BREATH TESTS - PRINCIPLES, TECHNOLOGY AND APPLICATIONS

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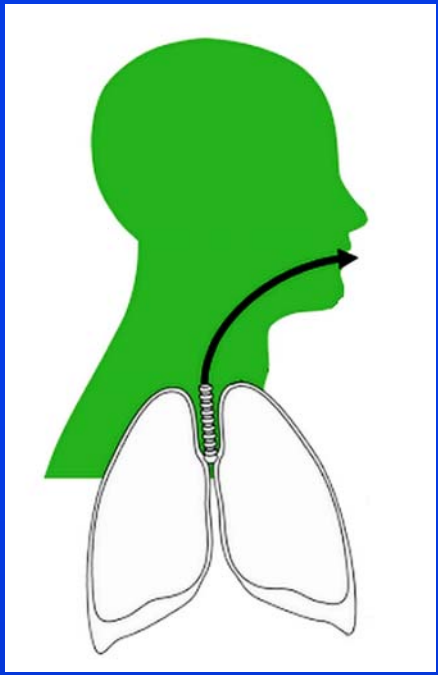
ÚLBLD VFN a 1.LF UK

1.LF UK tutorial, July 2024

The clinical significance of exhaled air analysis isl have known since the time of Hippocrates. Ancient doctors knew that the smell of a patient's breath was associated with certain illnesses



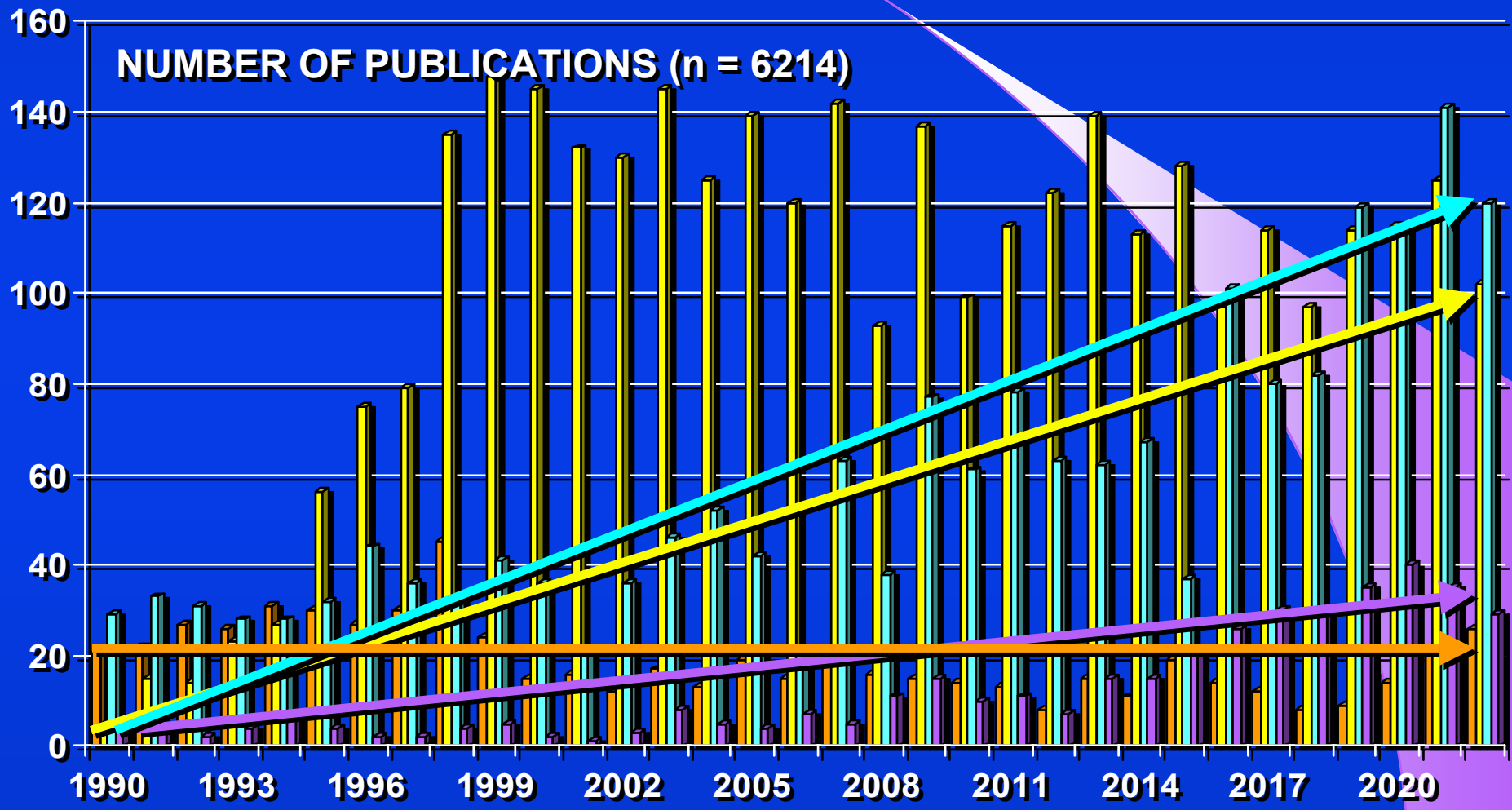
bad breath	disease
fruity	diabetes
fish	kidneys
sour	asthma
sweet	liver cirrhosis
ammoniacal	kidneys
feca	intestinal obstructionl

Recent Advances in Nanomaterial-Based Human Breath Analytical Technology for Clinical Diagnosis and the Way Forward. Kabir E, Raza N, Kumar V. et al. Chem. 2019; 5/12: 3020-3057

Non-invasive methods with the analysis of exhaled air offer very wide applications in clinical biochemistry, which are currently not sufficiently used. More than 8,500 publications are included in the NLM Pubmed database, and more than 40 13C-labeled substrates are described for methods with the stable carbon 13C isotope. With the development of new technologies, mass spectrometry analysis with selective, specific sensors based on nanochips, a higher use of non-invasive breath tests can perhaps be expected in the near future.

- Stable carbon isotope breath tests ^{13}C
- Breath tests with hydrogen and methane
- Analysis of nitric oxide in breath
- Determination of alcohol and ketone in breath
- Analysis of volatile organic compounds in breath

NLM - MEDLINE DATABASE ANALYSIS 1990 - 2023



BREATH TESTS TYPE: ^{14}C ^{13}C H_2 CH_4

^{13}C BREATH TESTS IN GASTROENTEROLOGY

ISOTOPE ^{13}C BENEFITS

^{13}C - IS A STABLE ISOTOPE OF CARBON
- IS NOT RADIOACTIVE
- COMMON OCCURENCE IN THE NATURE
- 1,1 % OF CARBON IN HUMAN BODY IS ^{13}C

ISOTOPE ^{13}C DISADVANTEGES

^{13}C - 1,1 % OF CARBON IN HUMAN BODY IS ^{13}C

^{13}C- BREATH TEST PRINCIPLE

matem.model

production CO_2

Change in ratio $^{13}C/^{12}C$ after substrate administration

DOB

hour output CO_2

PDR

kinetics

PET

cummulative output CO_2

cPDR

Peroral administration

^{13}C-substrate

determination ratio $^{13}C/^{12}C$

$^{13}CO_2$

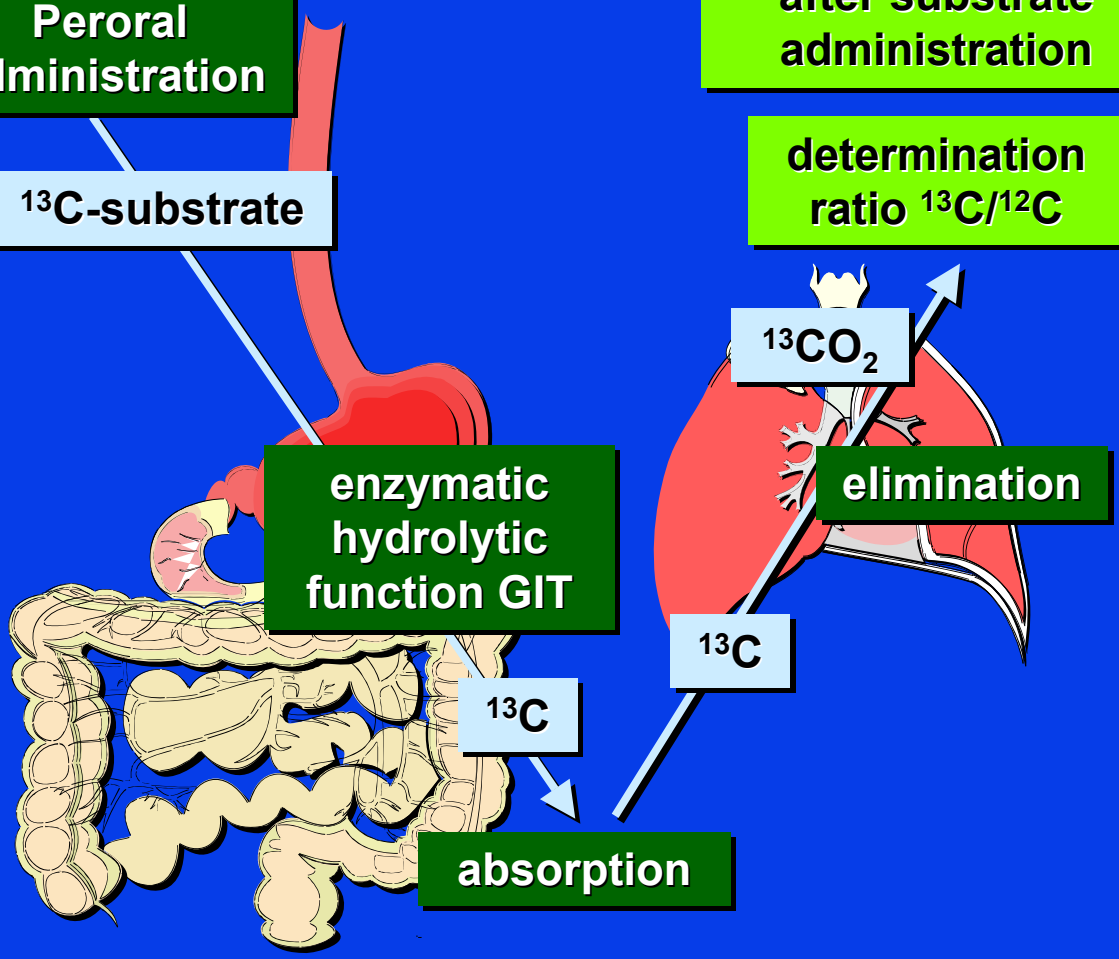
elimination

enzymatic hydrolytic function GIT

^{13}C

^{13}C

absorption



^{13}C BREATH TESTS - RESULTS COUNTING

δ – DELTA, δ is expressed in ‰ / per thousand

$$\delta\,(‰) = (R_{sample}/R_{standard} - 1) \bullet 1000$$

$$\delta^{13}C\,(‰) = ([^{13}C/^{12}C]_{sample}/[^{13}C/^{12}C]_{standard} - 1) \bullet 1000$$

DOB	**Delta Over Baseline**
PDR	**Percent Dose Recover**
cPDR	**Cummulative Percent Dose Recovery**
PET	**Peak Excretion Time**

^{13}C BREATH TESTS - PDB STANDARD

The PDB standard is the primary reference material for measuring natural changes in the content of the carbon isotope ^{13}C,determined in calcium carbonate from shells Cretaceous belemnites of the genus Belemnitella americana from the Pee Dee geological formation in South Carolina (US)

