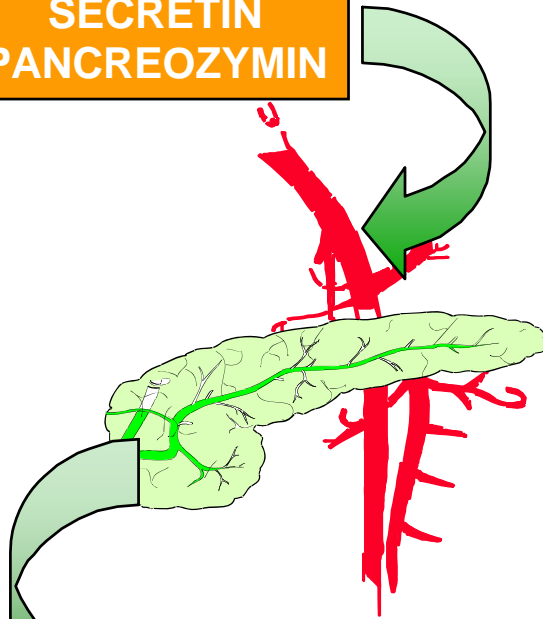
**Results.** Laboratory verified pancreatic exocrine insufficiency with  $^{13}\text{C}$ -MTG lower than 30%, was found only in 3/56 subjects, FELA less than 200  $\mu\text{g/g}$  was found in 11 patients. Substitution therapy, based on these tests, are still continued only in 8/56 i.e 14.28%.

**Conclusions.** Measurement of fecal elastase 1 is simple, non-invasive, robust test, which well correlates with morphological, static, extent of tissue damage.  $^{13}\text{C}$ -MTG breath test is better in evaluation of dynamic and kinetic aspects, real digestive ability and response to stimulation.  $^{13}\text{C}$ -MTG breath test is, contrary to FELA, suitable to evaluate pancreatic supplementation therapy. Clinical, therapeutical and economical benefit of exocrine pancreatic function tests is in possibility to exclude pancreatic substitution therapy in more than three-fourths patients with suspected pancreatic insufficiency.

# PANCREATIC FUNCTION TESTS

**DIRECT PZS TEST**

**SECRETIN  
PANCREOZYMIN**

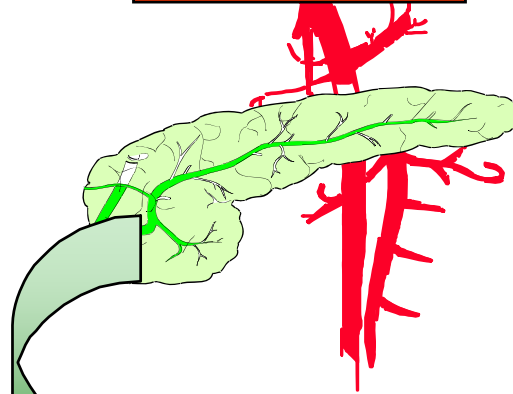


**AMYLASE  
LIPASE  
TRYPSIN  
BICARBONATE**

**DIRECT RESPONSE  
TO STIMULATION**

**FECAL ELASTASE**

**WITHOUT  
STIMULATION**



**FECAL  
ELASTASE**

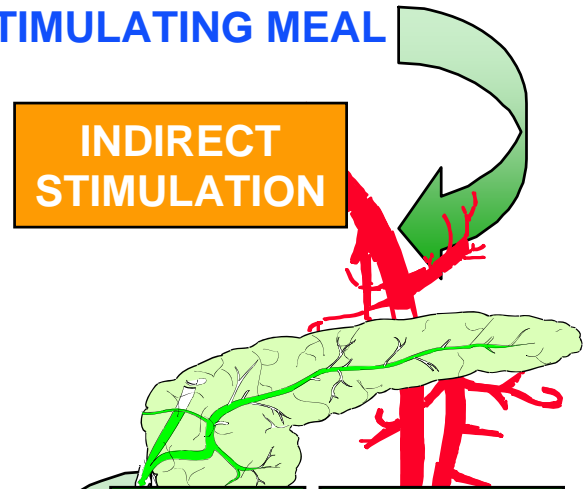
**ENZYMES FROM  
THERAPY/DRUGS  
WITH mAb NO REACTION**

**SECRETORY CAPACITY  
GRADING CHP**

**PABA, 13C-MTG**

**STIMULATING MEAL**

**INDIRECT  
STIMULATION**



**LIPASE**

**LIPASE  
ENZYME  
THERAPY**

**LIPID HYDROLYSIS  
TEST, SUBSTRATE**

**DIGESTIVE FUNCTION  
OF (LIPID) DIGESTION**

# INTRODUCTION

**Chronic pancreatitis** could be well diagnosed by histopathology, but for clinical purposes, differential diagnostics and patient follow-up we use mainly imaging procedures and non-invasive pancreatic function tests, if available.

