Chronic Pancreatitis

INSELSPITAL
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BERN UNIVERSITY HOSPITAL

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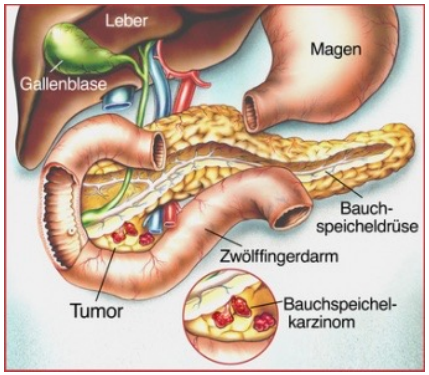
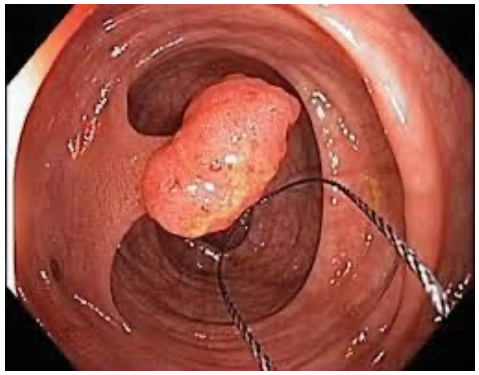
Terra
Incognita
AÇORES INSVLAE.
SEPTENTRIO.
Insula del Cuervo.
Insula de las Flores.
Insula Graciosa.
Insula Royal.
Insula S. Georgij.
Insula Terçera.
OCCIDENS.
ORIENS.
Has insulas perlustrauit summaque diligentia accuratissimè descripsit et delineauit Ludouicus Teixera Lusitanus, Regiæ Maiestatis cosmographus.
ANNO A CHRISTO NATO.
CIↃ IↃ LXXXIIII.
Insula S. Mariæ.
MERIDIES.



Pancreatology

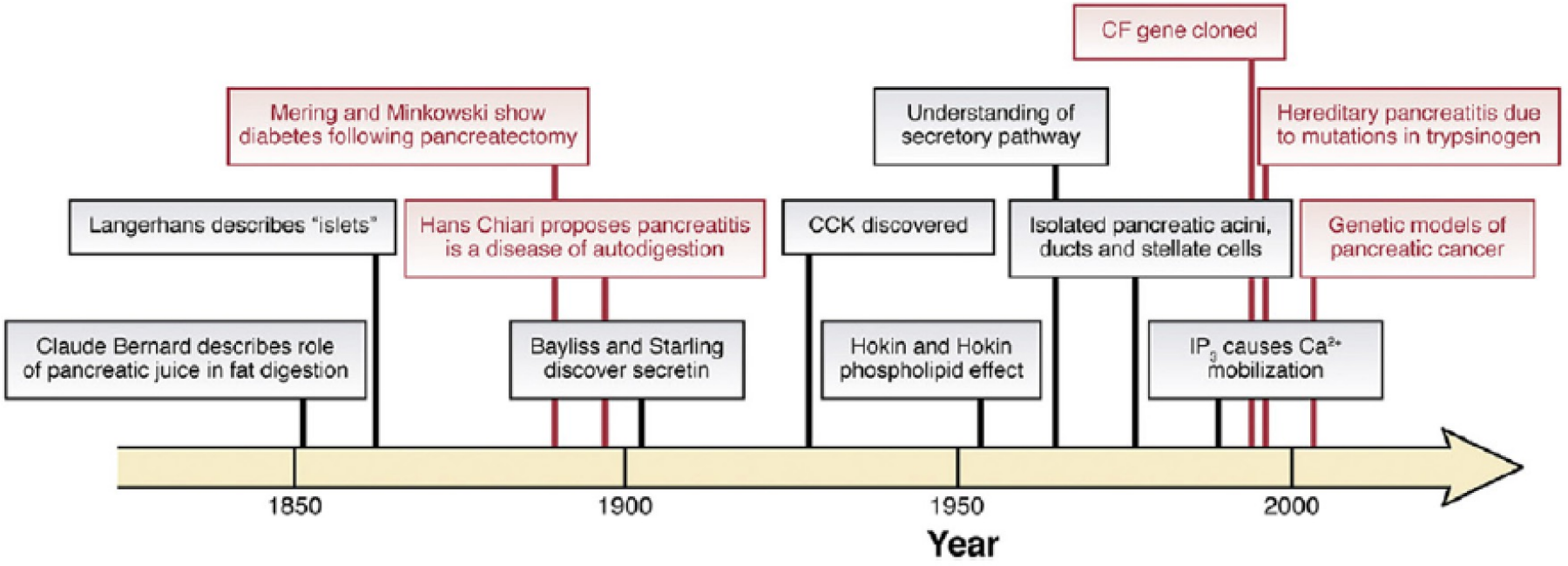


Pankreas	Other organs e.g. liver, colon
Access to organ - target: Histology – **Difficult**	Anytime blind liver biopsy Endoscopic access to colon **Easy, safe**
Operability: Morbidity, Mortality – **High**	Partial/ Liver-, Colon-resection Polypectomies .... – **fast track**

History and milestones in pancreatic pathophysiology

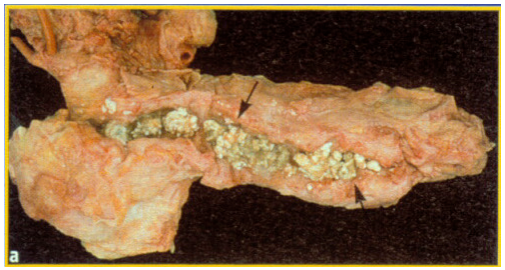
from "Terra incognita" to genetic + cellular delineation

Who and When discovery
Secretin – CF gene – "Islets" ?



Thiruvengadam Muniraj et al. Disease a month 2015

Definition of chronic pancreatitis ?



Statement 1 – 1 - 1 Definition

Chronic pancreatitis is a disease of the pancreas in which recurrent inflammatory episodes result in replacement of pancreatic parenchyma by fibrous connective tissue.

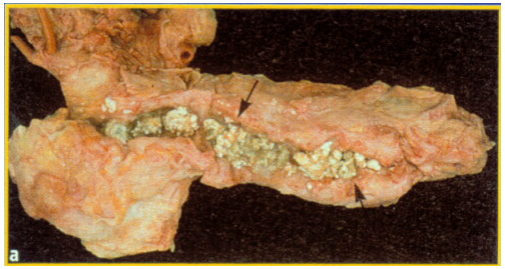
Morphological change

→ **Exo-, endocrine insufficiency**
Complications
Malnutrition
Pain
Risk for cancer

Functional consequences

→ **Reduced quality of life and life expectancy**

Definition of chronic pancreatitis ?



New concept of mechanistic definition and „bottom up“ approach

Not focusing on end-stage irreversible stage of disease but

differentiate at best

- **Pancreatic dysfunction**
- **Pancreatitis-related disorders**
- **Pancreatic disease**

Take into account all disease modifying genetic, environmental and Pathophysiological factors known to impact on pancreatitis-process

CP: consequences on work, life and survival ?

Work-Life:

Unable to persue profession: ca. 1/3

Forced to retire up to 40%

Mortality:

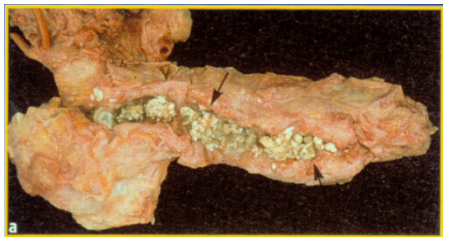
factor 3.6 increase as compared to age-control

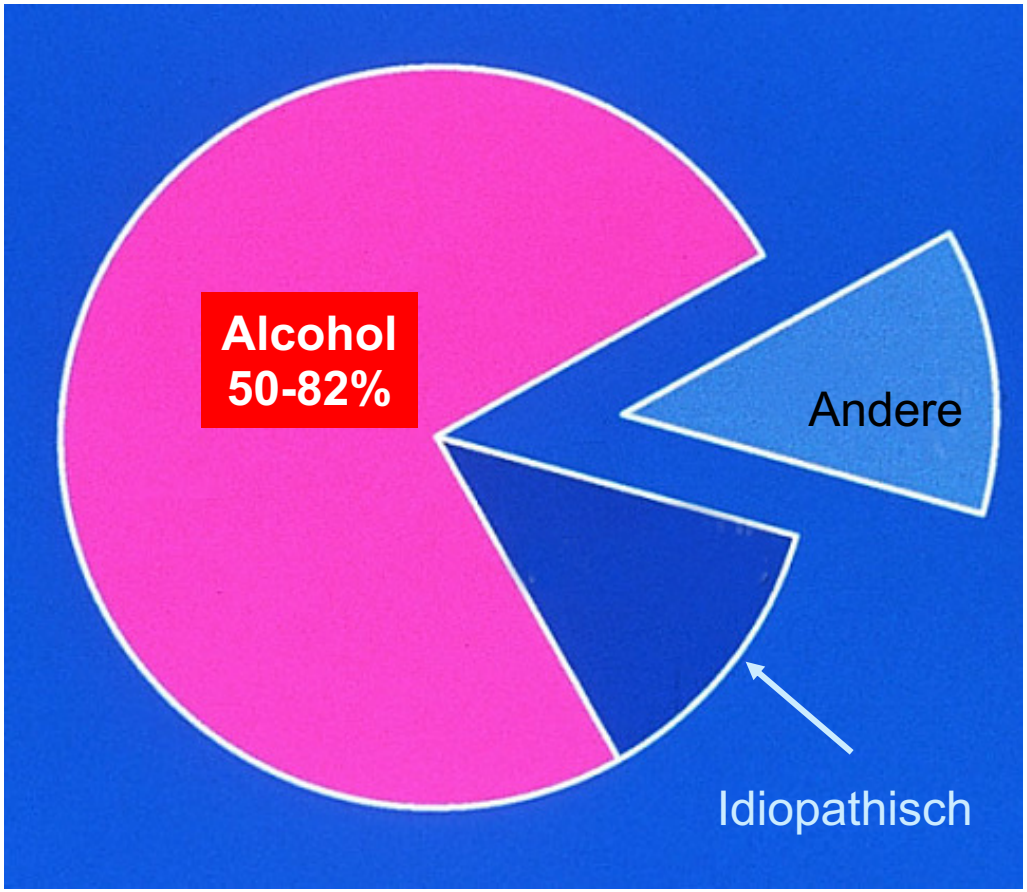
10y and 20y survival: 70% and 45%

as compared to 93% and 65% in normal population

Etiology / Riscfactors Chronic Pancreatitis

Causes of chronic pancreatitis
What is TIGAR-O ?