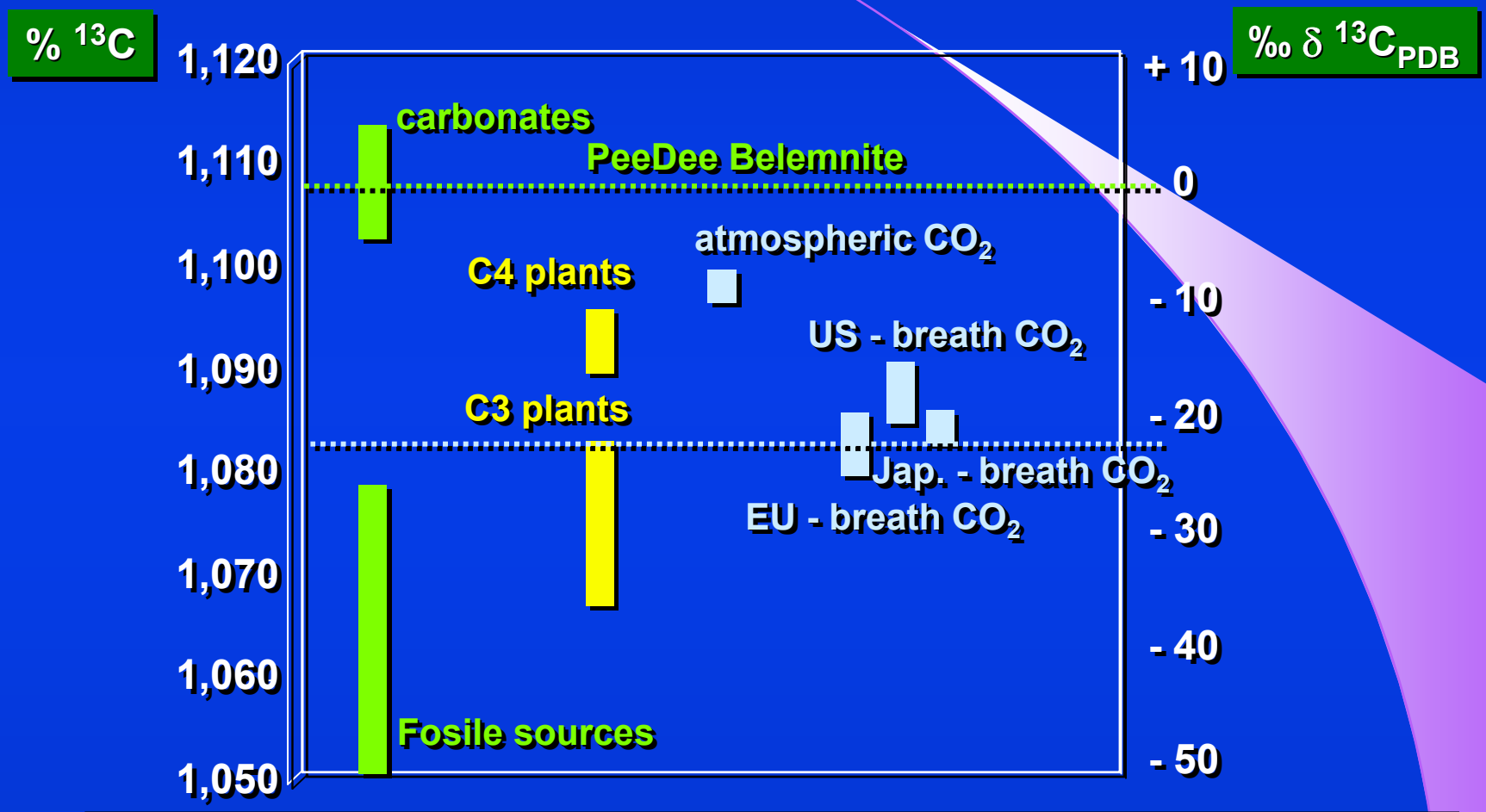
PDB Pee Dee Belemnitae

International standard ^{13}C = 1.11237 %

^{13}C BREATH TESTS - PDB STANDARD

PDB - Pee Dee Belemnitella americana

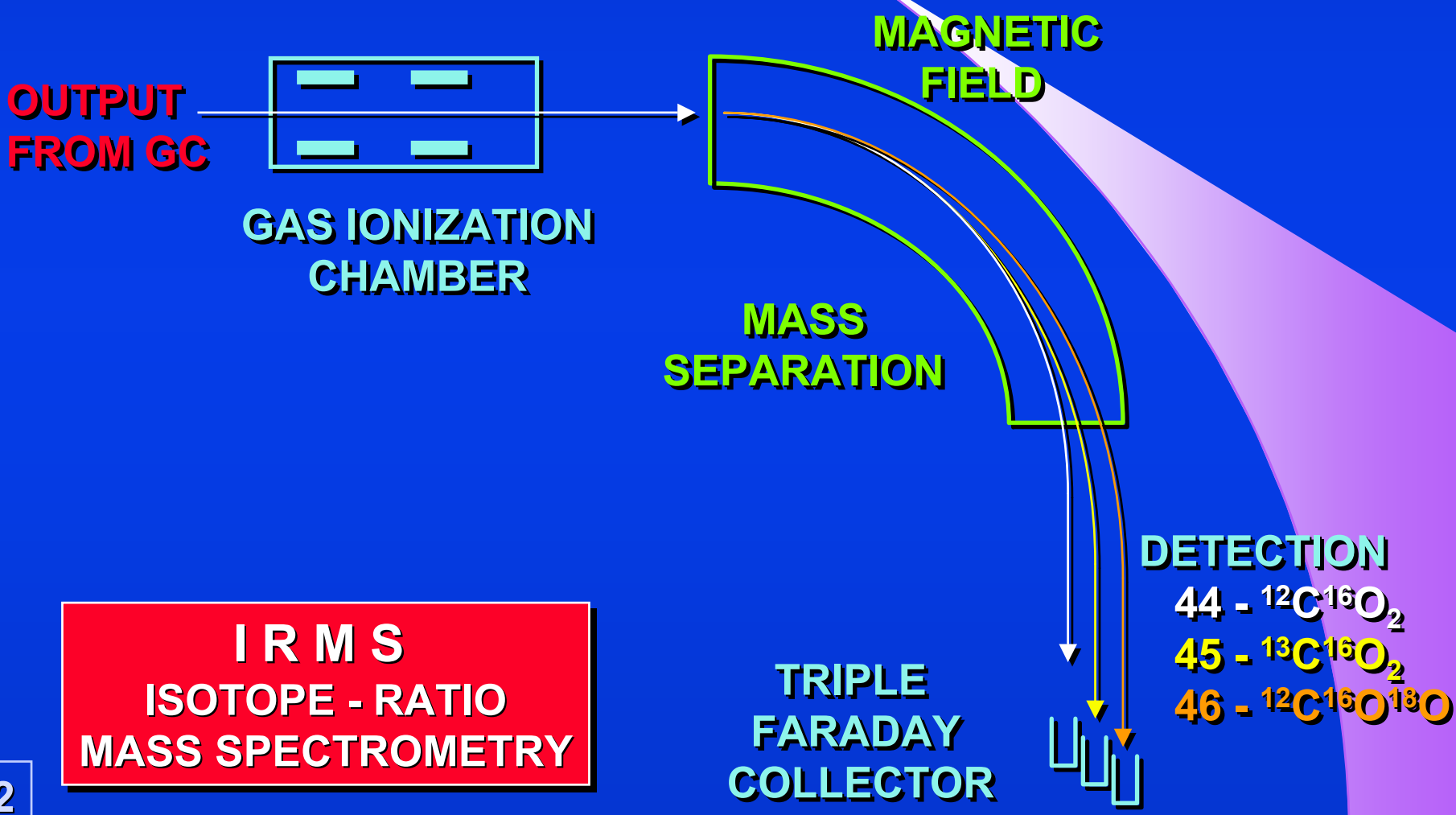
OCCURENCE ^{13}C IN NATURE



13C abundances of nutrients and the effect of variations in 13C isotopic abundances of test meals formulated for 13CO2 breath tests. Schoeller DA. et al.: Am J Clin Nutr. 1980; 33(11): 2375 - 2385

HeliView - IRMS ANALYSER OF BREATH TESTS BASED ON CARBON ^{13}C

IRMS - BREATH TEST ANALYSER - DETECTION

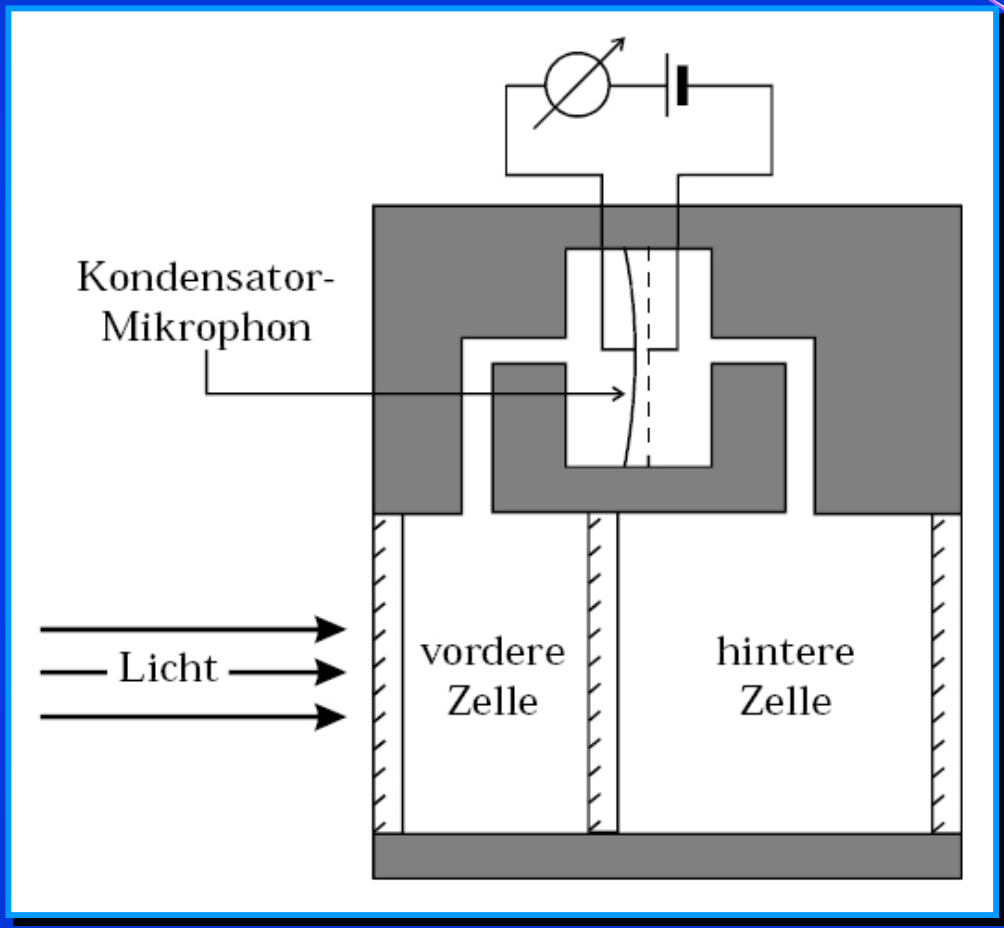


I R M S
ISOTOPE - RATIO MASS SPECTROMETRY

$^{13}CO_2$ ANALYSER WITH IR DETECTION

HeliFAN Plus
IR spectrophotometr
Fischer Analysen Instr.

$^{13}CO_2$ ANALYSER WITH IR DETECTION



OptoAcustic detection
Lehrer & Luft typ
Lehrer E and Luft K F 1938
German Patent No 730478

- IR absorption
- pressure change
- membrane deformation
- acoustic signal

An analytical model of the pneumatic non dispersive infrared detector
Daniel P Lucero: Journal of Physics E: Scientific Instruments, 1973; 6: 281 - 286

HELICOBACTER PYLORI GUIDELINES

Statement 1: **UBT is the most investigated and best recommended** non-invasive test in the context of a 'test-and-treat strategy'. **Monoclonal SAT can also be used.** Serological tests can be used only after validation. Rapid ('office') serology tests using whole blood should be avoided in this regard.
Level of evidence: 2a Grade of recommendation: B

Statement 9: The available data consistently recognise **pepsinogen (Pg)** serology as the **most useful non-invasive test to explore the gastric mucosa status (non-atrophic vs atrophic).** The PgI/PgII ratio can never be assumed as a biomarker of gastric neoplasia.
Level of evidence: 2a Grade of recommendation: A

Management of Helicobacter pylori infection-the Maastricht V/Florence Consensus Report.
Malfertheiner P. et all. - The European Helicobacter Study Group (EHSG). Gut. 2017 Jan; 66 (1): 6-30

^{13}C-UREA BREATH TEST FOR HELICOBACTER PYLORI

SUBSTRATE: ^{13}C-UREA
DOSAGE: 50 - 100 mg
TEST TIME: 30 minutes

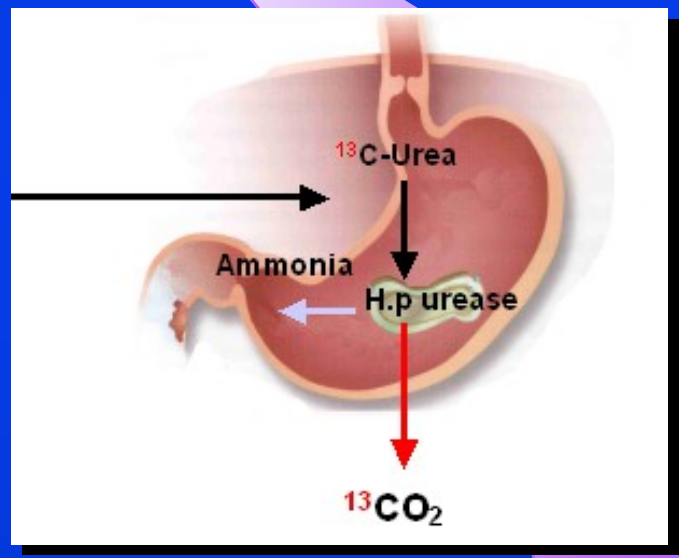
BREATH TEST

Hp - UREASE

$$NH_2\text{-}{}^{13}CO\text{-}NH_2 + H_2O = 2\ NH_3 + {}^{13}CO_2$$

RAPID UREASE TEST

global gastric test

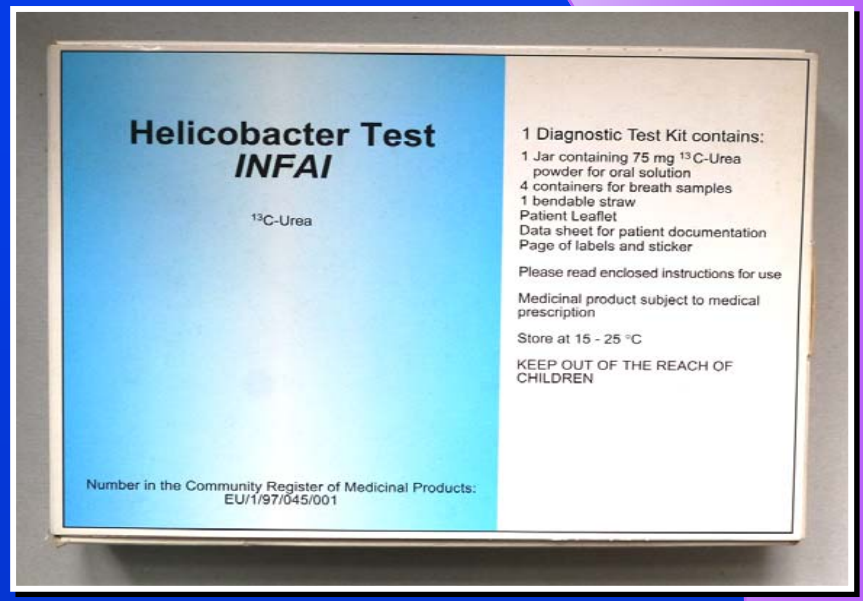


local test - biopsy

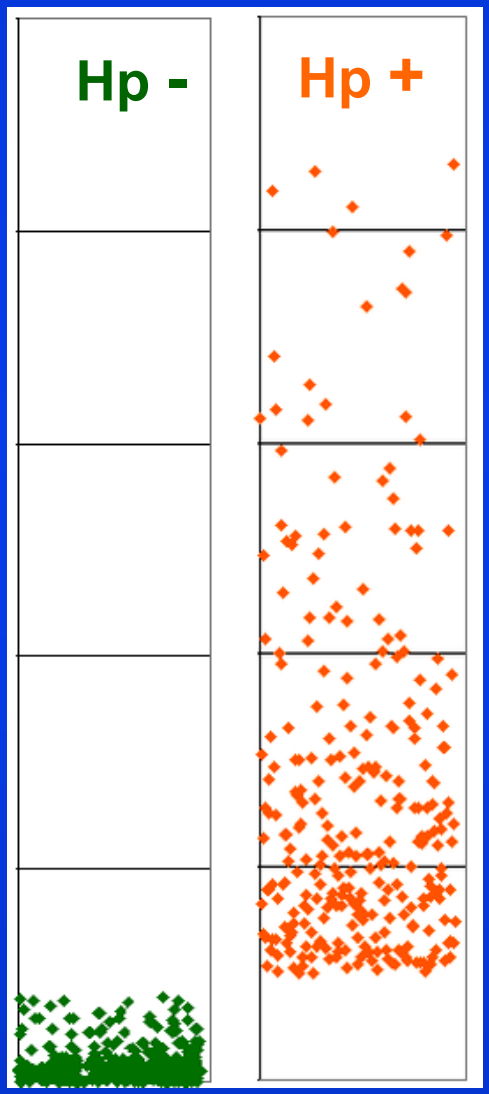
^{13}C-UREA BREATH TEST FOR HELICOBACTER PYLORI

^{13}C-UBT test, substrate - 75mg of labeled urea breath samples at T_0 and T_{30} minutes DOB up to 4‰ Hp negative, above 5‰ Hp positive,if the result is 4-5‰, we recommend repeating the test

UBT - Hp INFAI registered in Czech - SÚKL



^{13}C-UREA BREATH TEST FOR HELICOBACTER PYLORI



CLINICAL RESULTS:	
NUMBER OF UBT TESTS:	1621x
NEGATIVE RESULT:	1254x
POSITIVE RESULT:	333 x
GRAY SCALE 4 - 5:	36 x

POSITIVITY – 20.5%

DETERMINATION OF HpSA IN FACES (HELICOBACTER STOOL ANTIGEN)	
NUMBER OF HpSA TESTS:	1931x
NEGATIVE RESULT:	1678 x
POSITIVE RESULT:	253 x

POSITIVITY – 13.1%

^{13}C - BREATH TESTS FOR PANCREATIC FUNCTION

SUBSTRATE SELECTION

- ^{13}C - TRIOLEIN
- ^{13}C - HIOLEIN
- ^{13}C - MIXED TRIGLYCERIDE
- ^{13}C - CHOLESTERYL OCTANOATE
- ^{13}C - TRIPALMITIN
- ^{13}C - TRIOCTANOIN
- ^{13}C - STARCH
- ^{13}C - BzTyrAla

STEATORHEA > 11 - 14 g/day
INTRALUMINAL LIPOLYSIS
SPECIFICITY FOR PANCREATIC LIPASE
LIPASE OUTPUT < 90 kU/hr
PANCREAT. CHOLESTEROL ESTERASE
STEATORHEA > 11 g/day
FAT MALABSORPTION
TISSUE DAMAGE, FIBROSIS > 30%
AMYLASE SECRETION < 10%
CORRELATION with the PABA test

EXOCRINE PANCREAS INSUFFICIENCY GUIDELINES

Which test is clinically indicated
for diagnosing exocrine pancreatic insufficiency (PEI) ?
Statement 3-6. In a clinical setting, **a non-invasive pancreatic function test (PFT) should be performed.** The **FE-1 test** is feasible and widely available and is therefore most frequently used in this setting, while the **13C mixed triglyceride** breath test (13C-MTG-BT) offers an alternative. The s-MRCP test may also be used as an indicator of PEI but provides only semiquantitative data.
(Grade 1B, agreement)

Is a pancreatic function test required for the diagnosis of CP?
Statement 3-7. A function test is required for the diagnosis of CP.
(Grade 2B, strong agreement)

Should a pancreatic function test be performed at the time of diagnosis?
Statement 3-8. Every patient with a new diagnosis of CP
should be screened for PEI. (Grade 1A, strong agreement)