In this study we report clinical, therapeutical and economical benefit of two different **noninvasive tests of exocrine pancreatic function**, breath test with  $^{13}\text{C}$ -mixed triglycerides and fecal elastase-1. **Fecal elastase 1 (FELA)** determined by ELISA with monoclonal antibody is available for routine use. The **breath test with  $^{13}\text{C}$ -mixed triglycerides (MTG)**, measured by POCT instrument based on NDIRS was used as indirect function test for substitution optimalization.

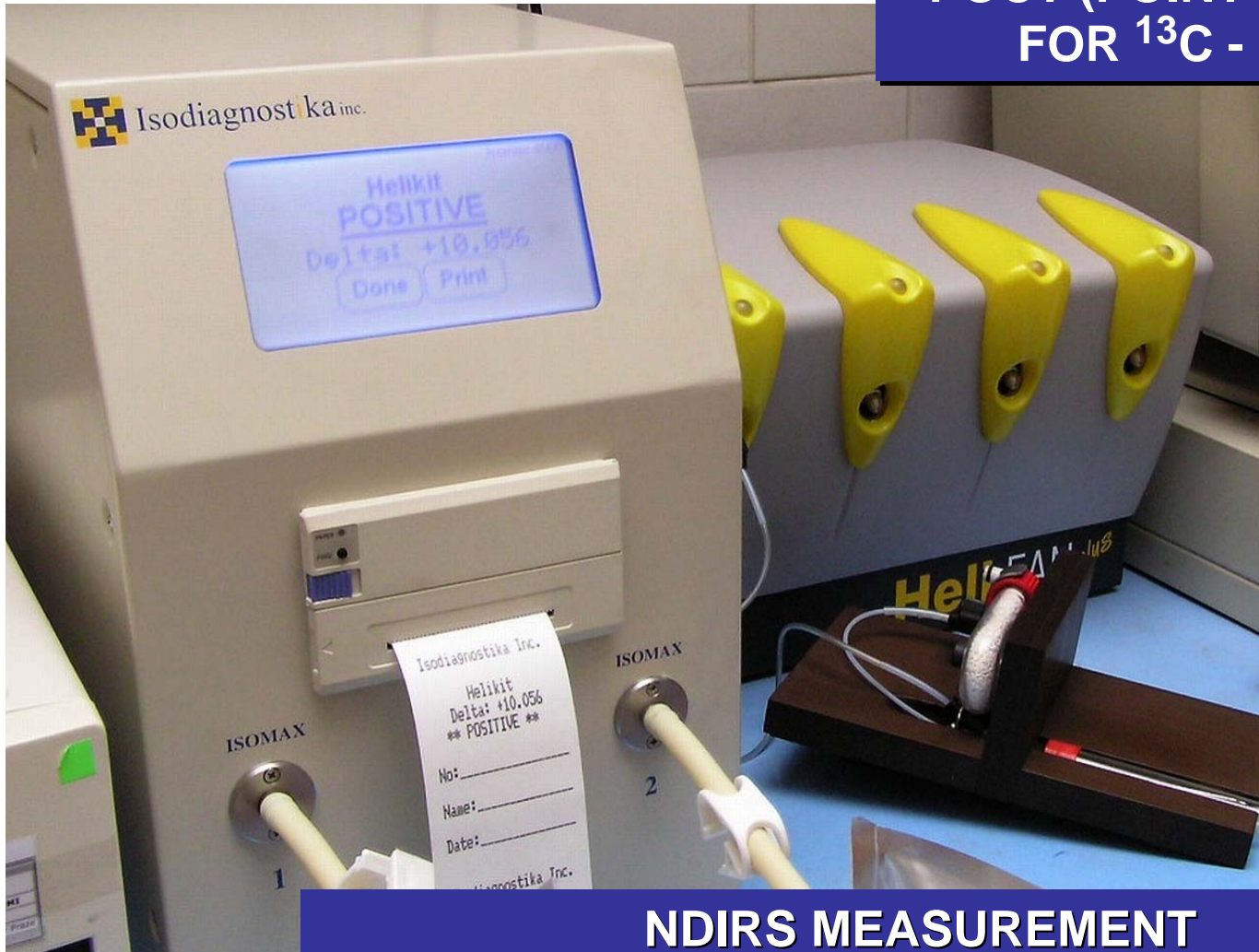
The new **clinically oriented classification of chronic pancreatitis** (Buchler and Malfertheiner, Bern 2009) applies following criteria: steatorrhoea (ST), diabetes mellitus (DM) and complications/organic changes of pancreas (CO). There are defined grade A (no-ST, no-DM, no-CO); grade B (no-ST, no-DM, with-CO); grade C (ST or DM, no-CO); grade D (ST and/or DM with CO).