TIGAR-O Version 1.0

risk/etiology factors

T	Toxic-Metabolic
I	Idiopathic
G	Genetic
A	Autoimmune
R	Recurrent active
O	Obstructive

TIGAR-O Version 2.0 Checklist

Toxic-metabolic

- Alcohol-related (susceptibility and/or progression)
  - 3–4 drinks/d
  - 5 or more drinks/d
- Smoking (if yes, record pack-years)
  - Nonsmoker (<100 cigarettes in lifetime)
  - Past smoker
  - Current smoker
  - Other, NOS
- Hypercalcemia—(ionized calcium levels >12.0 mg/dL or 3 mmol/L)
- Hypertriglyceridemia
  - Hypertriglyceridemic risk—(fasting >300 mg/dL; nonfasting >500 mg/dL)
  - Hypertriglyceridemic acute pancreatitis, history of (>500 mg/dL in the first 72 hr)
- Medications (name)
- Toxins, other
  - CKD—(CKD stage 5—ESRD)
  - Other, NOS
- Metabolic, other
  - Diabetes mellitus (with the date of diagnosis if available)
  - Other, NOS

Idiopathic

- Early onset (<35 yr of age)
- Late onset (>35 yr of age)

Genetic

- genotyping available
- Autosomal dominant (Mendelian inheritance—single-gene syndrome)
  - *PRSS1* mutations (hereditary pancreatitis)
- Autosomal recessive (Mendelian inheritance—single-gene syndrome)
  - *CFTR*, 2 severe variants in trans (cystic fibrosis)
  - *CFTR*, <2 severe variants in trans (CFTR-RD)
  - *SPINK1*, 2 pathogenic variants in trans (SPINK1-associated familial pancreatitis)
- Complex genetics—(non-Mendelian, complex genotypes +/− environment)
- Modifier genes (list pathogenic genetic variants)
  - *PRSS1-PRSS1* locus
  - *CLDN2* locus
  - Others
- Hypertriglyceridemia (list pathogenic genetic variants)

AIP/steroid-responsive

- AIP Type 1—IgG4-related disease
  - Isolated to the pancreas
  - Associated with other organs (IgG4-related disease)
- AIP Type 2
  - Isolated to the pancreas
  - With Crohn's disease
  - With ulcerative colitis
  - Associated with other organs
- AIP-NOS (Steroid responsive, not Type 1 or Type 2)

Recurrent

- Acute pancreatitis (single episode, including date of event if available)
- AP etiology—extrapancreatic (excluding alcoholic, HTG, hypercalcemia, and genetic)
  - Biliary pancreatitis
  - Post-ERCP
  - Traumatic
  - Undetermined or NOS
- RAP (number of episodes, frequency, and dates of events if available)

Obstructive

- Pancreas divisum
- Ampullary stenosis
- Main duct pancreatic stones
- Widespread pancreatic calcifications
- Main pancreatic duct strictures
- Localized mass causing duct obstruction

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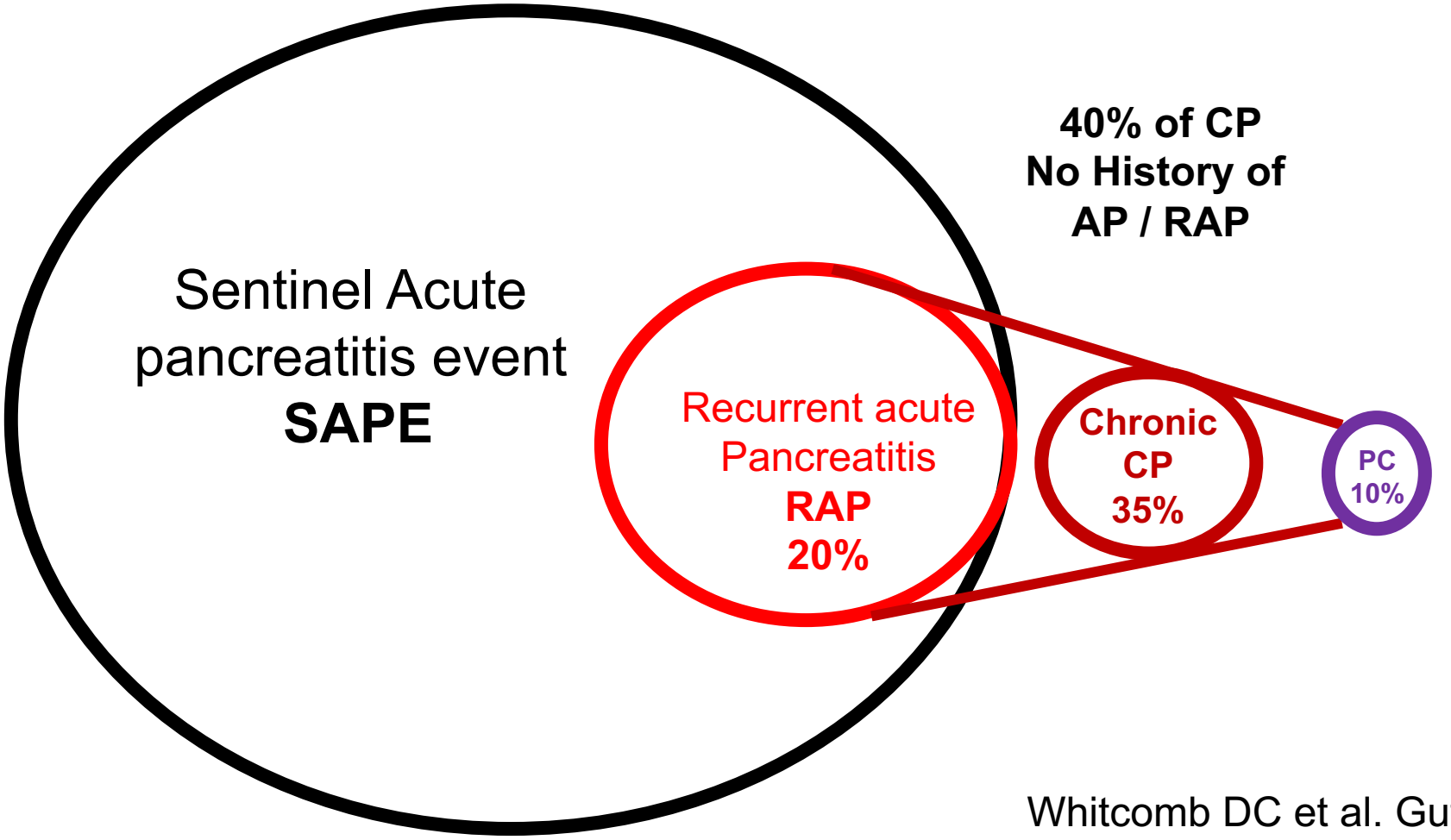
- Localized mass causing duct obstruction
  - Pancreatic ductal adenocarcinoma
  - IPMN
  - Other tumor
- Mass effect, NOS
- Anatomic Variants (other than pancreas divisum)
- Other NOS

Whitcomb et al.
Clinical and Translational Gastroenterology
2019

What is the course of disease after acute pancreatitis – life time risk for ….?



Whitcomb DC et al. Gut 1999

Causes of chronic pancreatitis
what do you know about alcohol?

Beer

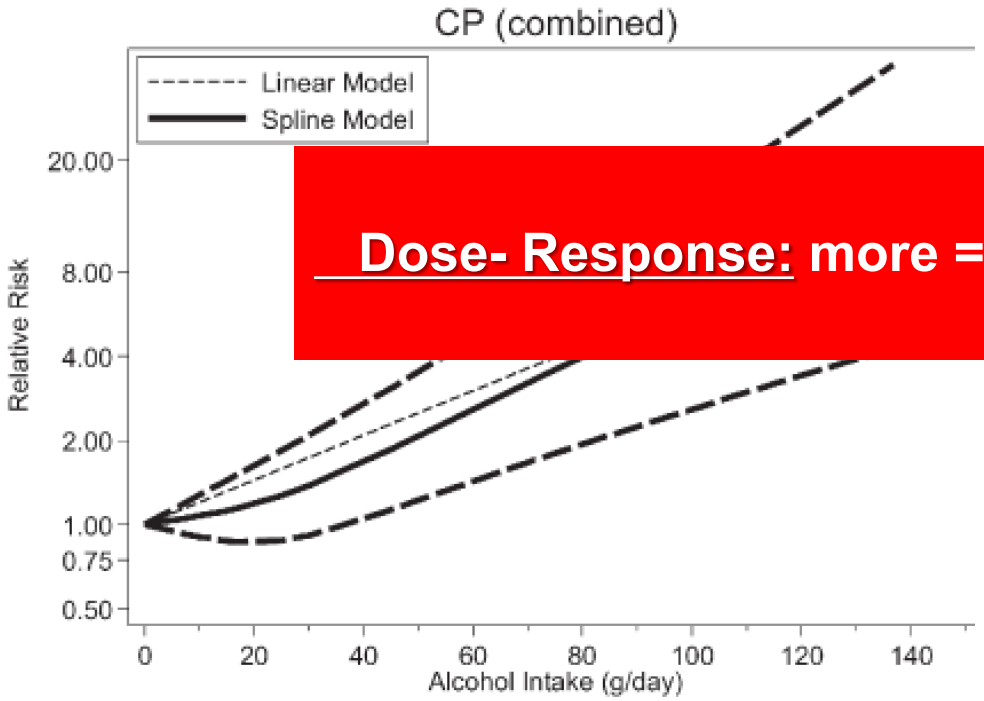
ALCOHOL

- **No threshold level ! Below which no risk**
- **5% of «heavy drinkers» (> 80g/d for > 10 years) get CP**
- **Accelerates progression from RAP to CP 2-times**
- **CP due to alcohol: highest risk for exokrine insufficiency**

Amann RW et al. Pancreas 1997

Alcohol and Pancreatitis

Alcohol Consumption as a Risk Factor for Acute and Chronic Pancreatitis: A Systematic Review and a Series of Meta-analyses