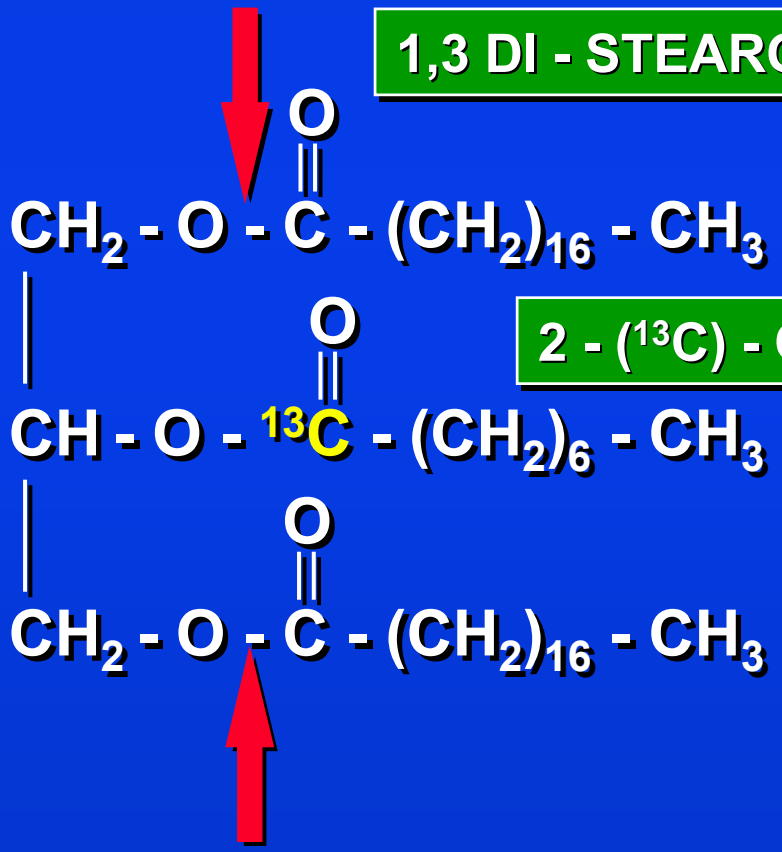
Löhr M. - HaPanEU/UEG Working Group, UEG Journal, 2017, Vol. 5(2) 153–199
United European Gastroenterology evidence based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPanEU)

METABOLIC PROCESSES FOR ^{13}C-MTG BREATH TEST

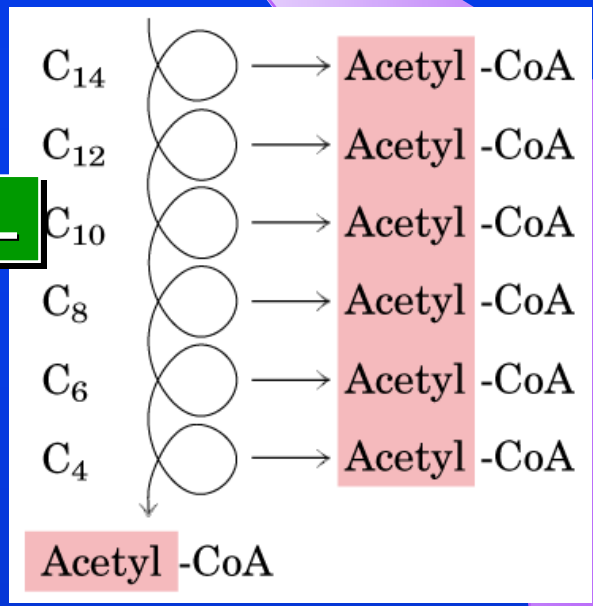
BREATH $^{13}CO_2$

PANCREATIC LIPASE

1,3 DI - STEAROYL



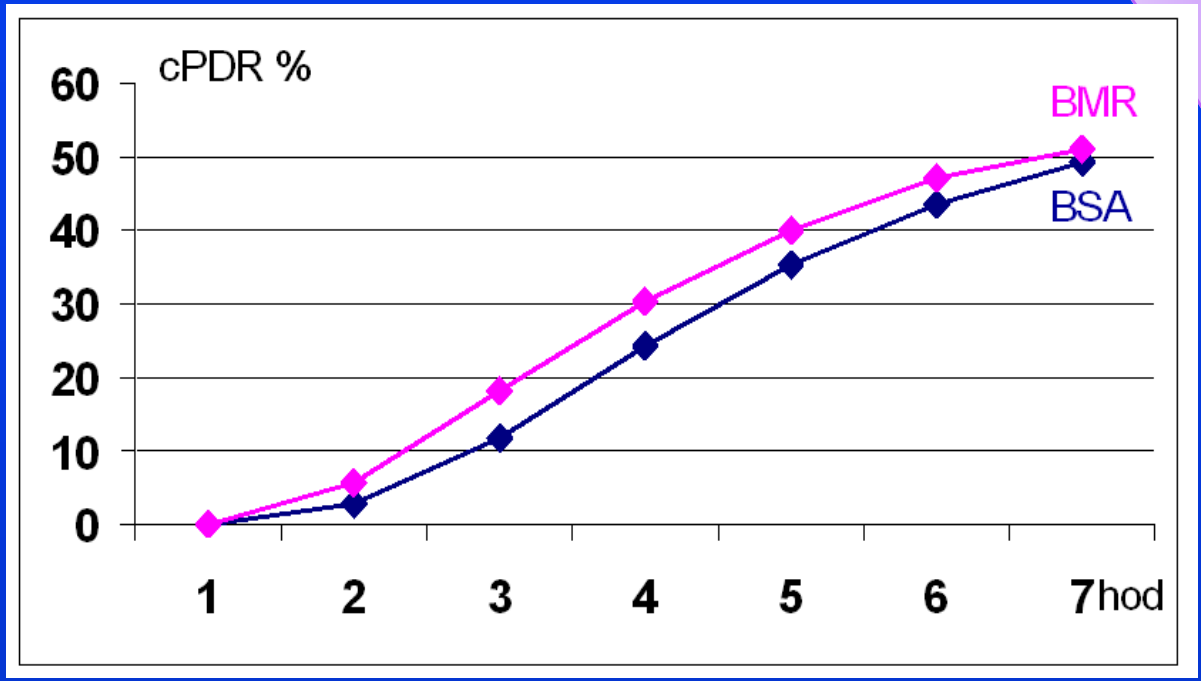
2 - (^{13}C) - OCTANOYL



HEPATAL β - OXIDATION

^{13}C-MTG BREATH TEST FOR EXOCRINE PANCREATIC FUNCTION

^{13}C-MTG test - in our arrangement we serve
100 g of gluten-free bread with
250 mg of mixed triglyceride in 20 g of margarine
breath samples at time T_0 to T_{360} minutes after 60 minutes
$cPDR_{6h}$ pathological below 30% (BMR)



^{13}C-MTG BREATH TEST FOR EXOCRINE PANCREATIC FUNCTION

CLINICAL RESULTS:
NUMBER OF MTG TESTS: 407 x

NORMAL VALUE: 365 x
PATHOLOGICAL VALUE: 41 x

DETERMINATION OF PANCREATIC ELASTASE-1 IN FACES (FELA)

COMPLIANCE OF ^{13}C-MTG TEST WITH FELA 327 x - MATCH is 83%

We recommend the determination of elastase-1 in the stool as a suitable static marker to assess the capacity of the exocrine pancreas, we suggest the ^{13}C-MTG breath test as a dynamic, functional test to assess the complex, digestive effect.

^{13}C - BREATH TESTS FOR LIVER FUNCTIONS

SUBSTRATE SELECTION

- ^{13}C - GALACTOSE
  CYTOSOL, PHOSPHORYLATION, DG.CIRRHOSIS
- ^{13}C - AMINOPYRINE
  CYP2C19, DEMETHYLATION, SEVERITY OF HCV FIBROSIS
- ^{13}C - PHENYLALANINE
  CYTOSOL, OXIDATION, FUNCTIONAL RESERVE ASSESSMENT
- ^{13}C - METHIONINE
  MITOCHONDRIA, OXIDATION, NAFLD ASSESSMENT
- ^{13}C - METHACETIN
  CYP1A2, DEMETHYLATION, LIVER DISEASE ASSESSMENT

Potential use of metabolic breath tests to assess liver disease and prognosis: has the time arrived for routine use in the clinic?
Stravitz RT, Ilan Y. Liver Int. 2016 Oct 8. doi: 10.1111/liv.13268. [Epub]

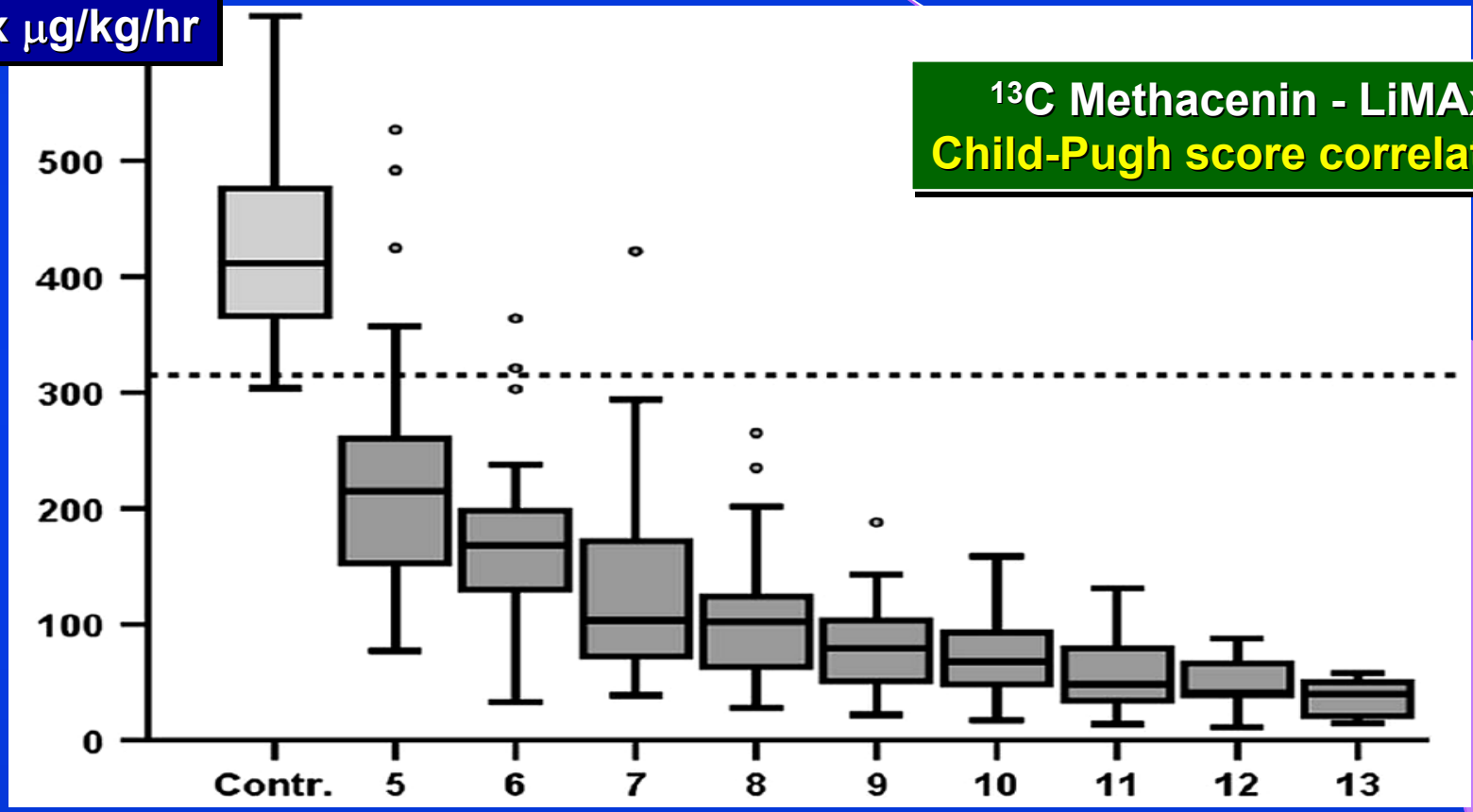
BREATH TEST WITH ^{13}C - METHACETIN

Exalenz BreathID POCT analyzer
continuous detection of the $^{13}C/^{12}C$ ratio
Molecular Correlation Spectroscopy (MCS)
Clinical studies 2016-2019 with ^{13}C-methacetin
Non-alcoholic hepatitis (NASH, NAFLD),
risk of cirrhosis in liver transplants

^{13}C Methacenin - MBT analyzing liver function, can reliably predict liver decompensation in patients with compensated NASH cirrhosis.

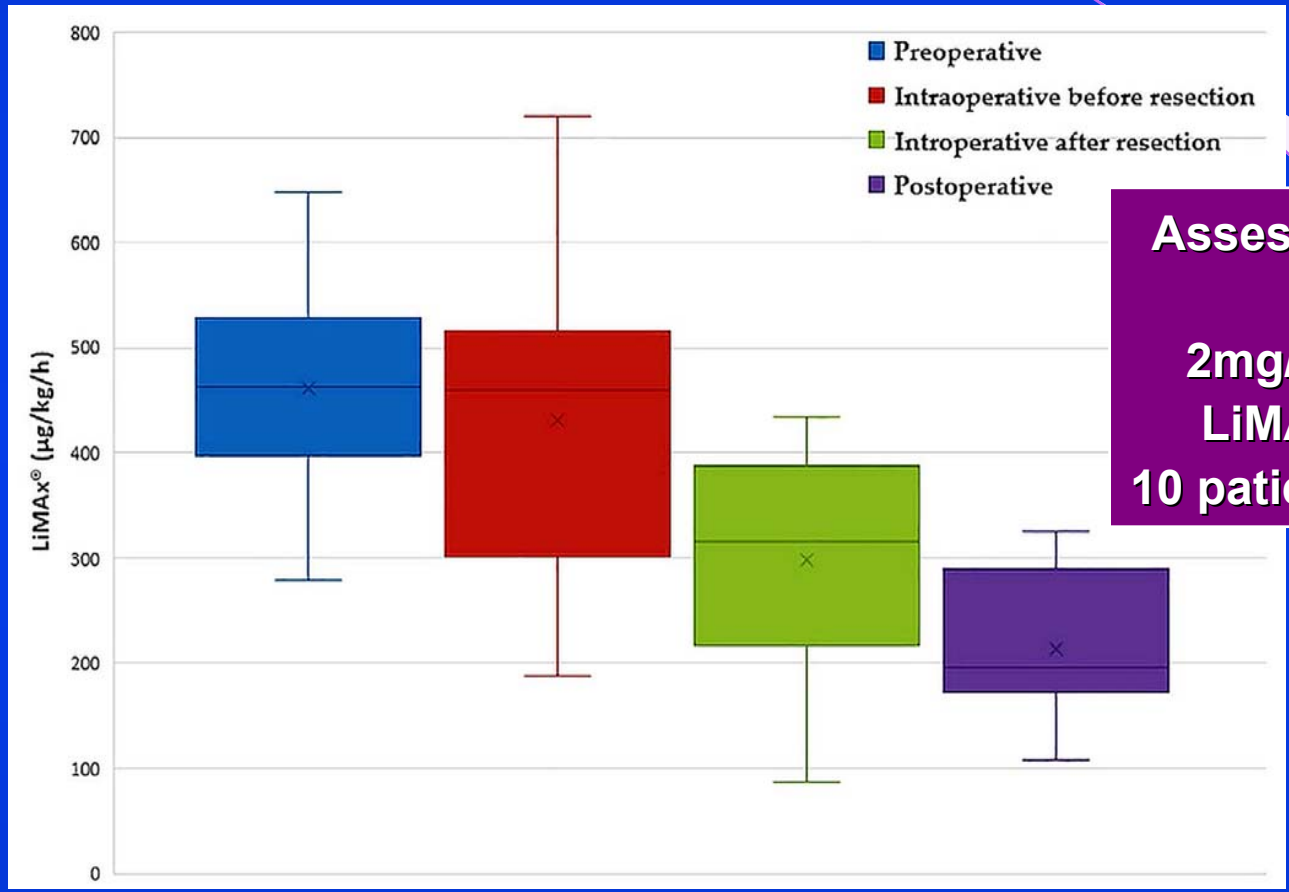
The noninvasive point of care MBT accurately predicts decompensation events better than MELD in compensated (MELD<15) NASH cirrhotics.
Chalasani N, Lawitz E, Abdelmalek M. et al.,
AASLD Liver Meeting, San Francisco, November 2018, Abstract No.1337

BREATH TEST WITH ^{13}C - METHACETIN



Enzymatic liver function capacity correlates with disease severity of patients with liver cirrhosis: a study with the LiMAx test.
Malinowski M, Jara M, Lüttgert K. et al. Dig Dis Sci. 2014 Dec;59(12):2983-2991