The group of 56 patients with chronic pancreatitis (CHP) or after severe acute pancreatitis (AP) were treated by pancreatic enzyme substitution.

**Is the substitution of pancreatic enzymes necessary?**

# <sup>13</sup>C-MTG ANALYSIS

**POCT (POINT OF CARE TESTING)  
FOR <sup>13</sup>C - BREATH TESTS**



**ISOMAX 4000  
Isodiagnostika  
2 channel system  
(Canada)**

**HeliFAN plus, FAN  
4 channel system  
(Germany)**

**NDIRS Opto-acoustic  
detector unit  
(Lehrer & Luft type)**

**NDIRS MEASUREMENT  
(NON-DISPERSIVE INFRARED SPECTROSCOPY)**



# <sup>13</sup>C-MTG TEST

## TEST PROCEDURE

TWO SAMPLE BAGS AFTER OVERNIGHT FASTING  
PANCREATIC SUBSTITUTION THERAPY 5DAY EXCLUDED  
STIMULATION MEAL

4 CRISP SLICES, MAIZE WITH FIBRES

(WITHOUT CHOLESTEROL, GLUTEN-FREE)

2 x 10g RAMA (VEGETABLE FAT WITHOUT MILK PROTEINS)

TEST SUBSTANCE ADMINISTRATION - 250mg <sup>13</sup>C-MTG

STIRRED INTO VEGETABLE FAT

HOURLY BREATH-BAG SAMPLING (1 - 6 hr)

## TEST ANALYTICS

DOB MEASUREMENT OF EACH SAMPLE <sup>13</sup>CO<sub>2</sub> : <sup>12</sup>CO<sub>2</sub> (in ‰)

T<sub>x</sub> SAMPLE AGAINST T<sub>0</sub> (DOB = Delta Over Baseline)

## EVALUATION OF PANCREATIC INSUFFICIENCY

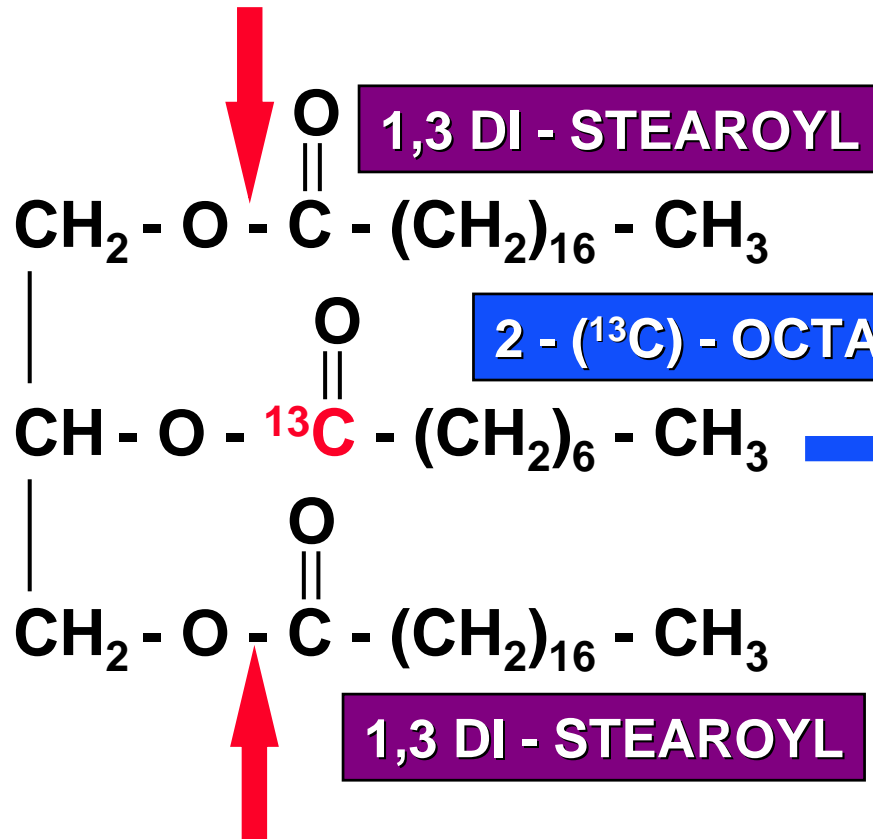
BSA CALCULATED (BASED ON WEIGHT, HEIGHT)