Dose- Response: more = worse = higher risk for AP/CP

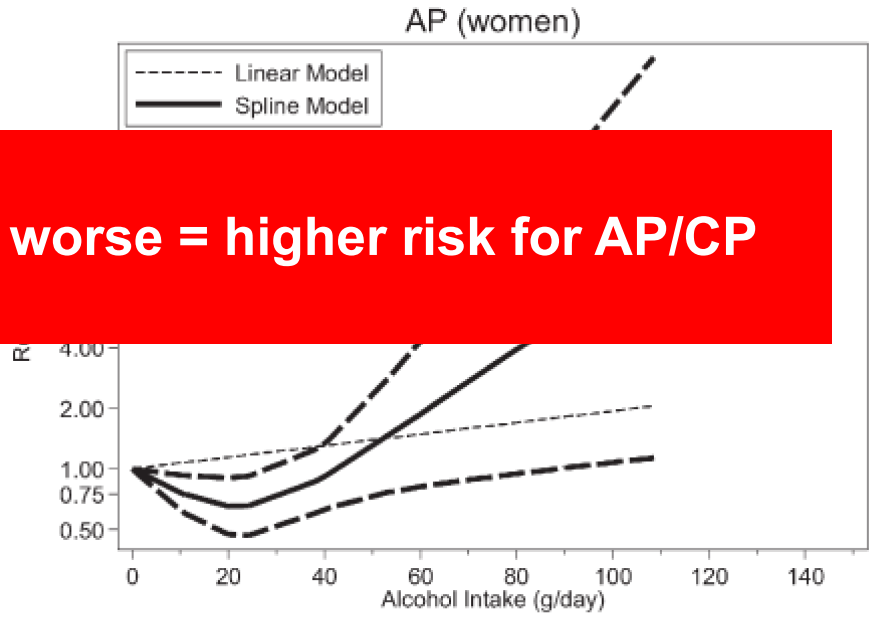


Fig. 4. Pooled dose–response risk relationships between average alcohol consumption and acute pancreatitis in women.

Samokhvalov et al. Ebio Med 2015

Smoking (+/- alcohol) and CP ?

	Alcohol consumption (g/month)			
	<400			
	RR† (95% CI)	p Val		ue
Smoking status*				
Never	1 (Ref)			
Former				
				<0.01
			(Ref)	
		0.20	1.97 (0.91 to 4.24)	0.08
	to 2.55)	0.21	3.96 (1.87 to 8.39)	<0.01
	1.69 (0.99 to 2.90)	0.06	2.13 (0.84 to 5.40)	0.11
≥20	1.94 (1.18 to 3.19)	<0.01	4.12 (1.98 to 8.60)	<0.01

Smoking accellerates progression of CP-disease
In hereditary pancreatitis: Ca 20y earlier!

After two decades of smoking cessation
risk of non-gallstone-related acute pancreatitis
is reduced to a level comparable to that of never smokers

Gut 2012 O-Sadr

Which genetic risk factors for CP do you know ?

Acinar cell dysfunction:

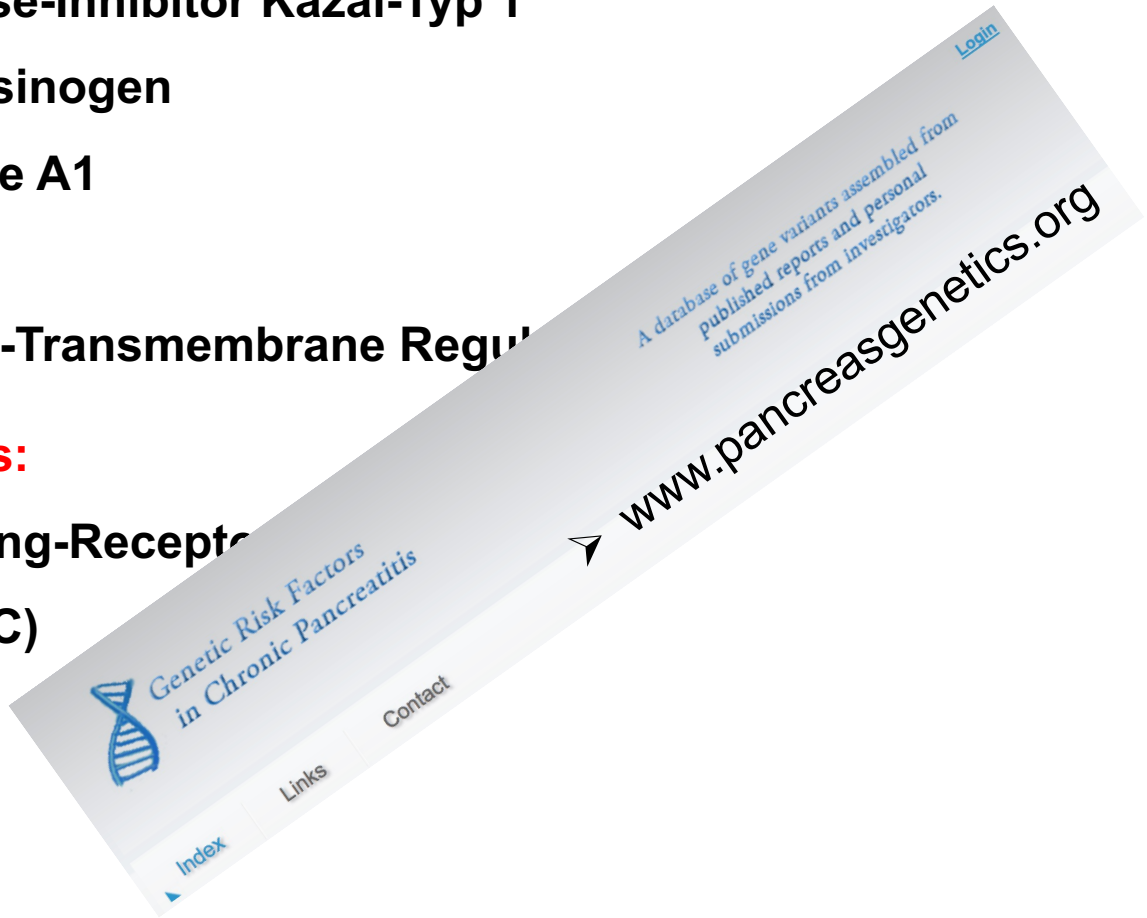
- **SPINK1: Serin-Protease-Inhibitor Kazal-Typ 1**
- **PRSS1: Cationic Trypsinogen**
- **CPA1: Carboxpepidase A1**

Ductal cell dysfunction:

- **CFTR: Cystic Fibrosis-Transmembrane Regu**

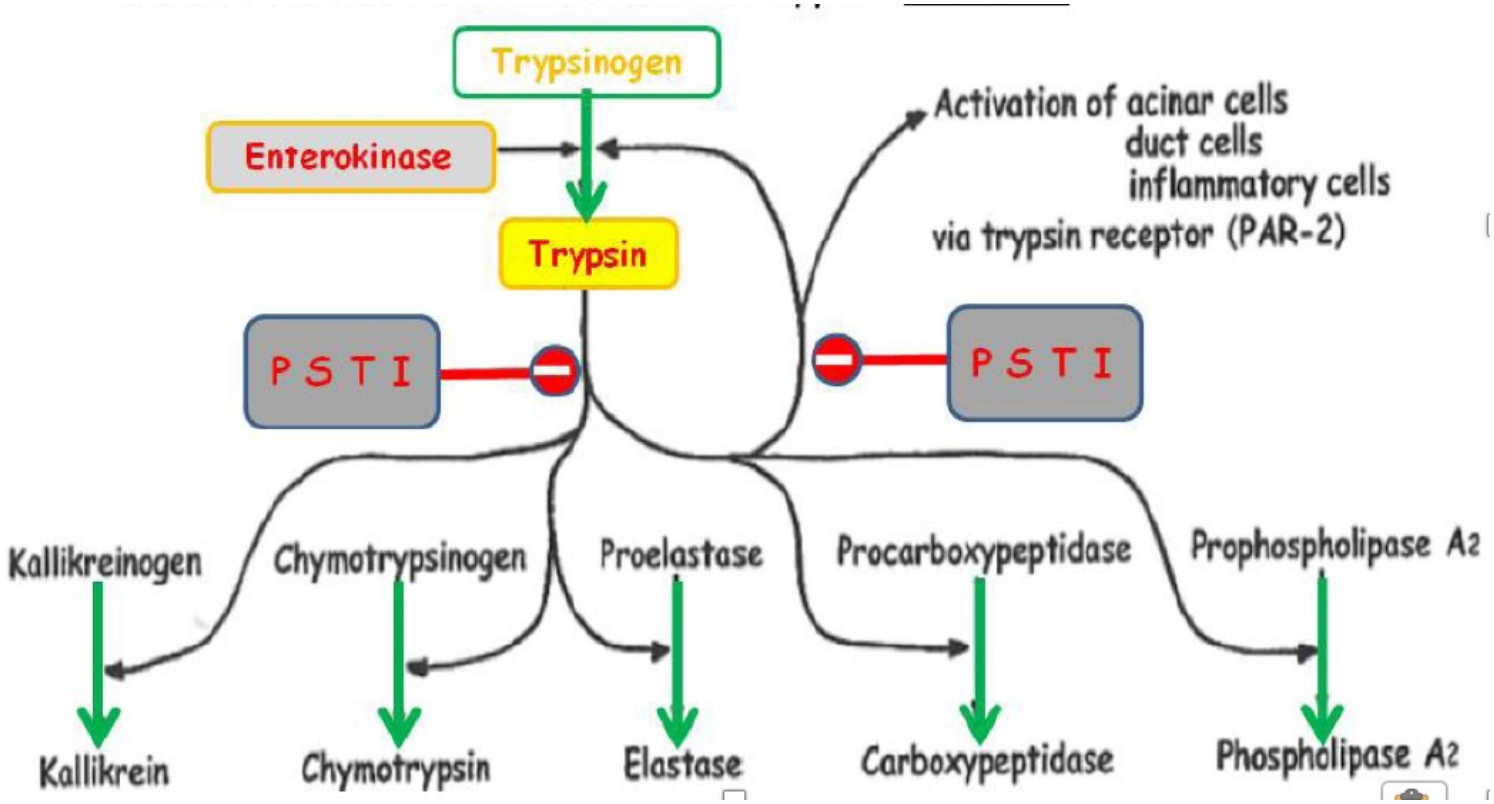
Disease-Modifying genes:

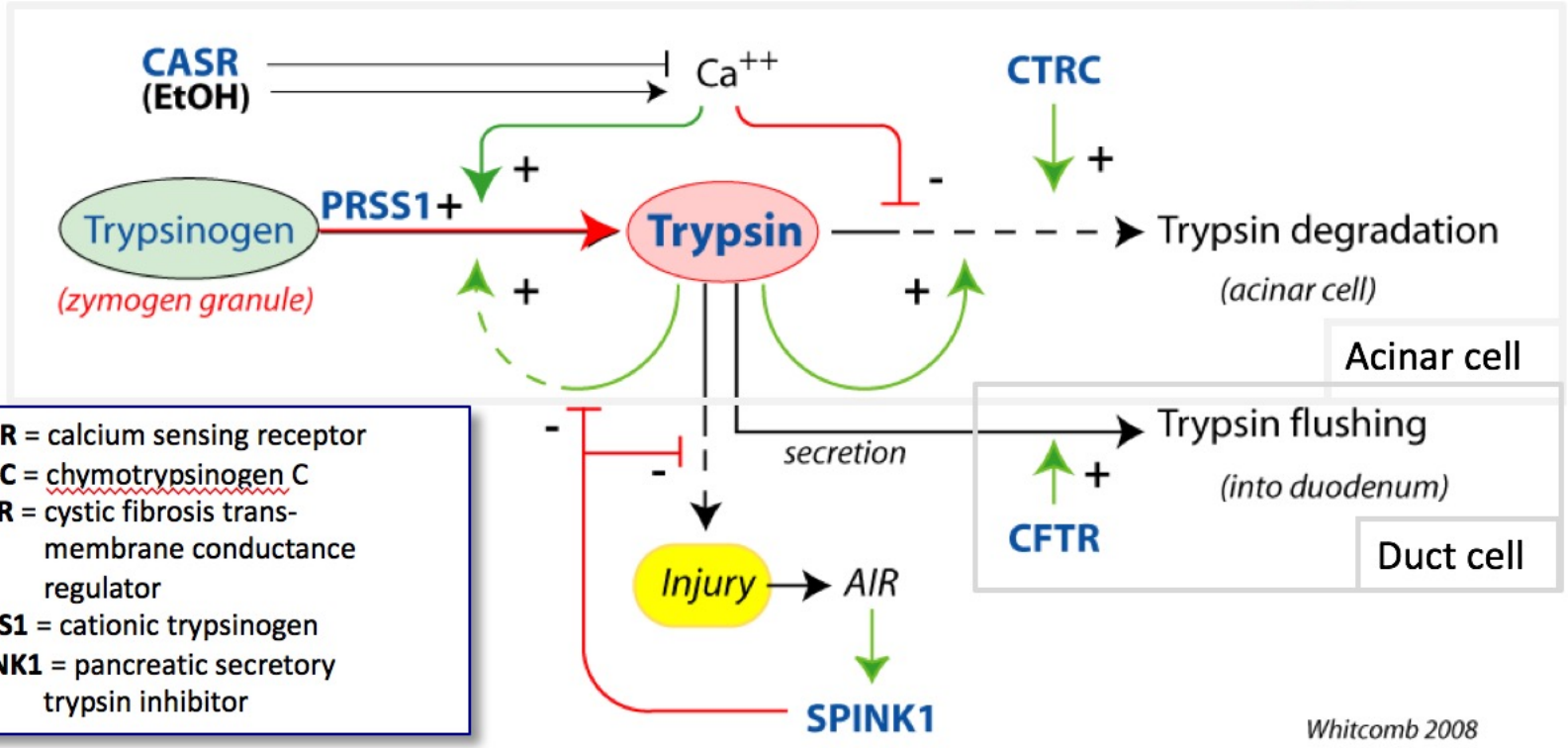
- **CASR: Calcium-Sensing-Recept**
- **CTCR (chymotrypsin C)**
- **Claudin-2/CLDN2. .....**



Trypsin-activation central for patho/physiology
How is trypsin inhibited ?

PSTI: Pancreatic Secretory Trypsin-Inhibitor
- Serin-Protease-Inhibitor, Kazal-Typ 1: **SPINK1**



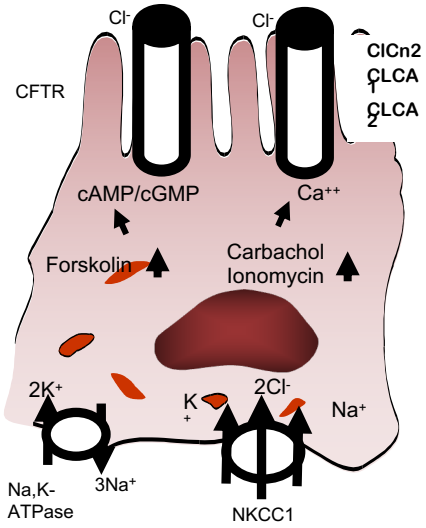


AIR = Acute inflammatory response (acute phase protein expression)

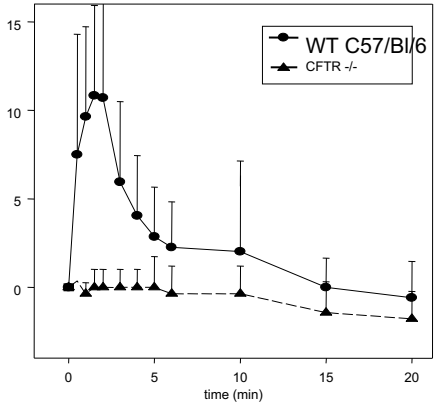
- Genes linked to **CP susceptibility** all regulate intra-pancreatic **trypsin** activity.
- Both the acinar cells and duct cells are linked with pancreatitis-causing variations

Whitcomb DC. *Annu Rev Med*. 2010;61:413-24.

CFTR ? Means – Does what ? Leads to ?



Change of potential difference after stimulation with Carbachol



- ***Cystic fibrosis transmembrane regulator gene*** mutations (> 2000 are known) lead to
- Alterations in secretion of ***Cl,*** Na and ***HCO3***
- Thick ***viscous mucus***
- Low pancreatic fluid volume
- Increased acidic pancreatic juice-> precipitations and thus, ***duct obstruction->*** longterm
- > 50% diabetes
- > 80% exocrine insufficiency

- Autosomal recessive inheritance
- Prevalence 1:2500, heterozygot: 1:25
- severe homozygous mutations: e.g. F508-delta/F508-delta typical multisystem CF phenotyp
- Mild variants: e.g. R75Q or BD (bicarbonate ....)

Diagnosis of hereditary pancreatitis (HP)
When to go for genetic testing ?

Consider when patients meet one or more of the following criteria:

- ✓A family history of idiopathic chronic pancreatitis, recurrent acute pancreatitis, or childhood pancreatitis
- ✓Relatives with known mutations associated with HP
- ✓Unexplained pancreatitis in a childhood, young adults=
- ✓Idiopathic chronic pancreatitis in patients <25 years old
- ✓Recurrent (≥ 2 episodes) acute pancreatitis of uncertain etiology

Aim: Testing before irreversible advanced stage of disease !

Surveillance of individuals with genetic predisposition for pancreatic cancer/ HP ?

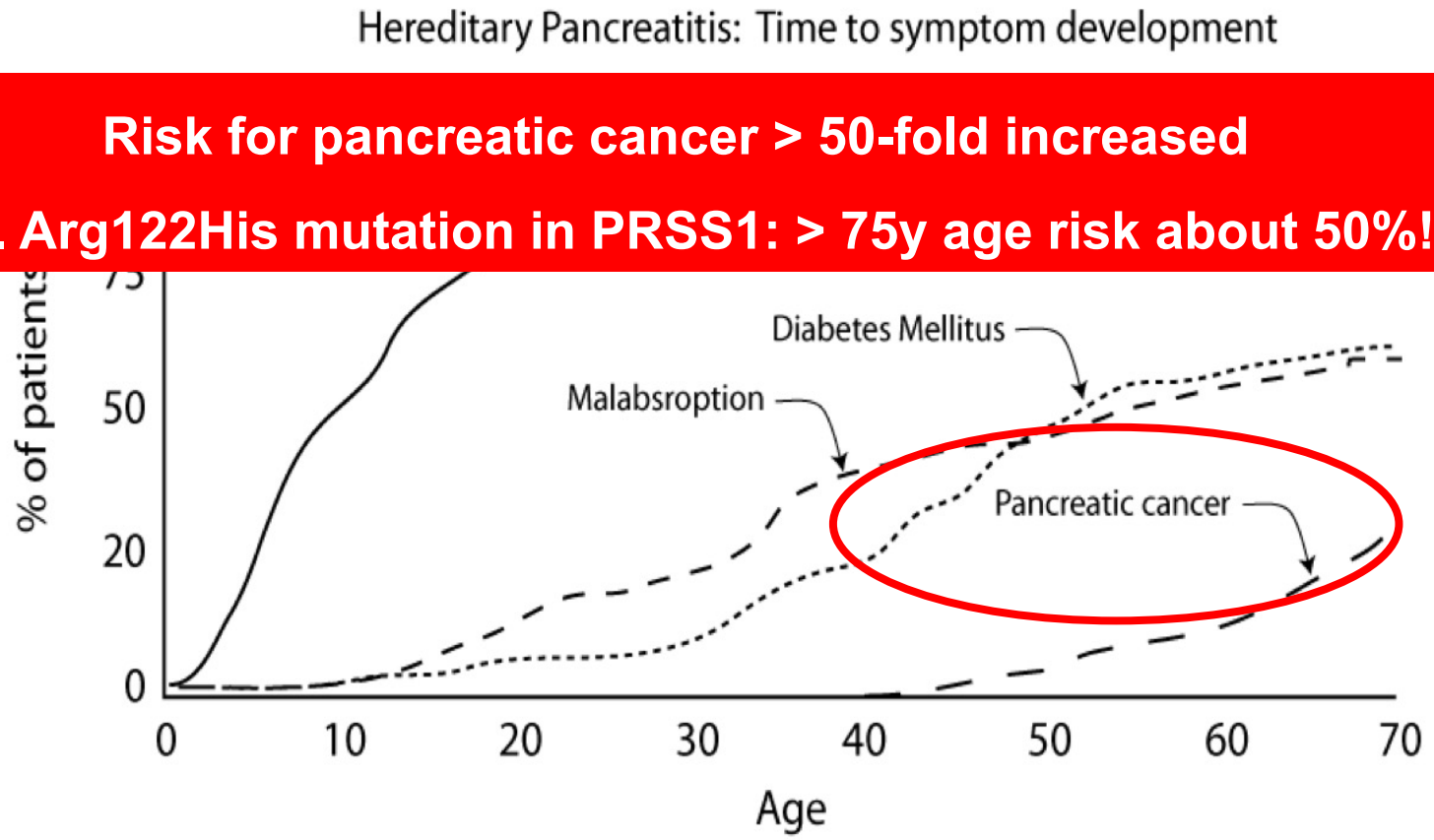
- **mutation carriers** for hereditay syndromes with increased pancreatic cancer risk, e.g. PJS, HP or
- **members** of familial pancreatic cancer kindreds with PCA-affected first degree
- **expert centres** (multidisciplinary and research capability)
- **EUS** or MRI, starting age 50 or 10 y younger than index pts
- **Avoidance** of i) medications with pancreatitis risk ii) environmental risk factors: C2, smoking, hig—fat-diet

- cystic lesions detected during surveillance of a hereditary pancreatic cancer-prone family member require evaluation by centers experienced in the care of high-risk individuals

Why do patients with HP need surveillance ?