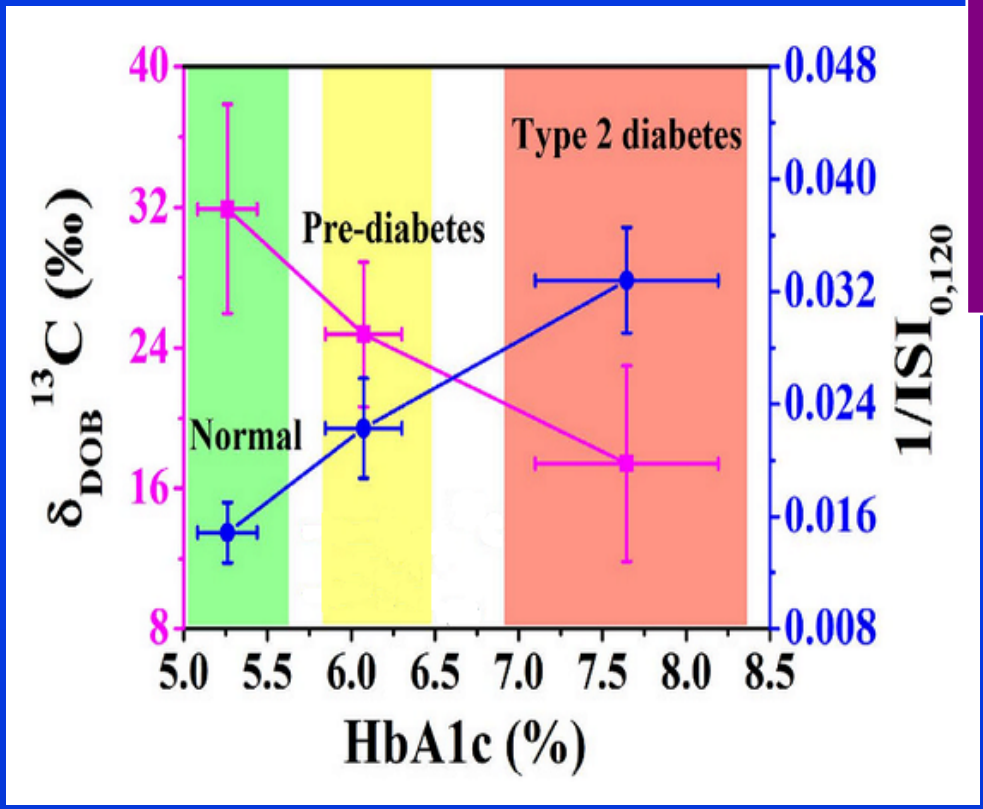
BREATH TEST WITH ^{13}C - METHACETIN



Assessment of liver function in real time
2mg/kg ^{13}C-methacetin i.v
LiMAx score in mg/kg/hr
10 patients with liver resection

First intraoperative measurement of liver functional capacity during liver surgery using the 13 C-methacetin breath test: early results of a pilot study. Makridis G, Oldhafer KJ. J Hepatobiliary Pancreat Sci. 2020; 27(5): 280-281

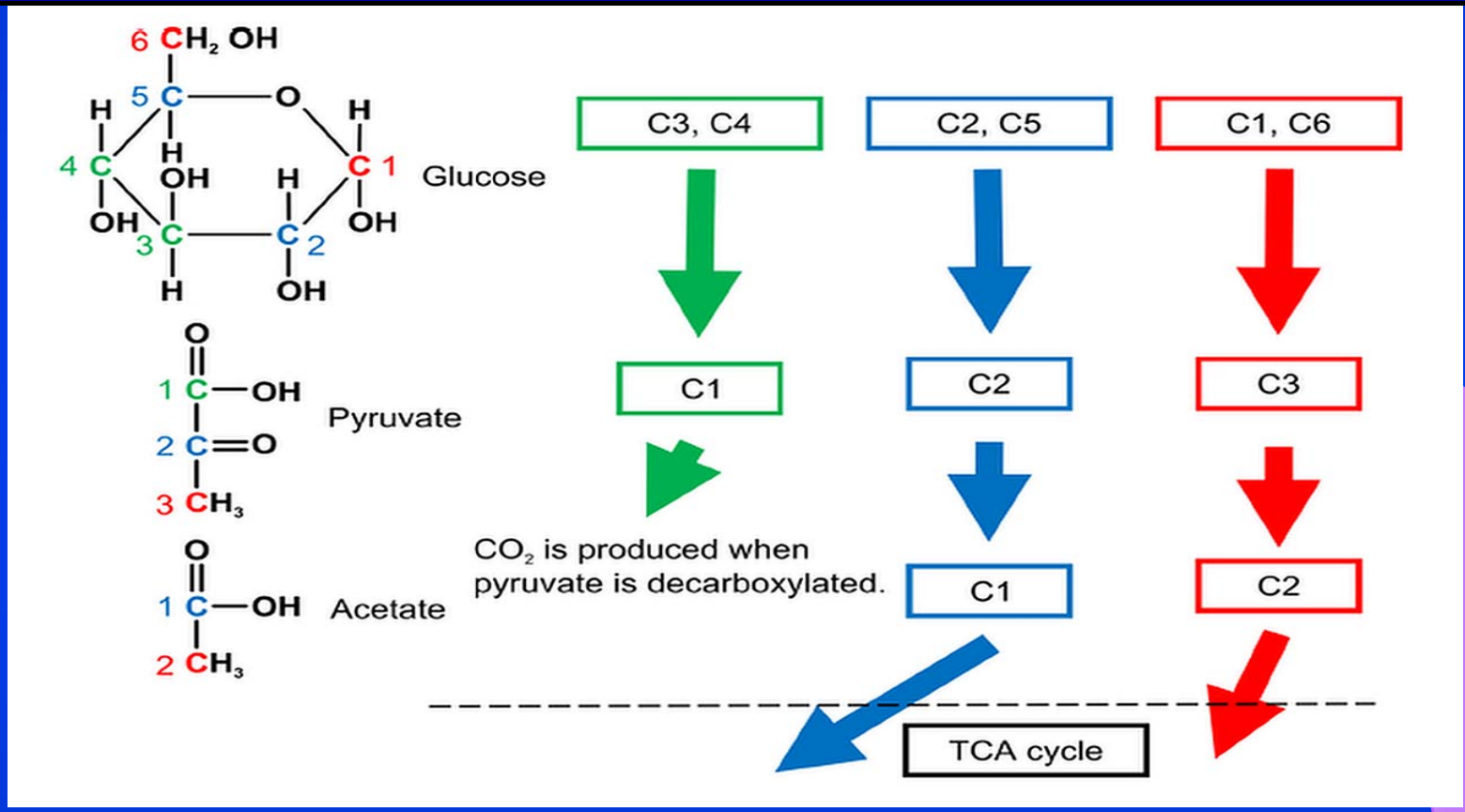
^{13}C-GLUCOSE BREATH TEST



Assessment of insulin resistance
Dg. pre-diabetes and type 2 diabetes
Insulin sensitivity index
Patients: 31 NDC, 38 PD and 47 T2D
75mg $^{13}C_6$ D-glucose (^{13}C-GBT)
ISI_{120} is more sensitive than HOMA-IR

Insulin sensitivity index (ISI0, 120) potentially linked to carbon isotopes of breath CO2 for pre-diabetes and type 2 diabetes. Ghosh C, Mukhopadhyay P, Ghosh S, Pradhan M. Sci Rep. 2015; 5: e11959

^{13}C-GLUCOSE BREATH TEST



Investigation of Metabolism of Exogenous Glucose at the Early Stage and Onset of Diabetes Mellitus in Otsuka Long-Evans Tokushima Fatty Rats Using [1, 2, 3-13C]Glucose Breath Tests. Kawagoe N, Kano O, Kijima S, Tanaka H, Takayanagi M, Urita Y. PLoS One. 2016; 11(8): e0160177

^{13}C- BREATH TEST IN ACUTE MEDICINE

Isomark Canary™ - BDV > 1.4% accurately differentiates subjects with emerging infections and predicts the presence of infection up to 48 hours before clinical confirmation. BDV can predict the onset of infection and help distinguish SIRS from infection, which could prompt earlier diagnosis, earlier appropriate treatment, and improve outcomes.

Changes in exhaled 13CO2/12CO2 breath delta value as an early indicator of infection in intensive care unit patients. O'Rourke AP, Buckman SA, Evans DC, Kerwin AJ, Breunig EA, Bütz DE. J Trauma Acute Care Surg. 2019 Jan;86(1):71-78.

^{13}C-EBT - BREATH TEST FOR ALCOHOL BREAKDOWN

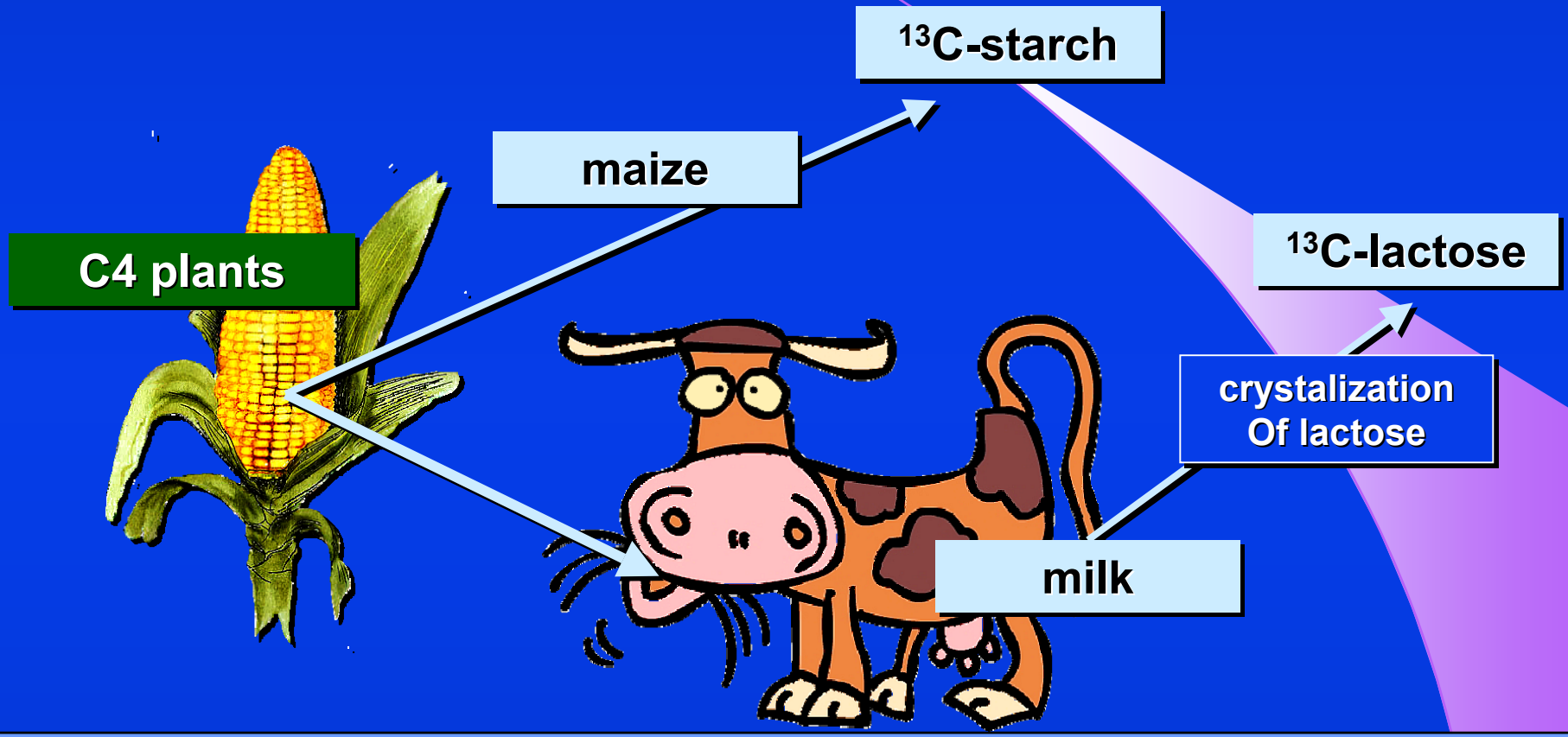
^{13}C-EBT - ^{13}C Ethanol Breath Test
the test substrate is
100 ml of ^{13}C-ethanol
in 100 ml of Asahi beer
polymorphism was tested
alcohol dehydrogenase (ADH) a
aldehyde dehydrogenase (ALDH)

Evaluation of alcohol metabolism in humans using the non-invasive [13C]-ethanol breath test – influence of gender, Helicobacter pylori infection and polymorphism of alcohol-oxidizing enzymes. Suzuki M, Tanaka S, Komatsu H, et al. Alimentary Pharmacology & Therapeutics 2006; 2: 177-181.

Breath test	Indication	Sensitivity	Specificity
^{13}C-Glykocholate	SIBO	76%	35%
^{13}C-Xylose	SIBO	89%	30%
^{13}C-Lactose	Malabsorption	84%	96%
^{13}C-Urea	Hp infection	96%	93%
^{13}C-Aminopyrin	Liver test	86%	68%
^{13}C-Metacetin	Liver test	93%	94%
^{13}C-Fenylalanin	Liver test	98%	60%
^{13}C-Mixed-triglyceride	Pancreat.insufficiency	89%	81%
^{13}C-Oktanoate	Gastric emptying	67%	80%

Update on diagnostic value of breath test in gastrointestinal and liver diseases.
Siddiqui I, Ahmed S, Abid S.
World J Gastrointest Pathophysiol. 2016 Aug 15;7(3):256-265

NATURAL SUBSTRATES WITH ^{13}C FOR BREATH TESTS



13C-enriched lactose, derived from milk of cows fed with silo corn (d= -10.885) for 5 weeks. Because it is known that it takes 14 days for cows milk to be in equilibrium with a diet, milk of seven cows was collected during the last 3 weeks of this 5-week period and pooled. Lactose was obtained by crystallization techniques.

NATURAL SUBSTRATES WITH ^{13}C FOR BREATH TESTS

J Gastroenterol Hepatol. 2005 Aug; 20(8): 1228 - 1234
Feasibility of a breath test with a substrate of natural 13C-abundance and isotope-selective non-dispersive infrared spectrometry: a preliminary study.
Jonderko K, Kasicka-Jonderko A, Syrkiewicz-Trepiak D, Blonska-Fajfrowska B.
Naturally (13)C-enriched starch and NDIRS provides background for future research on the clinical usefulness of this method for a non-invasive assessment of the pancreatic exocrine function.

J Lab Clin Med. 1988 Aug; 112(2): 193 - 200
13CO2 breath test using naturally 13C-enriched lactose for detection of lactase deficiency in patients with gastrointestinal symptoms.
Hiele M, Ghoos Y, Rutgeerts P, Vantrappen G, Carchon H, Eggermont E.
The 13CO2 breath test was found to be more sensitive (0.84 versus 0.68) and more specific (0.96 versus 0.89) than the H2 breath test in detecting low jejunal lactase activity.

The American Society for Nutritional Sciences J. Nutr. 134: 1193 - 1196, May 2004
A Combined 13CO2/H2 Breath Test Can Be Used to Assess Starch Digestion and Fermentation in Humans
Erin L. Symonds, Stamatiki Kritas, Taher I. Omari and Ross N. Butler
The 13CO2/H2 breath test can be used to estimate digestion and fermentation of starches in different physiologic and pathologic conditions.

^{13}C BREATH TESTS GUIDELINES - UEG

This recommendation should improve pan-European harmonization of diagnostic approaches to symptoms and disorders that are very common in gastroenterology practice, both by specialists and primary care in both adult and pediatric patients.

In addition, this guide identifies areas for future clinical research involving the use of ^{13}C breath tests

^{13}C-UBT Urea Breath Test
^{13}C GEBT Gastric Emptying Breath Tests
^{13}C PFBT Pancreatic Function Breath Tests
^{13}C MTGBT Mixed Triglyceride Breath Test
^{13}C LFBT Liver Function Breath Tests

European guideline on indications, performance and clinical impact of 13C-breath tests in adult and pediatric patients: An EAGEN, ESNM, and ESPGHAN consensus, supported by EPC. Keller J, Hammer HF, Afolabi PR et al. United European Gastroenterol J. 2021; 9: 598–625

^{13}C BREATH TESTS IN OTHER FIELDS OF MEDICINE

(13)C-tryptophan breath test detects increased catabolic turnover of tryptophan along the kynurenine pathway in patients with major depressive disorder. Teraishi T, Hori H, Sasayama D. et al.Sci Rep. 2015 Nov 3;5:15994.

Our results suggest that the 13C-TBT could be a novel biomarker for detecting a subgroup of MDD with increased tryptophan–KYN metabolism.

13C-phenylalanine breath test detects altered phenylalanine kinetics in schizophrenia patients. Teraishi T, Ozeki Y, Hori H. et al. Transl Psychiatry. 2012 May 22;2:e119

Our results suggest that 13C-PBT is a novel laboratory test that can detect altered phenylalanine kinetics in chronic schizophrenia patients.

A rapid non invasive L-DOPA-^{13}C breath test for optimally suppressing extracerebral AADC enzyme activity - toward individualizing carbidopa therapy in Parkinson's disease. Modak A, Durso R, Josephs E. et al. J Parkinsons Dis. 2012;2(4):349-56.