BMR AND CO<sub>2</sub> PRODUCTION CALCULATED (MS Excel)

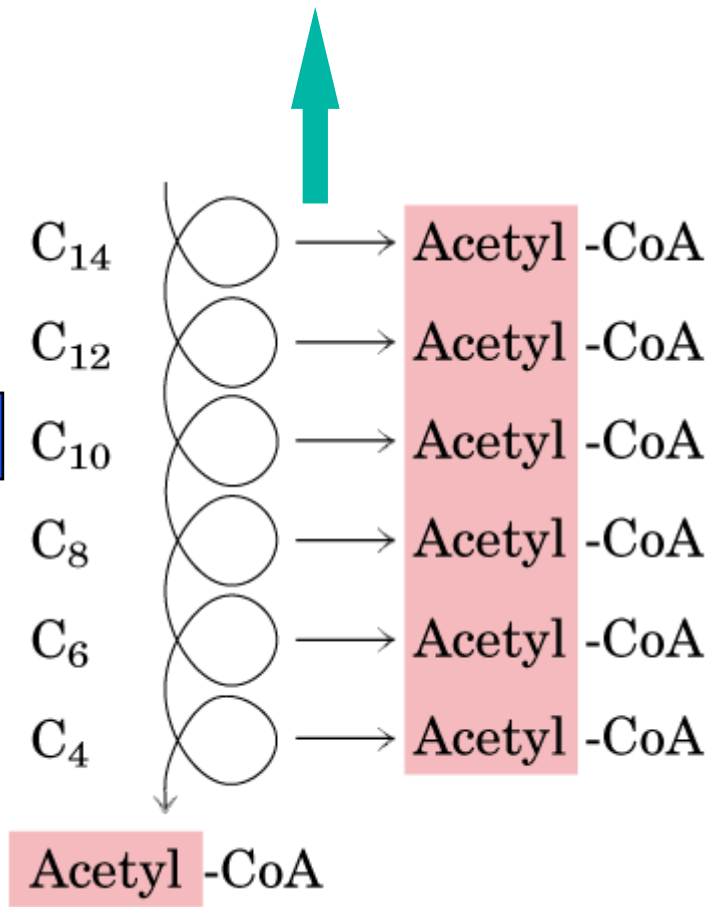
CUMMULATIVE RECOVERY FOR 6 HOURS CALCULATED

# <sup>13</sup>C-MTG - CHEMISTRY

PANCREATIC LIPASE



BREATH AIR <sup>13</sup>CO<sub>2</sub>



LIVER β - OXIDATION



# FECAL ELASTASE

## FECAL ELASTASE ELISA

**WE COMPARED TWO ELISA METHODS:**

**- SCHEBO BIOTECH (GERMANY) WITH**

**MONOCLONAL ANTIBODY TO ELASTASE IIA ISOTYPE**

**- BIOSERV DIAGNOSTICS (GERMANY) WITH**

**POLYCLONAL ANTIBODY TO ELASTASE IIIA AND IIIB ISOTYPES**

**CONCORDANT RESULTS WERE IN 85% WITH CORRELATION 0.72.**



*Comparison of two ELISA methods for determination of pancreatic elastase 1 in stool. Vaníčková, Z.; Kocna, P. et al. GUT, 2004, 53, Suppl.VI, A153*

## STOOL SAMPLES

**FECAL SAMPLES WERE STORED IN PLASTIC STOOL CONTAINERS AT 25°C FOR 1/2 WEEKS. THE VALUES OF ELASTASE-1 ARE HIGHLY STABLE, STORED AT TEMPERATURES FROM -25°C TO +37°C.**

*Determination of the interindividual variability with the ELISA test in the exocrine pancreas in the stool. Mrňák D. Thesis on 1.Medical Faculty, Charles University, Prague 2012*

# CHRONIC PANCREATITIS

THE CLASSIFICATION OF CHRONIC PANCREATITIS USED IN THIS STUDY INCLUDES TWO BASIC ASPECTS: MORPHOLOGY CHANGES AND CLINICAL SYMPTOMS OF FUNCTIONAL INSUFFICIENCY