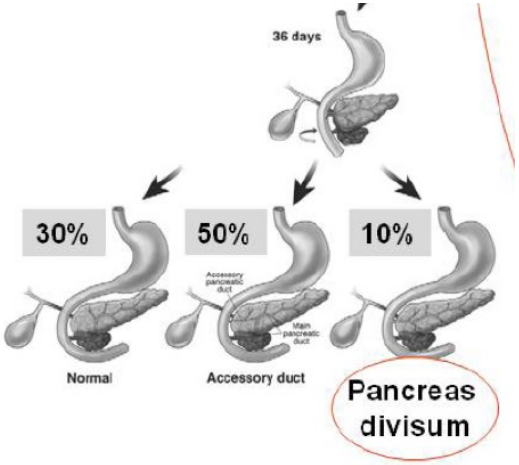
Risk for pancreatic cancer > 50-fold increased

e.g. Arg122His mutation in PRSS1: > 75y age risk about 50%!



Howes et al. Clin Gastroenterol Hepatol. 2004;2(3):252-61

Pancreas divisum: definition incidence, risk CP?



- Incomplete or lack of fusion D.santorini + D.wirsungianus with seperate drainage of ventral and dorsal pancreas in major and minor papilla
- Autopsies: 5-10% all individuals
- CP-cases: 6-26% of idiopathic CP-cases
- With other risk factors (genes, C2..): can cause CP
- Particularly in childhood pancreatitis search for it
- Endoscopic treatment can be/is appropiate individually

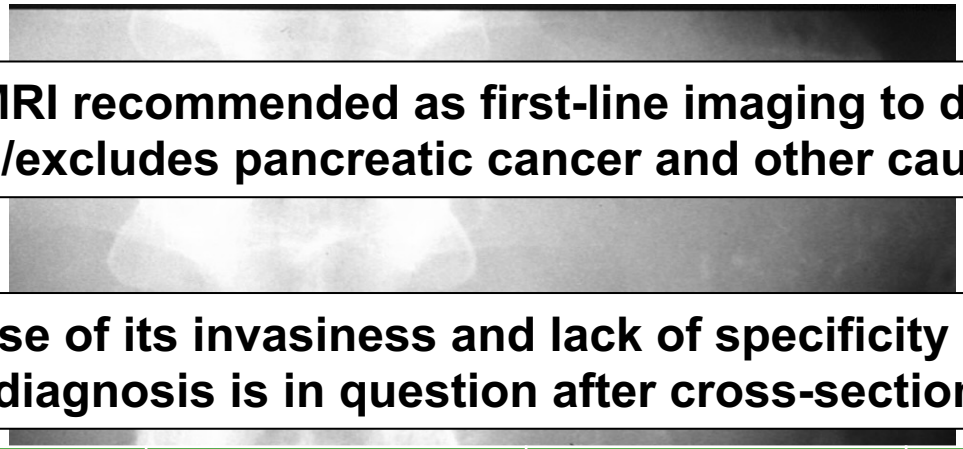
Diagnosing chronic pancreatitis

Diagnosis of chronic pancreatitis = summary of

Suspicion of Chronic Pancreatitis

	Clinical Features	← PLUS → Risk (TIGAR-O)	← PLUS → Biomarkers	
a	Pancreatitis-like pain Maldigestion Weight loss Glucose intolerance Older age	Alcohol / Smoking Hypertriglyceridemia Other metabolic / drugs AP / RAP Obstruction benign anatomic change Tumor	**Imaging** CT scan EUS (+/- FNA)	**Serum markers** High amylase/lipase High triglycerides High IgG4 High glucose Low vitamins (ADK B12) Tumor markers
b	Family history Early age of onset CF organ involvement Syndromic features	Genetic Testing (Genetic counseling: risk-based) Other toxic / metabolic risks	sMRCP	Sweat Chloride Exocrine function test
c	IBD or evidence of IgG4 disease Clinical response to Rx? Pain management with antioxidants Improved digestion with PERT Steroid trial for AIP Type 2	Known causes ruled out / unlikely Expand differential diagnosis Initiate low-risk therapy (lifestyle, antioxidants) Consider referral		Histology

Diagnosis of chronic pancreatitis- imaging ?



CT or MRI recommended as first-line imaging to diagnose CP differentiates/excludes pancreatic cancer and other causes of symptoms

EUS because of its invasiness and lack of specificity should be used Only if diagnosis is in question after cross-sectional imaging

	EUS	**MRI**	**CT**
Sensitivity	***81%*** *(CI 70-89%)*	78% (CI 69-85%)	78% (CI66-83%)
Specificity	***90%*** *(CI 82-95%)*	96% (CI 90-98%)	91% (CI 81-96%)

Strength of diagnostic EUS

Real-time – dynamic – individual adaptation

Which is the single best diagnostic imaging for CP in expert hands ?

Endoscopic Ultrasound

Pancreaticolithiasis + dilated duct > 80% probability for ExPI

but

poor negative predictive value (45%) compared with histology

= histo-changes can be overlooked easily

Which classification/s for CP-diagnosis e.g. by EUS ?

Rosemont – or - Cambridge-Classification

Chronische Pankreatitis-Rosemont-Classification

Parenchymal findings
Hyperechoic foci + shadowing = Major A
Lobularity = Major A
if honeycomb-typ = Major B
Hyperechoic foci without shadowing
Cysts
Stranding

Ductal findings
MPD calculi = Major A
Irregular MPD contour
Dilated side branches
MPD dilation
Hyperechoic MPD margin

I. Consistent with CP

A. 1 major A feature (+) ≥3 minor features

B. 1 major A feature (+) major B feature

C. 2 major A features

II. Suggestive of CP†

A. 1 major A feature (+) <3 minor features

B. 1 major B feature (+) ≥3 minor features

C. ≥5 minor features (any)

III. Indeterminate for CP†

A. 3 to 4 minor features, no major features

B. major B feature alone or with <3 minor features

IV. Normal

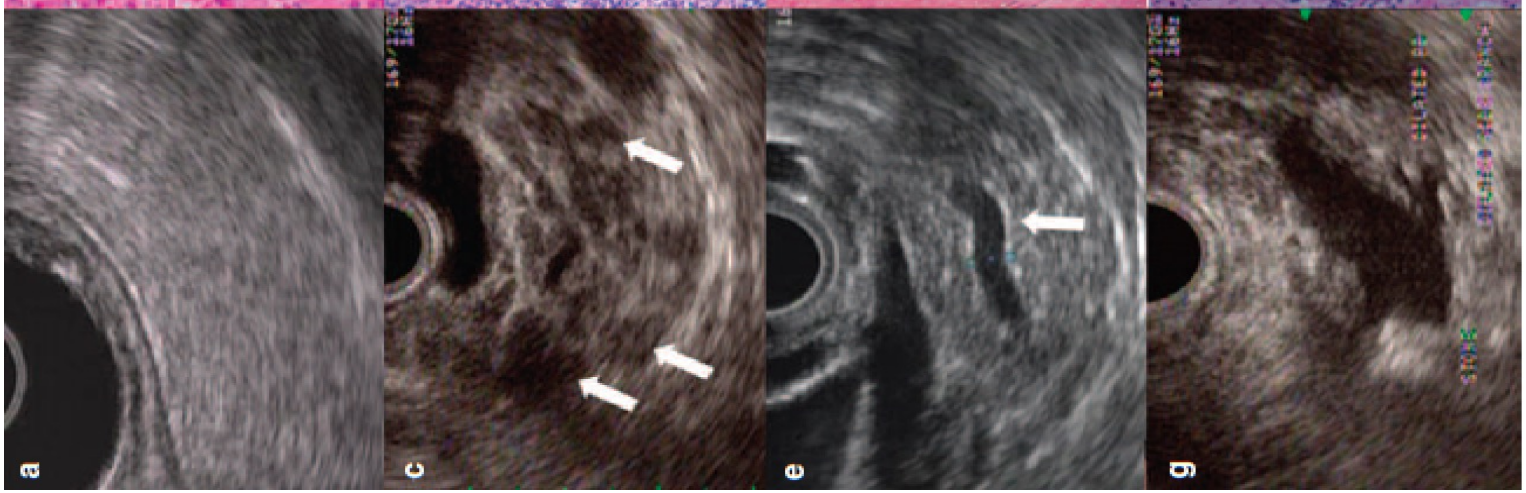
≤2 minor‡ features, no major features

*EUS diagnosis of CP should be made in the appropriate clinical setting.
†Diagnosis requires confirmation by additional imaging study (ERCP, CT, MRI, or PFT).