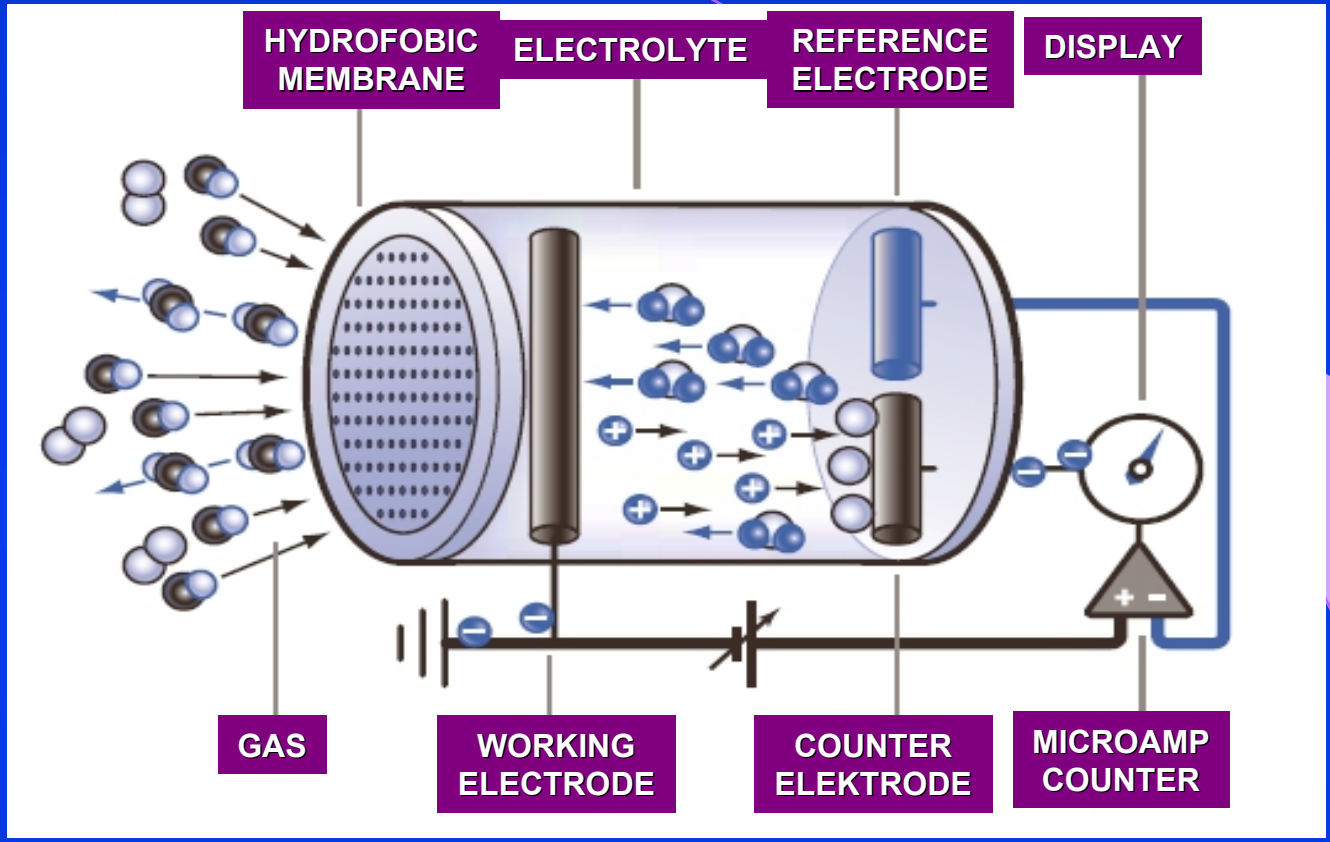
The LD-breath test can be a useful noninvasive diagnostic tool for evaluation of AADC enzyme activity using the biomarker 13CO2 in breath, a first step in personalizing CD doses for PD patients.

HYDROGEN HAND ANALYZERS

Gastrolyzer, Bedfont

H2 Check, MD Diagnostics

LactoFAN, FAN



H_2 ANALYZERS ARE ESTABLISHED ON THE ELECTROCHEMICAL HYDROGEN DETECTOR AMPEROMETRIC (MICRO-FUEL))

WHY IS JUST HYDROGEN ANALYSIS NOT SUFFICIENT?

Gas		Amount
Hydrogen	H_2	0 - 86%
Methane	CH_4	0 - 56%
Carbon dioxide	CO_2	3 - 54%
Nitrogen	N_2	11 - 92%
Oxygen	O_2	0 - 11%

Plyny v trávicím traktu, Lukáš K.
Čes a Slov Gastroent a Hepatol 2009; 63(1): 20-24

Methane is produced by 24 - 48% population

Role of hydrogen and methane breath testing in gastrointestinal diseases
Di Stefano M., Corazza GR. Dig. Liver Disease Suppl.3 (2009) 40–43

HOW BOWEL BACTERIA GENERATE GASES?

metanergic bacteria

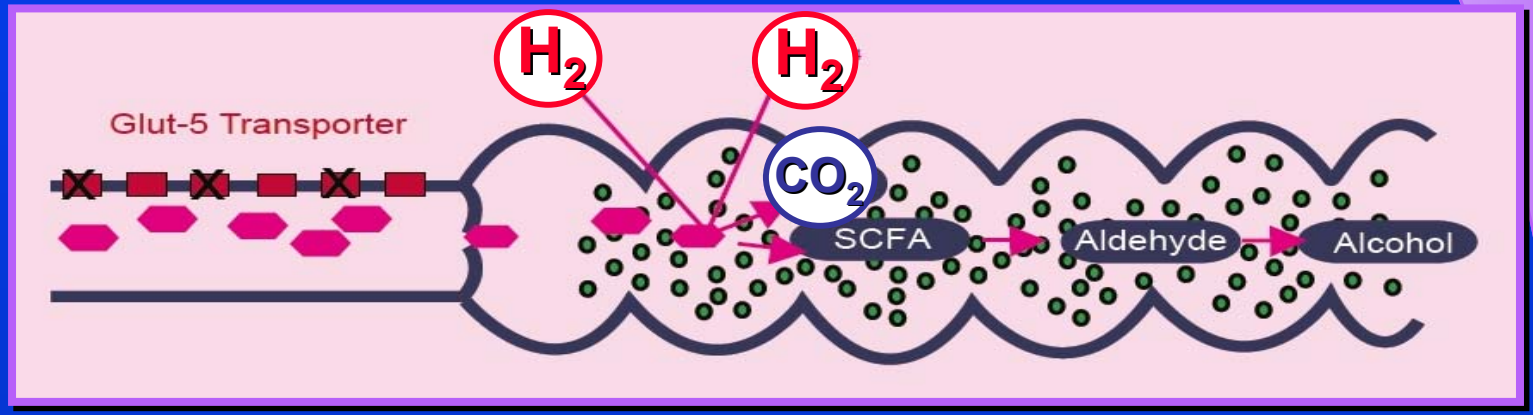
$$4H_2 + CO_2 \longrightarrow CH_4 + 2H_2O$$

sulfat reducing bacteria

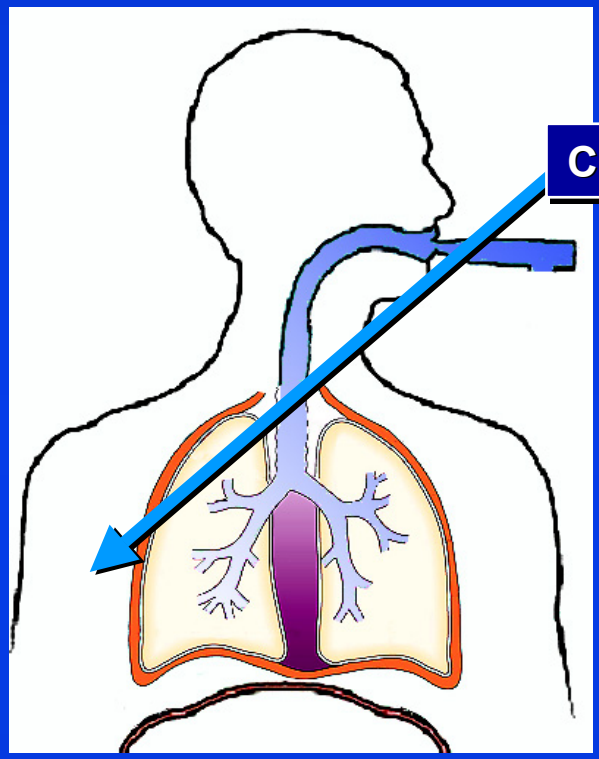
$$4H_2 + SO_4^{2-} \longrightarrow H_2S- + 4H_2O$$

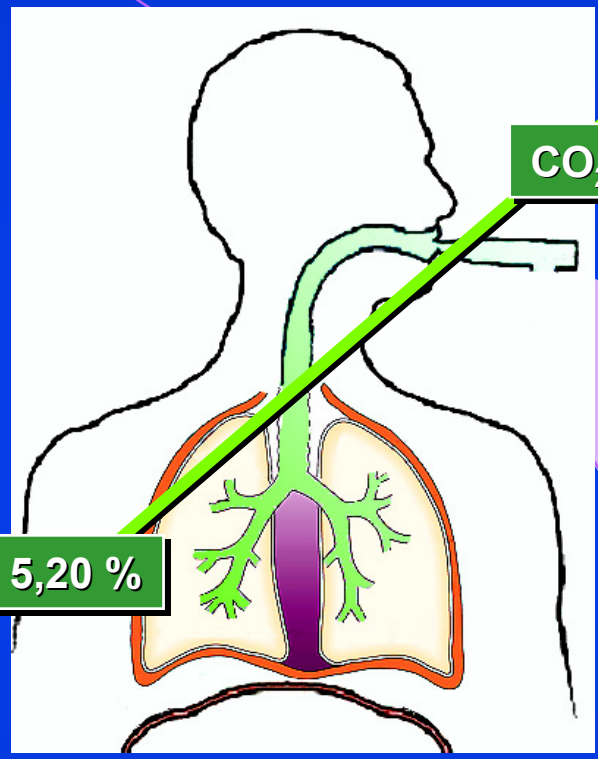
acetogenic bacteria

$$4H_2 + 2CO_2 \longrightarrow CH_3COOH + 2H_2O$$



WHY IS ANOTHER, THIRD ANALYST NEEDED?





INSPIRE-EXSPIRE - NO HOLDING ONE'S BREATH — LOW CONC.CO_2

INSPIRE-HOLD ONE'S BREATH SHORTLY - SHORT EXSPIRE — LOW CONC.CO_2

INSPIRE-HOLD ONE'S BREATH FOR 10 S - LONG EXSPIRE — CONC.CO_2 IS OK

WHY IS ANOTHER, THIRD ANALYST NEEDED?

If the alveolar air sample is contaminated with room air, the concentration of CO_2 in the sample will decrease, as will the other measured gases in the sample - H_2 and CH_4

Correction factor = alveolar CO_2 concentration / sample CO_2 concentration

Correction factor set according to CO_2 concentration minimizes errors caused by incorrect sampling

ALVEOLAR CO_2 CONCENTRATION

CO_2 is the physiological regulator of breathing, and the alveolar pressure pCO_2 is constant - 40 mm Hg (torr). Therefore, CO_2 is the most reliable "normalizer" of the measured gases in the sample.

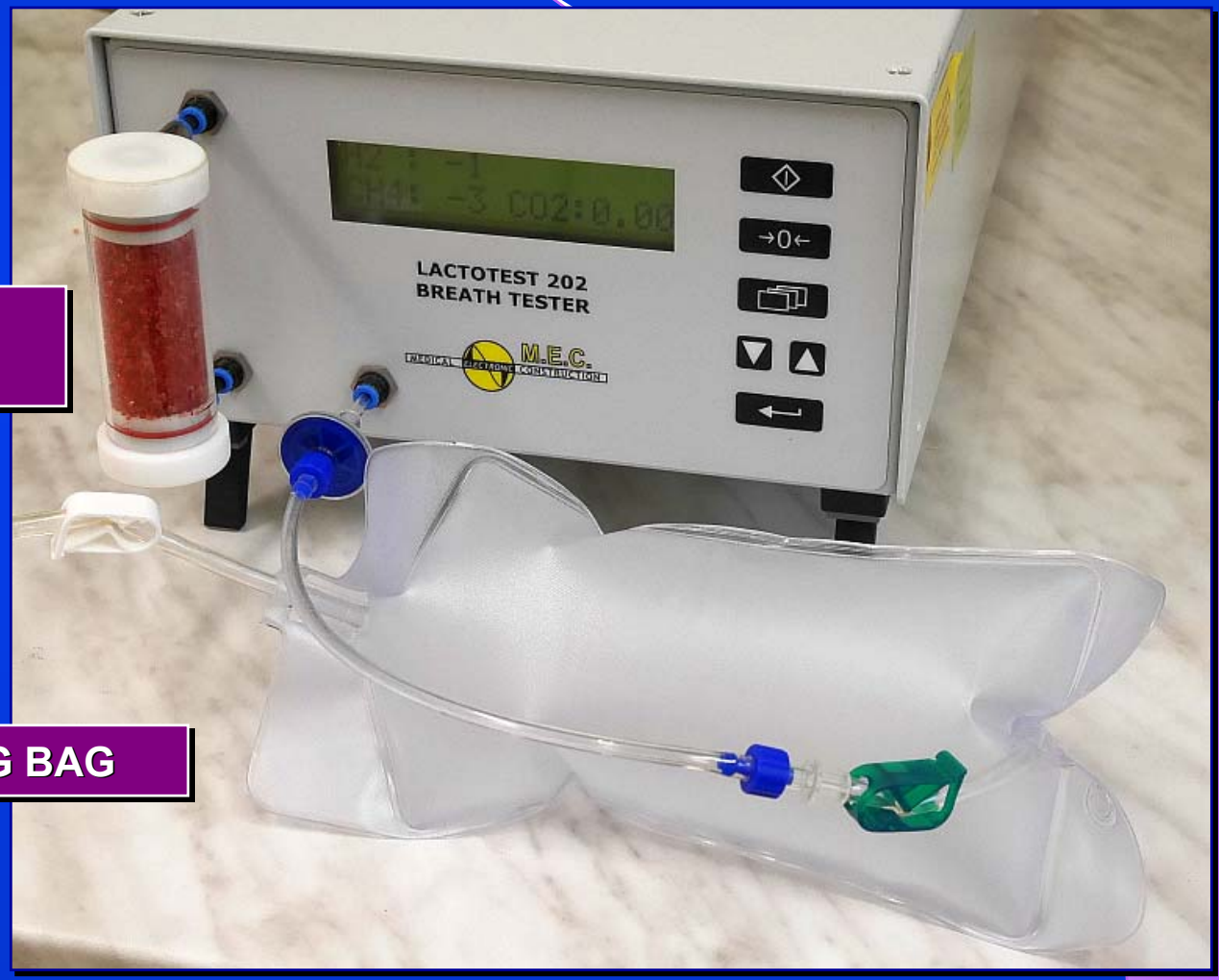
Foreign studies show that the use of an alveolar concentration of 5.5% is suitable for calculating the correction factor

Alveolar pCO_2 is constant - 40 mm Hg. The percentage of CO_2 in alveolar air is affected by barometric pressure.
Alveolar air with a pCO_2 of 40 mm Hg,
at sea level, will have a CO_2 concentration of about 5.5%
while alveolar air in, say, Denver will have CO_2 of 6.8%
(1610 m.a.s.l., barometric pressure is 625 torr)

HYDROGEN / METHANE - LACTOTEST-202 XTEND

ABSORBER
water and CO_2

SAMPLING BAG



HYDROGEN / METHANE BREATH TESTS

Breath test for SIBO, 75g glucose,
Breath samples are taken every 15 minutes for 3 hours
Breath test for lactose/fructose intolerance
20g lactose / 25g fructose
Breath samples are taken every 15 minutes for 4 hours
Test positivity – H_2/CH_4 rise of 10ppm against basal value