**MORPHOLOGICAL CHANGES**

**PANCREATIC COMPLICATIONS**

**FUNCTIONAL CHANGES**

**CLINICAL SYMPTOMS OF  
FUNCTIONAL INSUFFICIENCY  
DM, STEATORRHOEA**

	<b>NON</b>	<b>YES</b>
<b>NON</b>	CHP - A	CHP - B
<b>YES</b>	CHP - C	CHP - D

*A proposal for a new clinical classification of chronic pancreatitis.  
Büchler MW, Martignoni ME, Friess H, Malfertheiner P.  
BMC Gastroenterol. 2009 Dec 14; 9: 93*

# RESULTS

56 PATIENTS; 25 WOMEN AND 31 MEN; THE AVERAGE AGE 51 YEARS  
DIAGNOSIS: CHRONIC PANCREATITIS (CHP) OR AFTER SEVERE ACUTE  
PANCREATITIS (AP) TREATED BY PANCREATIC ENZYME SUBSTITUTION

	n	FELA↓	MTG↓	KREON	notice
NON	16	2 - 12.5%	0	1 - 6.2%	↓FELA →KREON
CHP-A	19	2 - 10.5%	1	2 - 10.5%	↓MTG →KREON
CHP-B	5	1 - 20 %	0	2 - 40%	↓FELA →KREON
CHP-C	6	2 - 33.3%	0	0 - 0%	
CHP-D	10	4 - 40 %	2	3 - 30%	↓MTG/FELA →KREON

**SUBSTITUTION OF PANCREATIC ENZYMES (KREON 25000 J)**

**ONLY 8 FROM 56 PATIENTS - i.e 14.28%**

**13 PATIENTS ↓ FELA/MTG - 6 PTS HAVE SUBSTITUTION**

**2 PTS WITH SUBSTITUTION DESPITE OF NORMAL VALUES OF FELA/MTG**

# RESULTS

## CASE REPORTS – THE IMPORTANCE OF FUNCTION TESTS FOR INDICATION OF PANCREATIC ENZYME SUBSTITUTION

- 3 PATIENTS WITH ACUTE NECROTISING PANCREATITIS
- MORE THAN 50% OF PANCREATIC GLAND DESTROYED
- HOME ENTERAL NUTRITION VIA NASOJEJUNAL TUBE, PPI, PANCREATIC ENZYME SUBSTITUTION
- AFTER HEALING OF PANCREATIC NECROSIS – RETURN TO PERORAL INTAKE – DIET WITH 60 G OF FAT, NO FRIED AND GRILLED DISHES
- **IS THE SUBSTITUTION OF PANCREATIC ENZYMES NECESSARY?**

# THREE SELECTED CASES

CASE	STORY	FUNCTION TEST RESULTS	SUBSTITUTION (KREON)
A.A. 1938	NO SYMPTOMS, NORMAL FREQUENCY OF STOOLS, NO ABDOMINAL PAIN	<sup>13</sup> C-MTG 51% FELA 378 µg/g	SUBSTITUTION EX
M.V. 1971	ABDOMINAL CRAMPS AFTER MEAL	<sup>13</sup> C-MTG 23% FELA 530 µg/g	SUBSTITUTION RETURNED
A.M. 1931	2-3 STOOLS, SOMETIMES ABDOMINAL PAIN AFTER MEAL	<sup>13</sup> C-MTG 45% FELA 57 µg/g	SUBSTITUTION LEFT

# CONCLUSIONS

**Measurement of fecal elastase-1** is simple, non-invasive, robust test, which well correlates with morphological, static, extent of tissue damage.

**$^{13}\text{C}$ -MTG-breath test** provides us the complex evaluation of digestive processes - lipid digestion. cPDR value of  $^{13}\text{C}$ -MTG is the cumulative value, covering the exocrine pancreatic function + substitution therapy  $^{13}\text{C}$ -MTG breath test is better in evaluation of dynamic and kinetic aspects, real digestive ability and response to stimulation.  $^{13}\text{C}$ -MTG breath test is, contrary to FELA, suitable to evaluate pancreatic supplementation therapy.

**Performance of both tests** could improve clinical values. Combination of both tests covering various aspects of exocrine pancreatic function

**Clinical, therapeutical and economical benefit** of exocrine pancreatic function tests is in possibility to exclude pancreatic substitution therapy in more than three-fourths patients with suspected pancreatic insufficiency.

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