EUS-diagnostic accuracy for chronic pancreatitis

25 Pts. with surgical wedge-resection; EUS and secrtin-test prior to operation

Goldstandard Fibrose-Histologie	Sensitivität	Spezifität
EUS	84%	100%
Secretin-Test	86%	67%



Albashir S et al. AJG 2010

CH-EUS for pancreatic adenocarcinoma (AC) diagnosis

227 pts. with solid pancreatic lesion
After CT/MR/MRCP and conventional EUS
Diagnosis: surgery (n=92) or negative FNA + 12 months FU

		Sensitivity	Specificity	AUC
All Lesions (n=277)	CH-EUS	95.1% (92.7-96.7%)	89.0% (83.0-93.1%)	0.91
	MDCT	91.7% (88.9-93.7%)	84.2% (76.9-89.7%)	0.88
Lesions < 2cm (n=67)	**CH-EUS**	**91.2%** (82.5%-95.1%)	**94.4%** (86.2-98.1%)	**0.93**
	MDCT	70.6% (60.3-76.1%)	91.9% (86.2%-98.4%)	0.81

p<0.03

Kitano et al. AJG 2012

CD-/CH-EUS for pancreatic adenocarcinoma diagnosis

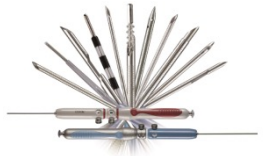
Meta-Analysis 12 Studies and 1139 Patients

All pancreas-adenocarcinoma

Sensitivity	**94%**
Specificity	**89%**

AUC-ROC 0.9732

Gong TT GIE 2012



EUS-FNA: Problems in Differentiation chronic pancreatitis (CP)- Carcinoma

Diagnostic accuracy < 75%

	No pts./ With CP	Sensitivity Without CP %	Sensitivity With CP %	P-Value
Fritscher-Ravens 2002	200/ 74	89.3%	**53.5%**	-
Varadarajulu 2005	300/75	91.3%	**73.9%**	0.02

Significantly lower sensitivity of EUS-FNA in CP due to:

- ✓ Calcified stones can hamper vision
- ✓ desmoplastic stroma traps cancer cells, yielding only a scant aspirate.
- ✓ Collaterals make FNA challenging: considering expert-recommendation of «funnel-technique» and > 7 passes/per puncture
- ✓ Occasional atypical cells can mimic malignancy
- ✓ *Well-differentiated Ca* overlooked: lack hyperchromasia; modest increase N/C-ratio

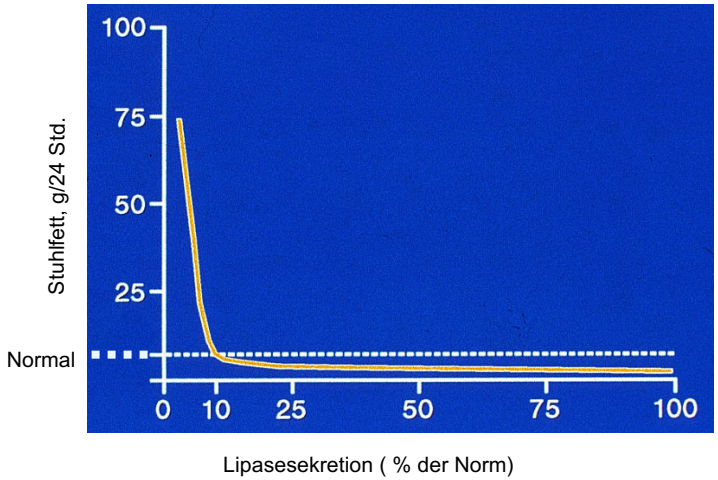
Exokrine Pancreas Insufficiency

What you need to know about steatorrhoe ?

Large volume, stinky stool, osmotic diarrhoe
undigested fibres (muscle), similar to coeliac
>7g fat/d at 100g fat ingestion/d

Clinically no reliable detection
(neither NPV nor PPV sufficient)

Usually (very) late manifestation:
after 15-20 years first symptoms
> 90% reduction in lipase-secretion



Testing exokrine pancreas function – how ?

Nonhormonal tests

Fecal elastase-1: universally available, easy
Requires only small amount of faeces
Is stable at room tempreture for 3 days
Only does test human elastase
(measures also substitution/drug-effect)
< 200 mikrog/d suggests moderate
< 100 mikrog/d suggests severe ePI

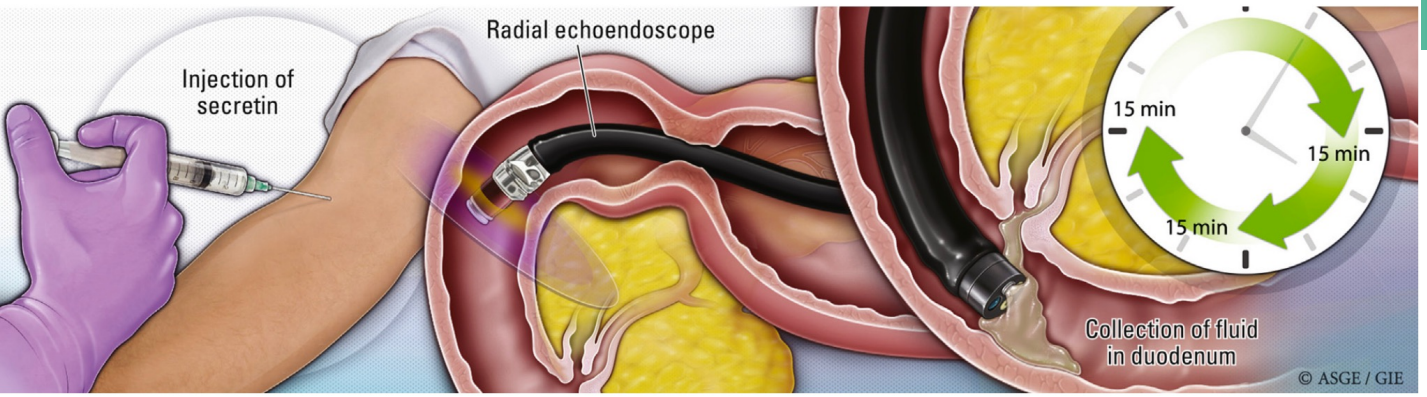
C13-mixed triglyceride-test
Test duration 4-6 h
Easy obtainable

Serum trypsinogen/trypsin
does not measure digestive tract encymes
Elevated with pancreatic pain

Hormonal tests

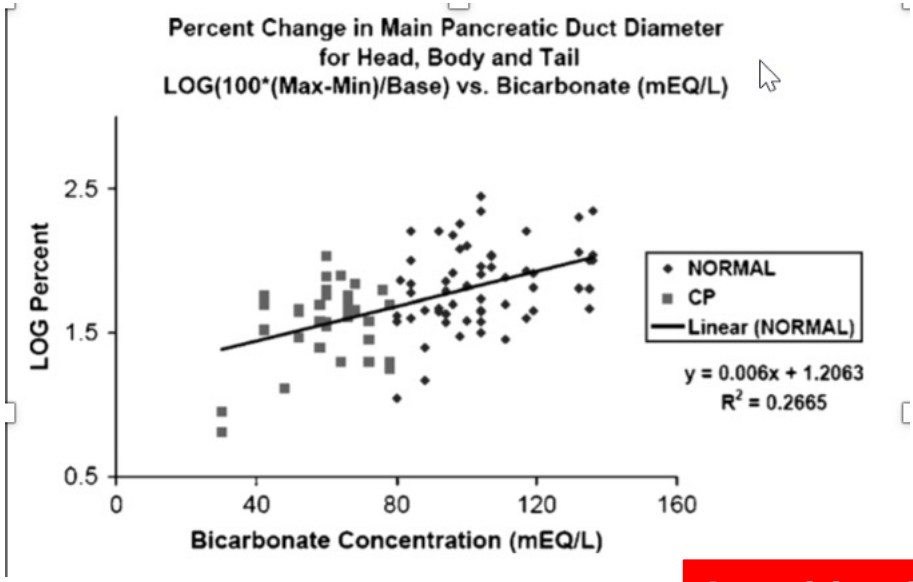
CCK-stimulation test:
acinar cell stimulation
Measuring trypsin and/or lipase
Can detect subtle ePI but
Cumbersome, specialized lab

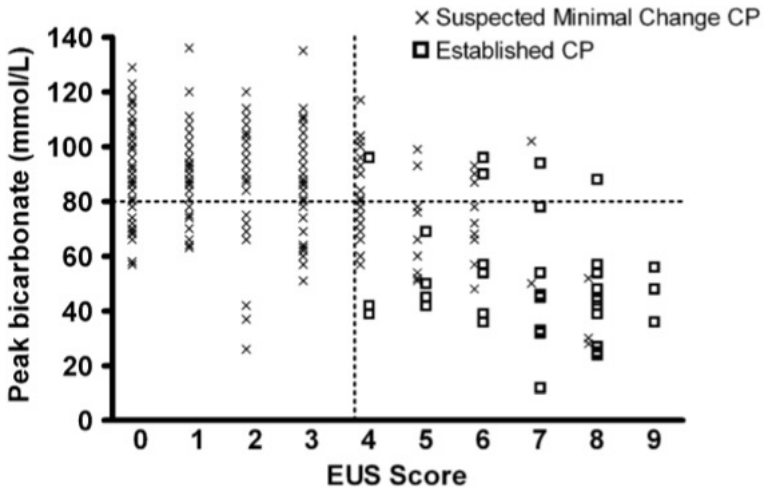
Secretin-stimulation test
Ductal cell stimulation
Measuring bicarbonate
Risk + cost endoscopy



De Witt GIE 2021

Secretin-Stimulated EUS-testing





Low bicarbonate duodenal aspirate + High EUS-score predicts CP

ExPI: Diagnosis – Testing – How and When

Test	Minimal ePI	Moderate ePI	Severe ePI	Specificity
	Sensitivität	Sensitivität	Sensitivität	
Fecal Elastase	**54%**	75%	**95%**	**>90%**
Qual. Stuhlfett*	0%	0%	78%	70%
Fecal Chymotrypsin	<50%	Ca. 60%	80-90%	80-90%
C13 breath thest (mixed triglyceride)	**62-100%**	**-**	**90-100%**	**80-90%**

Fecal pancreatic Elastase: < 200 mikrogramm/g Feces
False positive/low levels in diarrhoe (= adjust for water content)

C13-Breath-test-Triglyceride:
More/also sensitive at early stages of ExPI
test feasable/utilize to monitor replacement therapy!

Exocrine pancreas insufficiency (ExPI): Does normal morphology rule out ExPI ?

Even at normal EUS/MRI 28% pts. exhibit ExPI/reduced encyme activity in duodenal juice

Less common causes of ePI other than CP ?

- Coeliac disease
- HIV
- IBS-D
- Alcohol-related liver disease
- Sjoegren Syndrome
- Shwachman-Diamond syndrome
- Johanson-Blizzard syndrome

Pancreatic Encyme Replacement Therapy (PERT) in chronic pancreatitis

Basic considerations: if you do it do it right !

- Take with (and not before or after) and ***throughout the meal***
- If not to be swallowed then open capsule and take on spoon with cold acidic food (e.g. joghurt)
- Start with ***minimum 50.000 units*** per meal (and 25.000 for snacks)

- Eventually ***use PPI*** to suppress gastric acid = effective action of PERT
- If no response despite PPI and dose increase switch preparation
- ***No maximum dose*** of PERT in adults but if exceeding 100.000 units (10.000 u/kg/d): comorbidities other causes ?