CLINICAL RESULTS:	
NUMBER OF BREATH TESTS:	2300 x
SUSPECTED SIBO	80.4% of tests
SUSPECTED MALABSORPTION	19.6% of tests

POSITIVITY – 39.3%

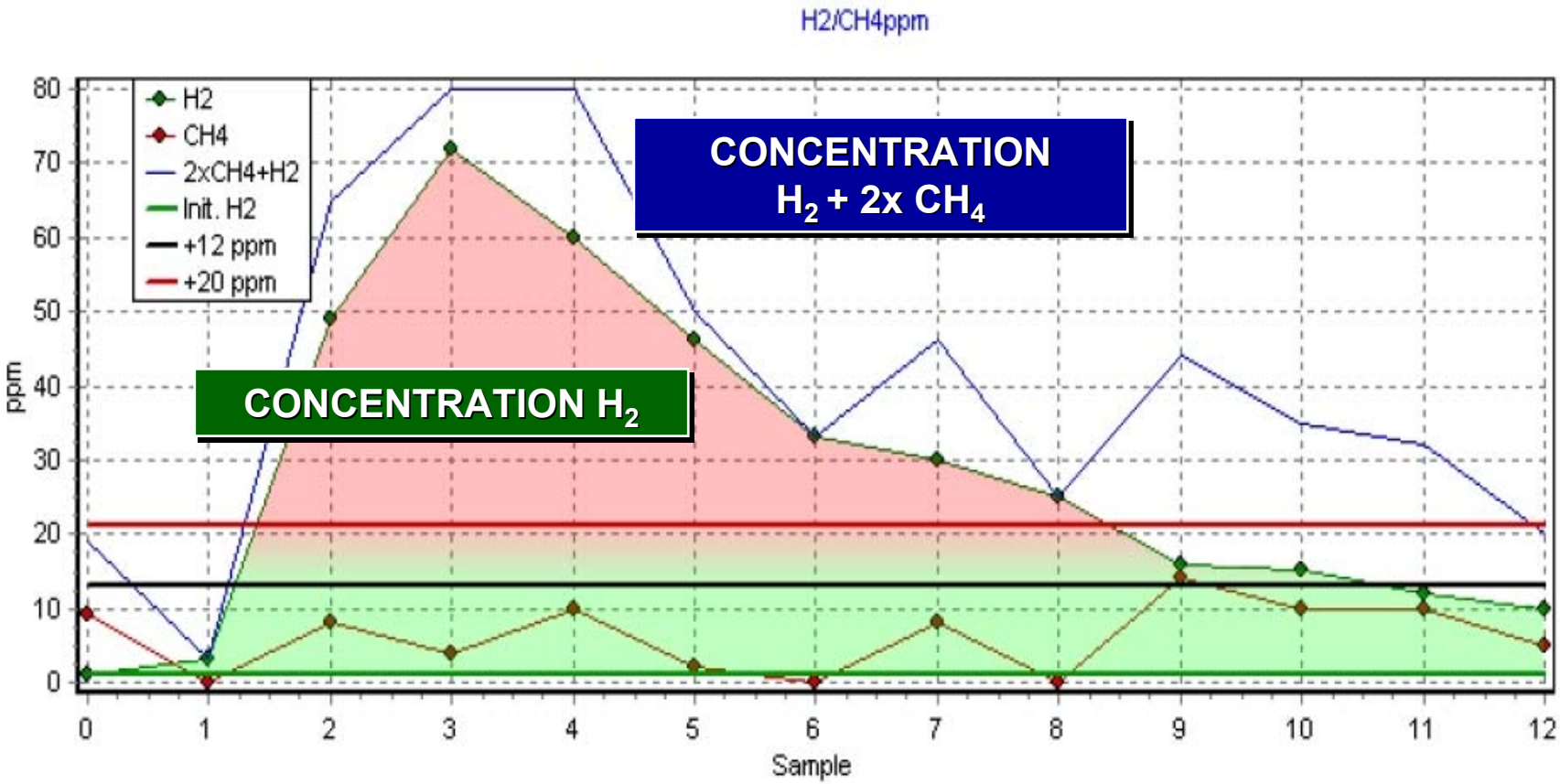
POCITIVITY – 55.0%

H_2 /CH_4 BREATH TESTS, INDICATIONS, RELIABILITY

Breath test	Indication	Sensitivity	Specificity
Glucoze HBT	SIBO	62%	83%
Lactulose HBT	SIBO	31%	86%
Fructose HBT	Malabsorption	98%	86%
Lactoze HBT	Malabsorption	80%	100%

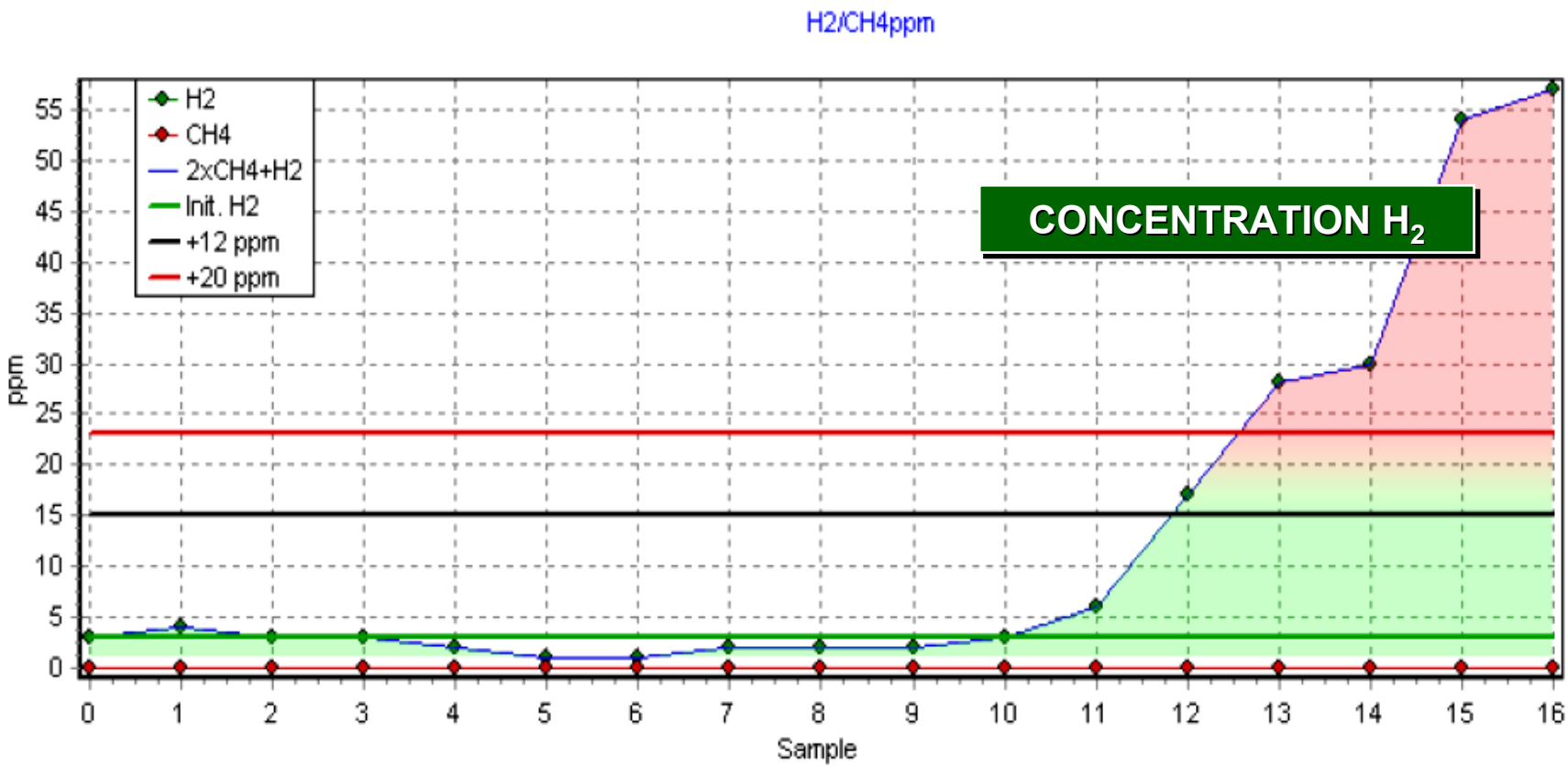
Update on diagnostic value of breath test in gastrointestinal and liver diseases.
Siddiqui I, Ahmed S, Abid S.
World J Gastrointest Pathophysiol. 2016 Aug 15;7(3):256-265