- Mild side effects: nausea, vomiting, abdominal discomfort=***VERY SAFE***
- Can (should) be used with high-fat (high-protein) diet but avoid high-fibre content (> 25g/day)

Fecal elastase < 200: rate of response to PERT in > 80%

Pancreatic Encyme Replacement Therapy (PERT) in chronic pancreatitis

Effectiveness:

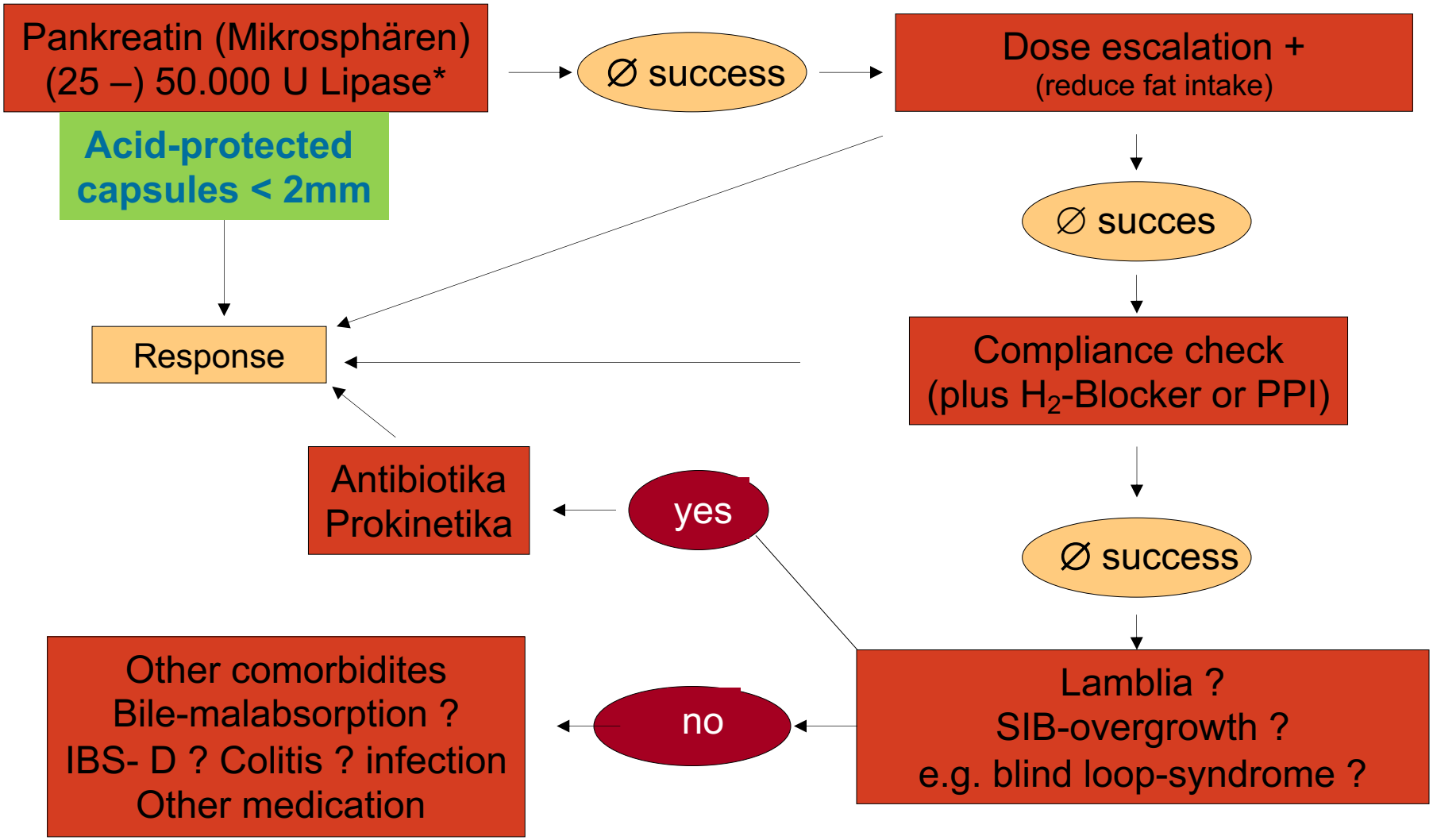
- Improves digestion, symptoms, fat and nitrogen absorption=
- PERT independent factor related to survival (e.g. in PA-cancer for surgery)
- UK propensity-matched observational study:

  adjusted increase in median survival time 262% with vs. without PERT

  in chronic pancreatitis with ePI and pancreas-cancer
- Improves quality of life in ePI

Winny M et al. Surgery 2014; Roberts KJ et al. Pancreatology 2019;
Dominguez-Munoz JE et al. BMC Cancer 2018; D`Haese JG et al. Pancreas 2014

Encyme replacement in chronic pancreatitis



*abhängig von der Art der aufgenommenen Nahrung

Indication and handling of encyme replacement in CP

Indications:

- ✓ **Loss in BW > 10% due**
- ✓ **Malassimilation**
- ✓ **Steatorrhoe > 7-15g/d**
- ✓ **Abdominal symptoms**
- ✓ **Fecal Elastase < 200**

Monitoring success:

- ✓ **Body weight**
- ✓ **Clinical symptoms**
- ✓ **Vitamin status**
- ✓ **If doubts ^{13}C breath test TG**

Relevance: CP with ePI: increased mortality on multivariate analysis (OR 2.6)

De la Iglesia-Garcia et al. J Clin Gastro 2018

Malnutrition and exocrine pankreatic-insufficiency

- **Maldigestion due to reduced encyme secretion**

  + Ca-loss (saponified fatty acids)
    -> Oxal acid-resorption increases
    -> Nephrolithiasis (Oxalate stones)
  + Deficiency fat-soluble vitamins A D E K

  + Azothorrhoe/ Protein-loss often late phenomenon

- **Pain-related lack of appetite and nutrition**

- **Ongoing alcohol-abuse limiting balanced nutrition**

ExPI and micronutrients + vitamin deficiency ?

Mg Nausea, Vomiting, Inappetence, Cramps

Vit-A Night blindness, Xerophtamia, skin hyperkeratosis,..

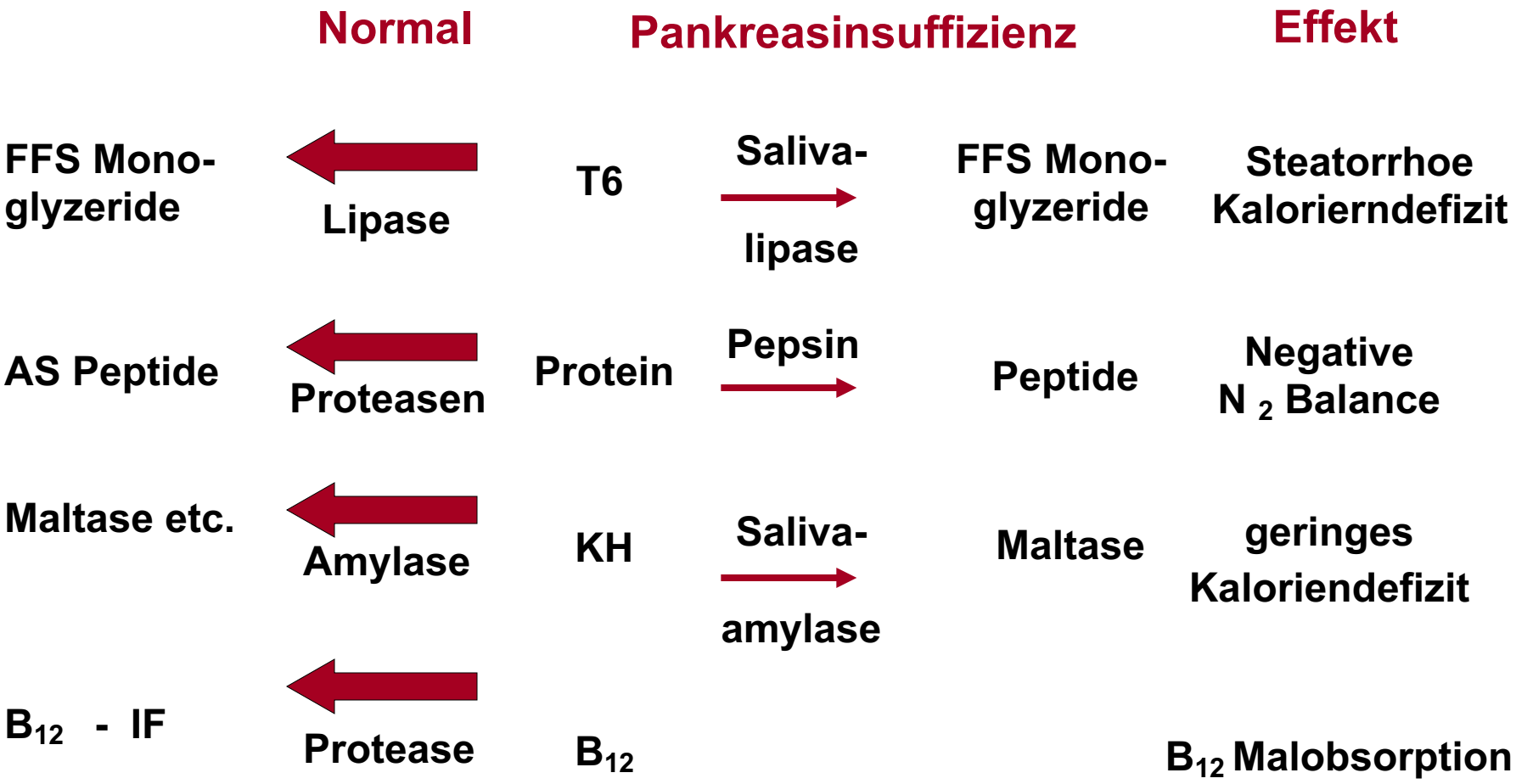
Vit-E Peripheral Neuropathy, Cerebellar Injury, Myopathy

Vit-K Plasmatic Homeostasis: INR-reduction

Vit-D Bones: Osteomalazie, ***Osteoporosis***

- Low fecal elastase associates with low bone mineral density
- Correlating with Vit-D- and Calcium levels
- About 65% of CP/ePI suffer either osteoporosis or osteopenia
- DXA-scan every 2 years recommended

ExPI and absorption problems ?