H_2 /CH_4 /CO_2 - GLUCOSE TEST FOR SIBO



75 g GLUCOSE

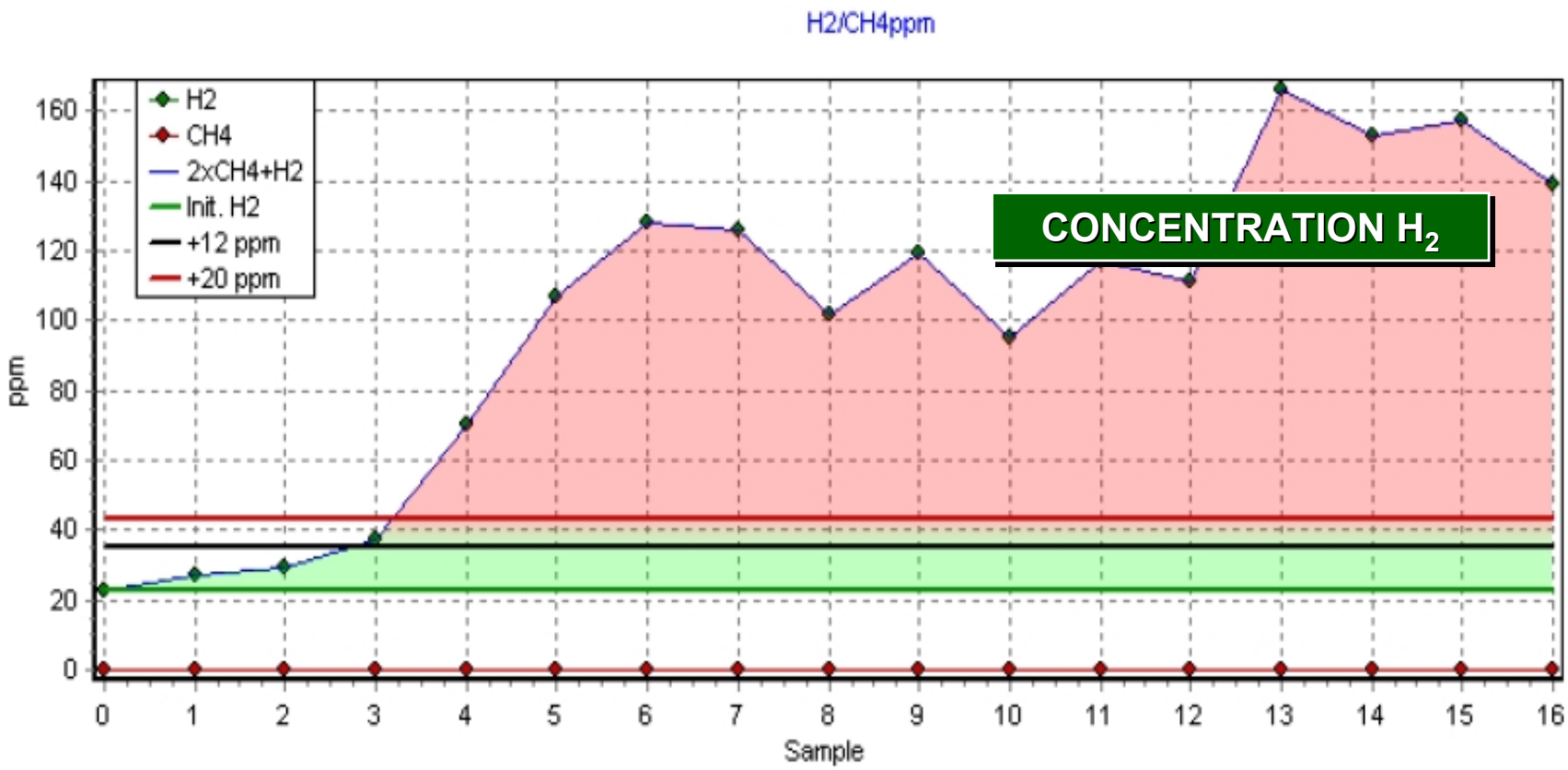
H_2 /CH_4 /CO_2 - LACTOSE MALABSORPTION



CONCENTRATION H_2

20 g LACTOSE

H_2 /CH_4 /CO_2 - LACTOSE MALABSORPTION + SIBO

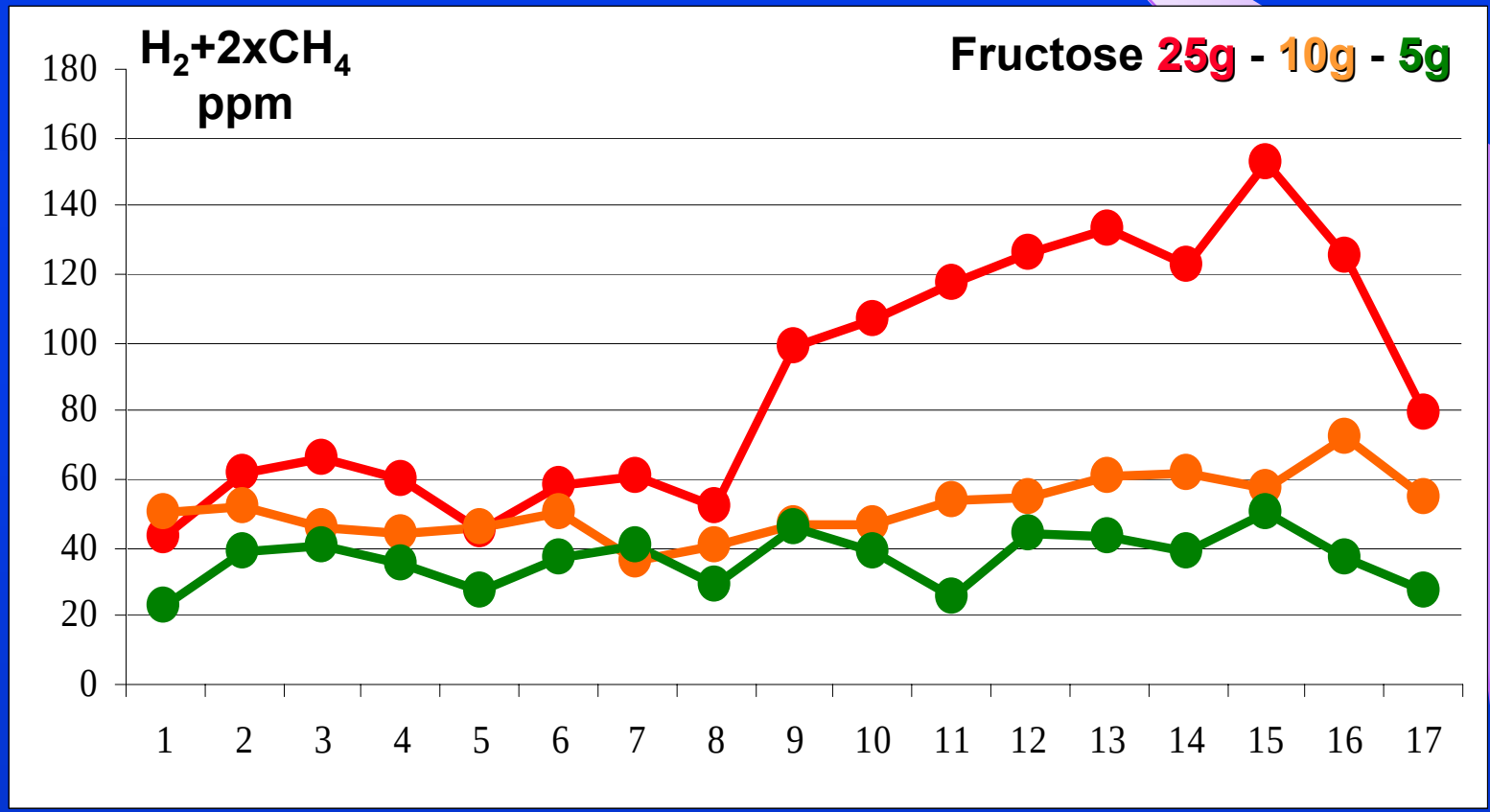


CONCENTRATION H_2

20 g LACTOSE

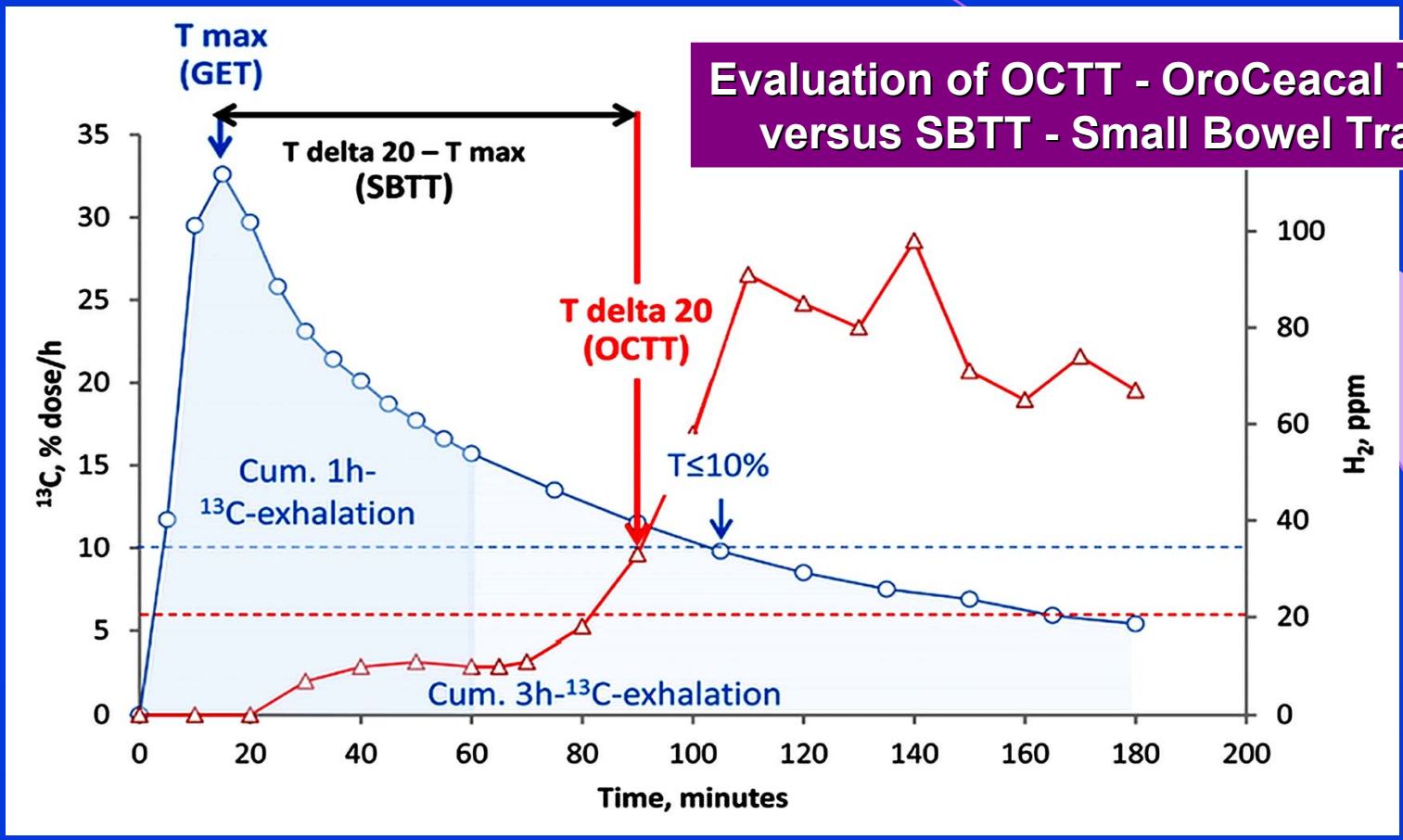
H_2-FRUCTOSE BREATH TEST

Fructose breath test - 46-year-old patient L.S.
Breath test performed with fructose in doses of 25g, 10g and 5g during 6 weeks
Samples taken every 4 hours and 15 minutes



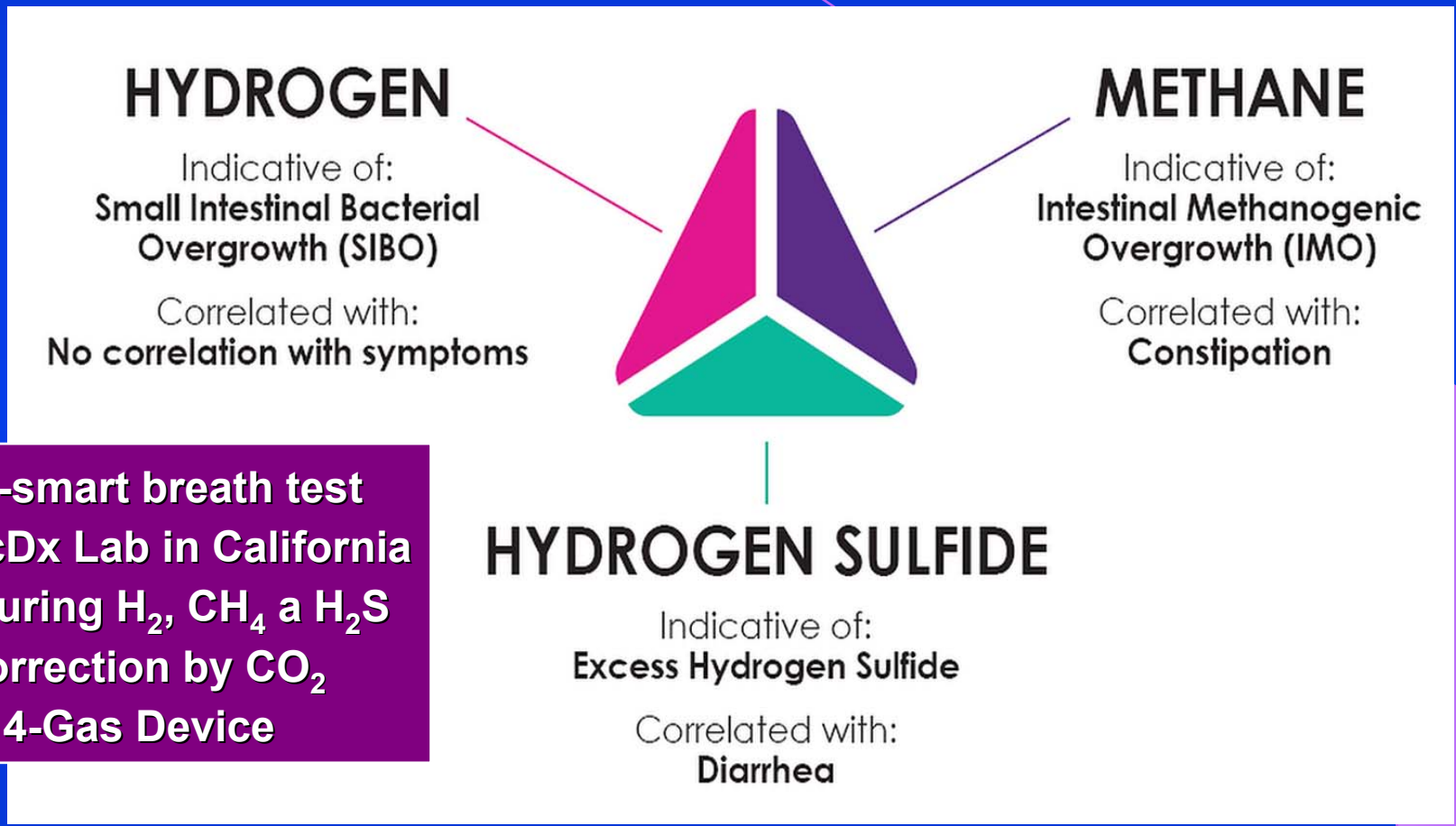
^{13}C-ACETATE WITH H_2-LACTULOSE BREATH TEST

Evaluation of OCTT - OroCeacal Transit Time versus SBTT - Small Bowel Transit Time



Simultaneous non-invasive measurement of liquid gastric emptying and small bowel transit by combined 13C-acetate and H2-lactulose breath test. Bertram F, Andresen V, Layer P, Keller J. J Breath Res. 2014; 8(4): e046007

DETECTION OF HYDROGEN, METHANE AND HYDROGEN SULFIDE



Trio-smart breath test
PacificDx Lab in California
Measuring H_2, CH_4 a H_2S
Correction by CO_2
4-Gas Device

Validation of a 4-Gas Device for Breath Testing in the Determination of Small Intestinal Bacterial Overgrowth. Singer-Englar T, Rezaie A, Gupta K. et al. Gastroenterology, 2018, 154(6), s. 281

HYDROGEN BREATH TESTS GUIDELINES - UEG

This clinical practice recommendation should facilitate Europe-wide harmonization of diagnostic approaches to symptoms and disorders that are very common in specialist and primary care gastroenterology practice, both in adult and pediatric patients. In addition, it identifies areas of future research needs to clarify diagnostic and therapeutic approaches.

H_2BT - Hydrogen Breath Tests
Small intestinal bacterial overgrowth - SIBO - glucose, lactulose
Oro-cecal transit time - OCTT - lactulose, inulin
Carbohydrate malabsorption:
Lactose malabsorption - lactose, Fructose malabsorption - fructose

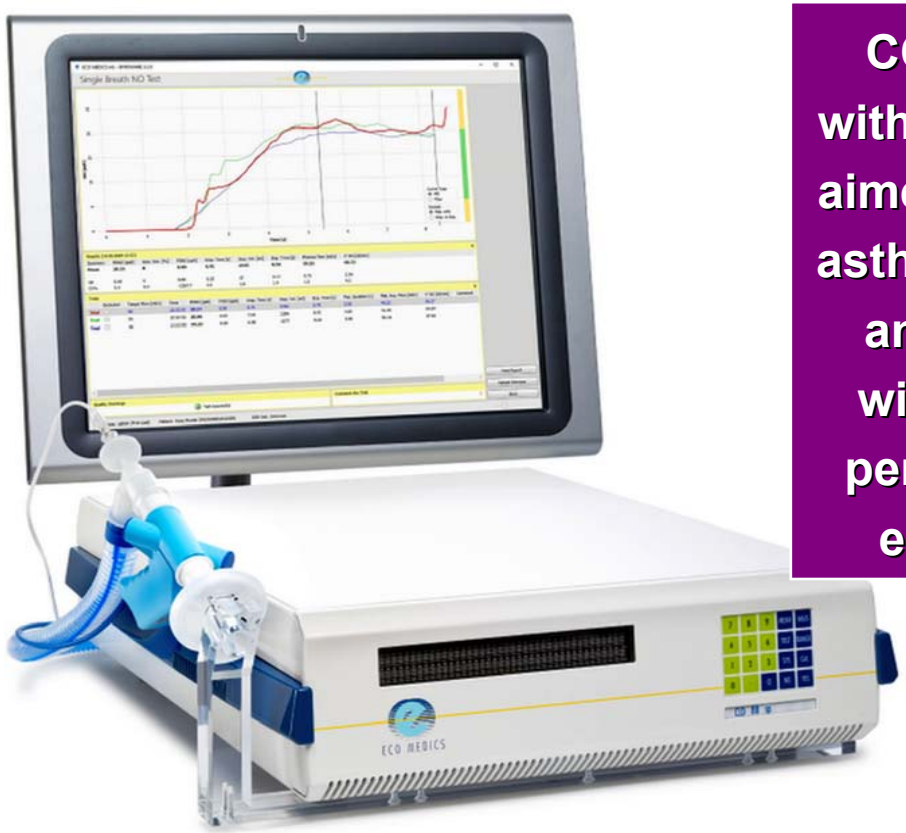
European guideline on indications, performance, and clinical impact of hydrogen and methane breath tests in adult and pediatric patients. EAGEN, ESNM and ESPGHN consensus. Hammer HF, Fox MR, Keller J. el at. United European Gastroenterol J. 2022; 10: 15-40.

ROUTINE ALCOHOL TEST – CLINICAL BENEFIT

A 37-year-old previously healthy man
when entering service in a submarine
routinely tested for alcohol
Diabetic ketoacidosis
a positive result of a manual breathalyzer

Early Detection of Diabetic Ketoacidosis by Breathalyzer in a Sailor Reporting for Duty. Reinhart J. Mil Med. 2019; 184(11-12): e951-e952

ANALYSIS OF NITRIC OXIDE (FeNO) IN PNEUMOLOGY

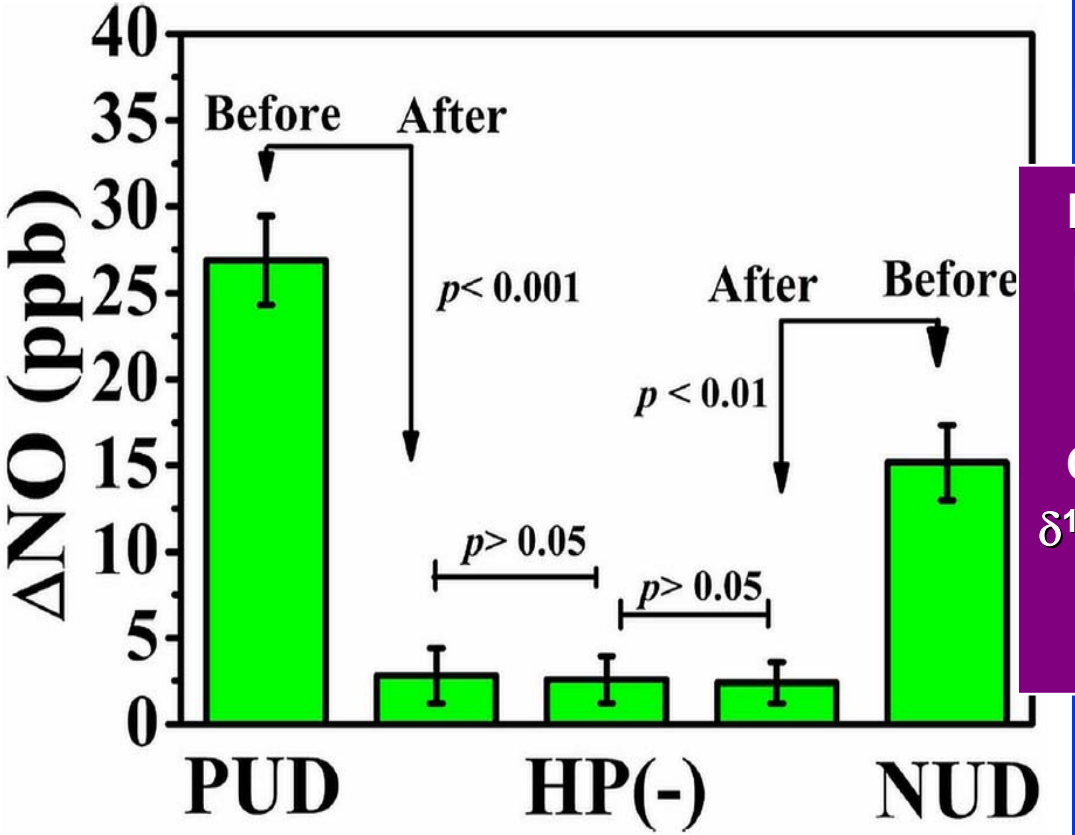


COPD is a heterogeneous disorder with different phenotypes. The study is aimed at determining the prevalence of asthma history, peripheral eosinophilia and elevated FeNO levels, together with the diagnostic effectiveness of peripheral eosinophilia in identifying eosinophilic airway inflammation.

FeNO
Fractional exhaled Nitric Oxide

Eosinophilia and fractional exhaled nitric oxide levels in chronic obstructive lung disease. Annangi S, Nutalapati S, Sturgill J et al. Thorax. 2021 Aug 20. Epub. PMID: 34417353.

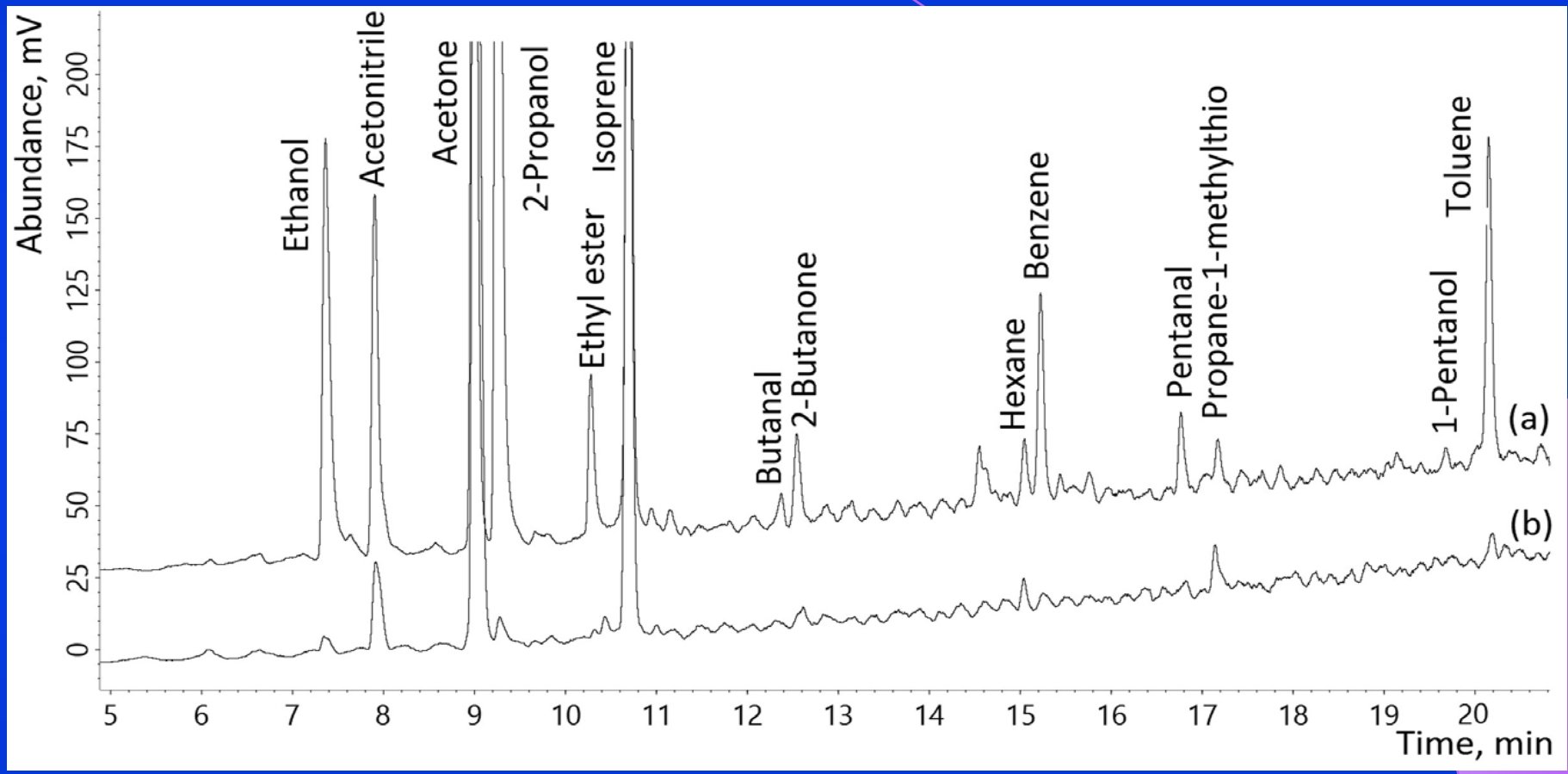
ANALYSIS OF NITRIC OXIDE (NO) IN GASTROENTEROLOGY



NUD (Non Ulcer Dyspepsia) n=64
PUD (Peptic Ulcer Disease) n=56
Hp negative controls n=49
ΔNO (ppb) detection CRDS
Cavity Ring-Down Spectroscopy
$\delta^{13}C$ (< 3‰) ^{13}C-UBT detection ICOS
Laser-Based Integrated
Cavity Output Spectroscopy

Exhaled nitric oxide as a potential marker for detecting non-ulcer dyspepsia and peptic ulcer disease. Som S, Dutta Banik G, Maity A et al. J Breath Res. 2018; 12(2): e026005

VOC - VOLATILE ORGANIC SUBSTANCES IN BREATH



Investigation of different approaches for exhaled breath and tumor tissue analyses to identify lung cancer biomarkers. Gashimova E, Temerdashev A, Porkhanov V. et al. Heliyon. 2020; 6(6): e04224.

OFFLINE

ReCIVA

GCxGC-MS
✓ Complex matrices
x Requires expertise

GC-MS
✓ Gold standard
x Time consuming

APCI-MS
✓ Compact, tuneable
x Low scan rate

ONLINE

PTR-MS
✓ High sensitivity
x Low scan rate

GC-IMS
✓ Compact, tuneable
x Low scan rate

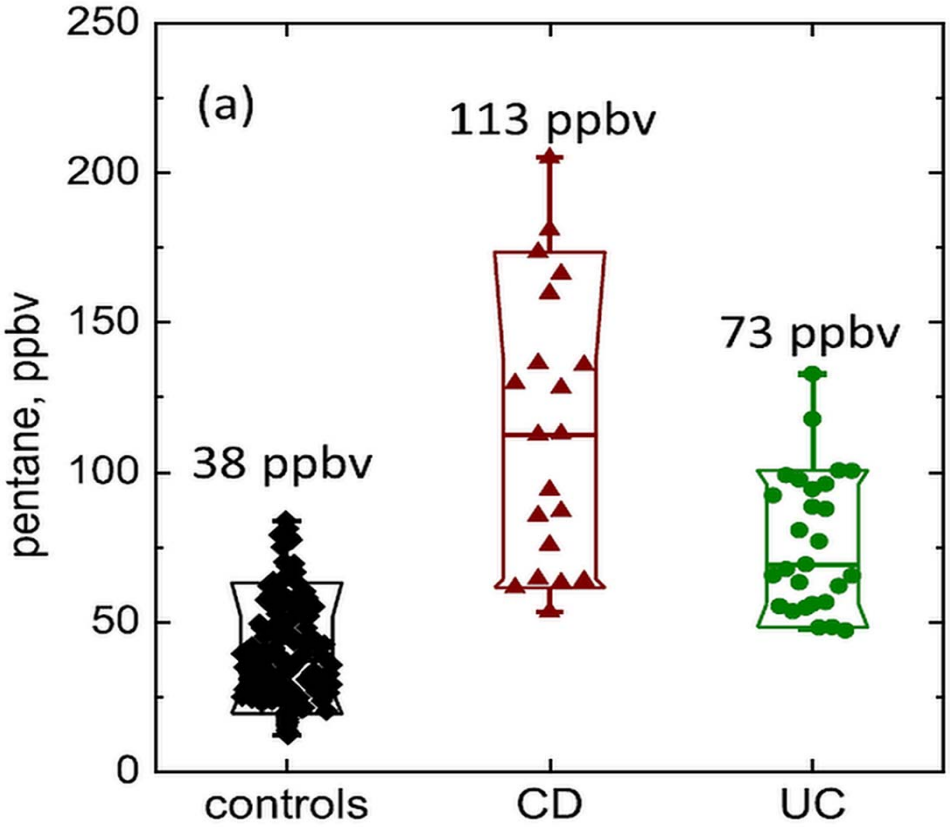
GCxGC-MS	Comprehensive two-dimensional gas chromatography
GC-MS	Gas Chromatography Mass Spectrometry
APCI-MS	Atmospheric Pressure Chemical ionisation- Mass Spectrometry
PTRMS	Proton Transfer Reaction Mass Spectrometry
GC-IMS	Gas Chromatography Ion Mobility Spectrometry

Assessment of breath volatile organic compounds in acute cardiorespiratory breathlessness: a protocol describing a prospective real-world observational study. Ibrahim W, Wilde M, Cordell R. BMJ Open. 2019; 9(3): e025486

Acetone	diabetes, chronic kidney disease, lung CA
Acetaldehyde	CA breast
Formaldehyde	CA lung
Hexanol	CA lung
Octanol	Alzheimer's
Ethanol	liver steatosis, diabetes, CA lic
Ethylbenzene	Parkinson's, diabetes
Isoprene	chronic kidney disease, lung CA
Styrene	Alzheimer's, Parkinson's, chronic kidney disease, lung CA
Benzene	Alzheimer, Parkinson, TB, CRCA
Hexane	Alzheimer's, CA of the lungs, head and neck
Decane	Alzheimer, CA of the lungs, head and neck, breast and prostate
Octane	Alzheimer's, Parkinson's, chronic kidney disease, lung CA, head, neck

Investigation of different approaches for exhaled breath and tumor tissue analyses to identify lung cancer biomarkers. Gashimova E, Temerdashev A, Porkhanov V. et al. Heliyon. 2020; 6(6): e04224.

ANALYSIS OF VOC IN PATIENTS WITH IBD



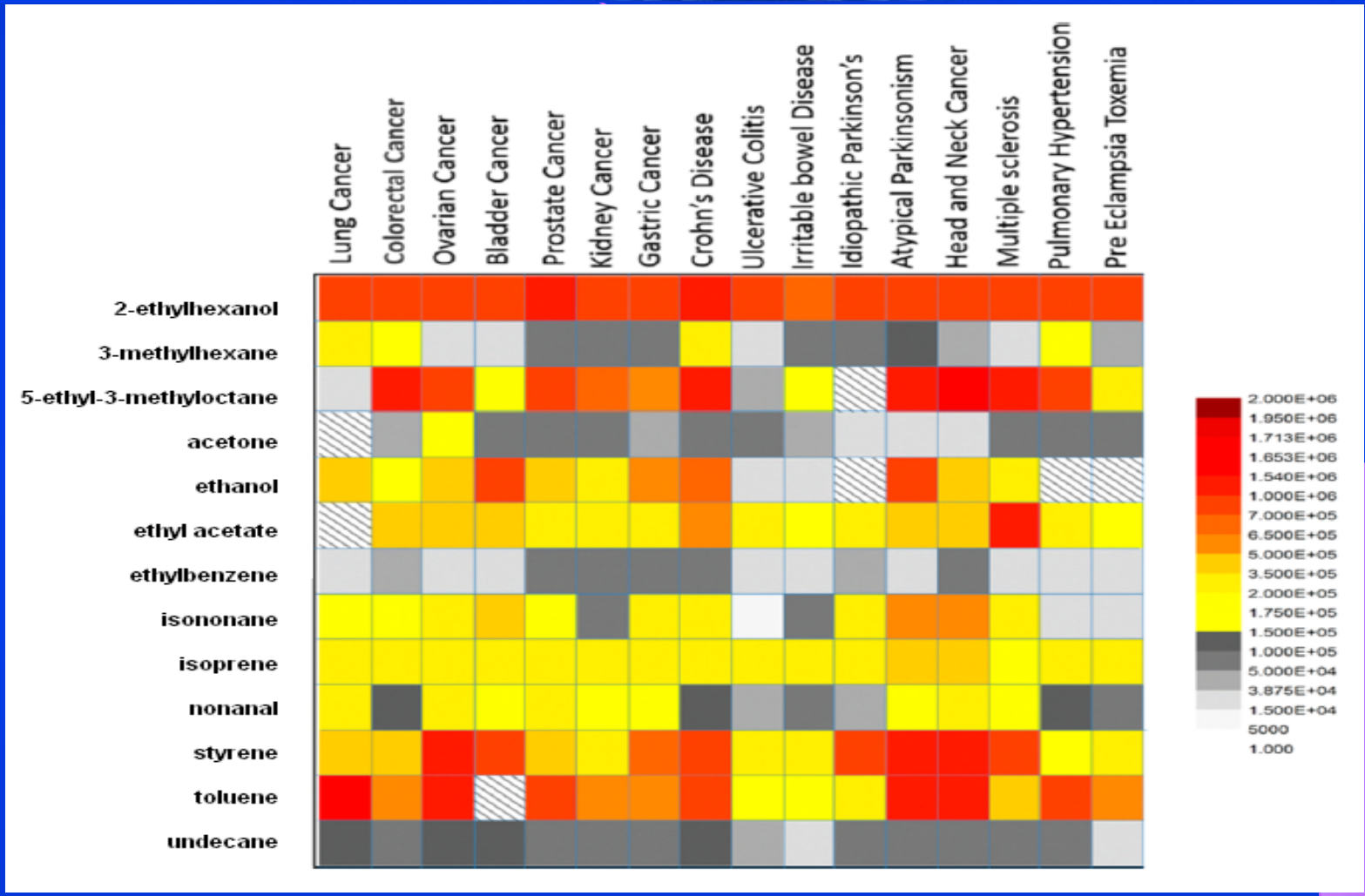
The study was conducted on VOC in exhaled air
Inflammatory Bowel Disease (IBD)
136 with Crohn's disease (CD)
51 with ulcerative colitis (UC)
Control - 14 healthy people
Breath samples into Nalophan bags
Mass spectrometry analysis with ion flow (SIFT-MS)

Pentane and other volatile organic compounds, including carboxylic acids, in the exhaled breath of patients with Crohn's disease and ulcerative colitis. Dryahina K, Smith D, Bortlík M. et al. J Breath Res. 2017; 12(1): e016002

ARTIFICIAL INTELLIGENCE IN VOC ANALYSIS

Study of 57 authors from 21 workplaces (Israel, France, USA)
Exhaled air samples of 1404 persons
A VOC 'breathprint' was defined for 17 diseases
lung cancer, colorectal cancer, ovarian cancer,
prostate cancer, kidney cancer, stomach cancer,
head and neck cancer, bladder cancer,
Crohn's disease, ulcerative colitis, IBS,
Parkinson's disease, multiple sclerosis,
pulmonary arterial hypertension, pre-eclampsia, chronic renal failure
Reliability of artificial intelligence to diagnose 17 diseases is 86%

Diagnosis and Classification of 17 Diseases from 1404 Subjects via Pattern Analysis of Exhaled Molecules. Nakhleh MK, Amal H, Jeries R. et al. ACS Nano. 2017; 11(1): 112-125



Diagnosis and Classification of 17 Diseases from 1404 Subjects via Pattern Analysis of Exhaled Molecules. Nakhleh MK, Amal H, Jeries R. et al. ACS Nano. 2017; 11(1): 112-125

BREATH BIOPSY – BREATH SAMPLING TECHNOLOGY

While blood, urine and stool tests became common ways disease identification, the development of breath tests faltered because it didn't exist yet reliable way breath sample collection and analysis.

The Great Exhale Using Breath Analysis to Detect Disease.
Mertz L.: IEEE Pulse. 2020; 11(3): 7-11

http://www1.lf1.cuni.cz/~kocna/glab/glency1.htm

http://gelab.zde.cz

Skupina metodik funkce tenkého střeva, malabsorpce, screening céliakie, střevní propustnost, bakteriální přerůstání

- Anti-endomysium IgA
- Anti-gliadin IgA, IgG
- Anti-tTG IgA, IgG
- Anti-gliadin, tTG ve stolici
- A-vitamin zátěžový test
- ß-karoten
- ß-karoten zátěžový test
- Céliakie - screening
- Dechový test s laktózou
- Dechový test s xylózou
- Laktózový toleranční test
- Laktulózo/mannitolový test
- Xylózový toleranční test

Intro

Abecední přehled metodik

Miniencyklopedie laboratorních metod v gastroenterologii

GastroLab

Protilátky ke tkáňové transglutamináze (atTG) - IgA a IgG

Tkáňová transglutamináza má přímý vztah k patogenezi onemocnění a byla popsána jako vlastní, chemický substrát endomysia. Tkáňová transglutamináza - (isoenzym transglutaminasa II, TG2 - EC 2.3.2.13, je transferázou, systémový název je protein-glutamin:amin-g-glutamyltransferasa. Je to Ca2+ dependentní enzym, katalyzující deaminaci glutaminu na glutamát, rovněž vede ke vzniku intramolekulární vazby glutaminu na další primární amin, např. lysin a vede k agregaci glutaminových peptidů. Stanovení protilátek ke tkáňové transglutamináze (atTG) má proto rovněž velmi vysokou diagnostickou efektivitu, podobně jako EmA protilátky (senzitivita 87-97% a specificita 88-98%). Stanovení atTG je prováděno klasickou metodou ELISA, což je pro rutinní diagnostiku technika dostupnější než immunofluorescenční průkaz EmA.

Protilátky atTG lze na rozdíl od EmA stanovovat ve třídě IgA i IgG, což má význam pro nemocné se selektivním deficitem IgA. Metoda byla popsána s použitím morčecího antigenu, který je použit ve většině starších souprav, novější soupravy již používají jako antigen tkáňovou transglutaminázu izolovanou z lidských buněk, z lidských erytrocytů, nebo rekombinantní tTG izolovanou na E.coli. Referenční hodnoty se liší u jednotlivých souprav, většinou je pro IgA protilátky uváděna horní hranice normy 10 - 15 IU/l, některé soupravy definují i tzv. gray-zone v rozsahu 10 - 20 IU/l. Stanovení protilátek atTG s lidským, rekombinantním antigenem vykazuje nižší falešnou pozitivitu než metody s morčecím antigenem. Nejnovější studie porovnávají protilátky třídy IgA a IgG, a POCT metodiky stanovení atTG protilátek. Stanovení protilátek atTG ve třídě IgA je doporučeno jako základní screeningový test pro diagnostiku celiakie. Pro screening byla v roce 2011 použita i technologie detekce atTG ve slinách, a nejnovější studie popisují zcela nové technologie detekce protilátek elektrochemickými imunosenzory.

Reference

Volta U. - Gastroenterol Hepatol Bed Bench. 2023, Medline - link PubMed

Infantino M. - J Immunol Met... 2021, Medline - link PubMed

NČLP

Done

Medline online latest publication

Direct link to MZČR National code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