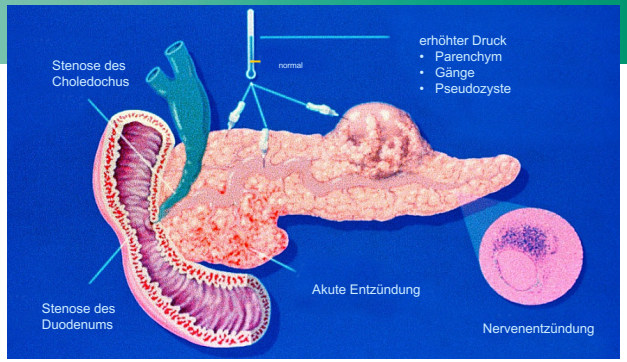
What is the chronic pancreatitis prognosis score ?

Chronic Pancreatitis Prognosis Score (COPPS), adapted from (28)

1 point	2 points	3 points
NRS (0–10), most severe pain intensity in the last 7 days		
0–2	3–6	7–10
HbA1c (%)		
> 6.0	5.5–6.0	< 5.5
CRP (mg/L)		
< 3.1	3.1–20	> 20
BMI (kg/m²)		
> 25	18–25	< 18
Platelets (Gpt/L)		
150–400	100–150	< 100, > 400
COPPS A = 5–6 points	**COPPS B = 7–9 points**	**COPPS C = 10–15 points**

Pain
in chronic pancreatitis

Pain in chronic pancreatitis –> how to handle/treat ?



Active/invasive interventions in patients actively using alcohol
Should be considered very cautiously.
Urgent/Emergency cases = different

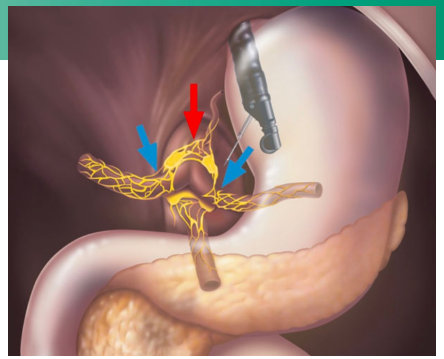
Pharmakological-conservative:
tricyclic antidepressants or gabapentin

<u>WHO-3-step-ladder:</u>
Paracetamol/Novalgin/NSAR → low-> high potent long-acting opiate
if other options are exhausted (since side effects, risk addiction etc.)

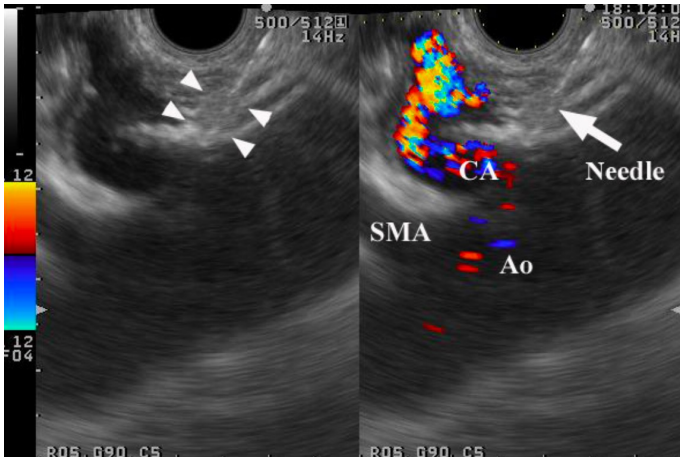
<u>Use anti-oxidative therapy (reducing oxidative stress)</u>
e.g. daily doses of 600 µg organic selenium, 0.54 g ascorbic acid, 9000 IU -carotene, 270 IU alpha- tocopherol and 2 g methionine (Betamore G, USA)

Gardner T et al. Guidelines AJG 2020, Bhardawaj et al. Gastroenterology 2009; Cai GH Pain Phys 2013

Pain in chronic pancreatitis –> interventional handling ?



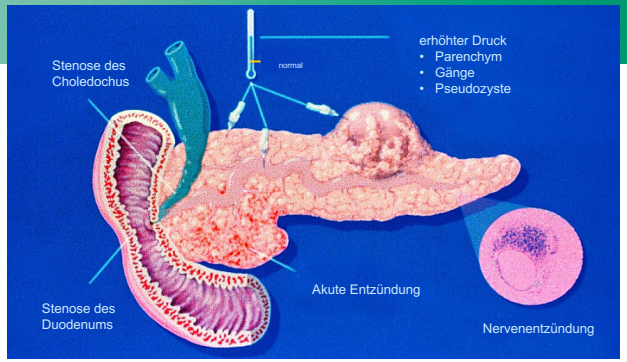
Endoscopic EUS-based bilateral **coeliac plexusblockade**
Single treatment: effect 3-6 months – wide range of pain reduction
median response rate* ca. 68% (week 2) -50% (week 4)
25 publications, case series with low evidence (meta-analysis *)



Bupivacain plus Triamcinolon
Ethanol 10-20 ml
Central or bilateral injection or
If identified ganglia direct into

Park W et al. GIE 2017; *Koulouris Pancreatology 2021; Yasuda et al. Dig Endoscopy 2017

Pain in chronic pancreatitis –> surgical handling ?



Pancreas-resection, debulking of fibrosis
e.g. plus pancreatico-jejunostomy (or Beger, Frey, Bern-mode)

Surgical approach achieves best longterm results

i**n chronic pancreatitis with dilated duct (> 5mm) +**
main duct stone or stricture with severe chronic (refractory) pain

RCT vs. endoscopy (ERC with lithotrypsy, multiple stenting)
79 mo follow-up: 5% vs. 68% need for Re-Intervention
> 50% of endoscopically treated cases needed sugery afterwards
free of pain 15% vs. 34% (endoscopy vs. surgery)

Dite P et al. Endoscopy 2003; Cahen DL et al. **N Engl J Med 2007** + Gastroenterology 2011; Cochrane 2015

Endoscopy in Complicated CP with Pancreaticolithiasis Still often first line treatment and choice as ESG recommends:

ESWL first: any obstructive stone > 5 mm (head or corpus)

since ERCP alone successful in minority (9-13%) of cases

+ complication rate for such ERP 3-times higher than biliary lithotrypsy

Success: fragmentation into fragments <3 mm

+/- Endoscopic drainage (with stent insertion) after ESWL =

Effective in up to 80%; particularly for pain resolution/reduction (ca. 50%)

Caveat: Relapse in 30-50%

Predictive factors (goal) for sustained clinical response: complete stone removal

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EUS-guided transenteric pancreatic duct drainage

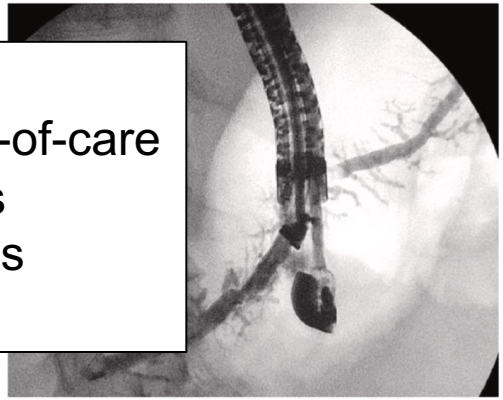
M. Giovannini

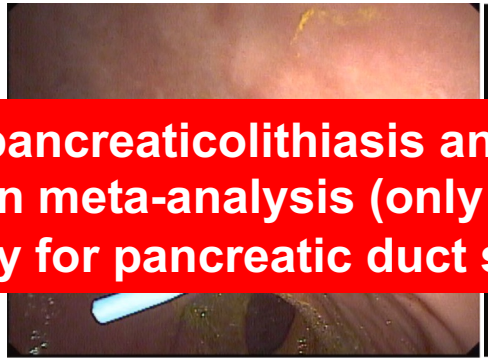
Head of Gastroenterology and Endoscopy Department, Paoli-Calmettes Institute, Marseille, France

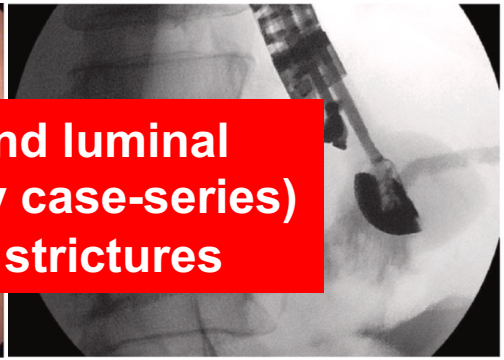
Studies on EUS-guided pancreatico-gastrostomy.

AUTHORS	NB PTS	% SUCCESS	% COMPLICATION	FOLLOW-UP
TESSIER GIE, 2007	36	70%	11%	16.5 months
KAHALEH GIE, 2007	13	92%	16%	14 months
BARKAY GIE, 2010	21	48%	2%	13 months
ERGUN ENDOSCOPY, 2011	20	90%	10%	37 months
Fuji GIE,2013	45	74%	6%	32 months
Will WJG, 2015	94			
Oh * GIE, 2016	25			
Tyberg Endosc ultrasound, 2020	56			
Krafft GIE,2020	28			
• FCSEMS				

Summary: feasable
Potential for standard-of-care
Meta-analysis 503 pts
81% technical success
AE-rate 21%







No seperate data on pancreaticolithiasis and luminal Endoscopic lithotrypsy in meta-analysis (only case-series) but used so far mainly for pancreatic duct strictures

CP and MPD-strictures- definitions – handling ?

Dominant stricture: upstream dilatation > 6 mm

Endoscopic approach as for ERP includes:

- **Pancreatic sphincterotomy**
- **Dilatation (or Sohendra-Retreiver-crossing of) stenosis**
- **10 Fr-stenting (or multiple) and if pain-relief -> with**
- **Exchange within 1 year (rather on-demand, but > 6 months)**

EUS-guided pancreatic drainage for pancreatic strictures after failed ERCP: a multicenter international collaborative study

Amy Tyberg, MD,[1] Reem Z. Sharaiha, MD,[1] Prashant Kedia, MD,[2] Nikhil Kumta, MD,[1] Monica Gaidhane, MD,[1] Everson Artifon, MD,[3] Marc Giovannini, MD,[4] Michel Kahaleh, MD[1]

New York, New York; Dallas, Texas, USA; São Paulo, Brazil; Marseille, France

Conclusions: With appropriate endoscopic expertise, EUS-PD offers a minimally invasive, more effective, and safer alternative to some surgical PD procedures. Prospective studies are needed to evaluate long-term outcomes. (Clinical trial registration number: NCT01522573.) (Gastrointest Endosc 2017;85:164-9.)

Biliary obstruction due to chronic pancreatitis Indications and type of treatment ?

Efficacy of self-expandable metal stents in management of benign biliary strictures and comparison with multiple plastic stents: a meta-analysis

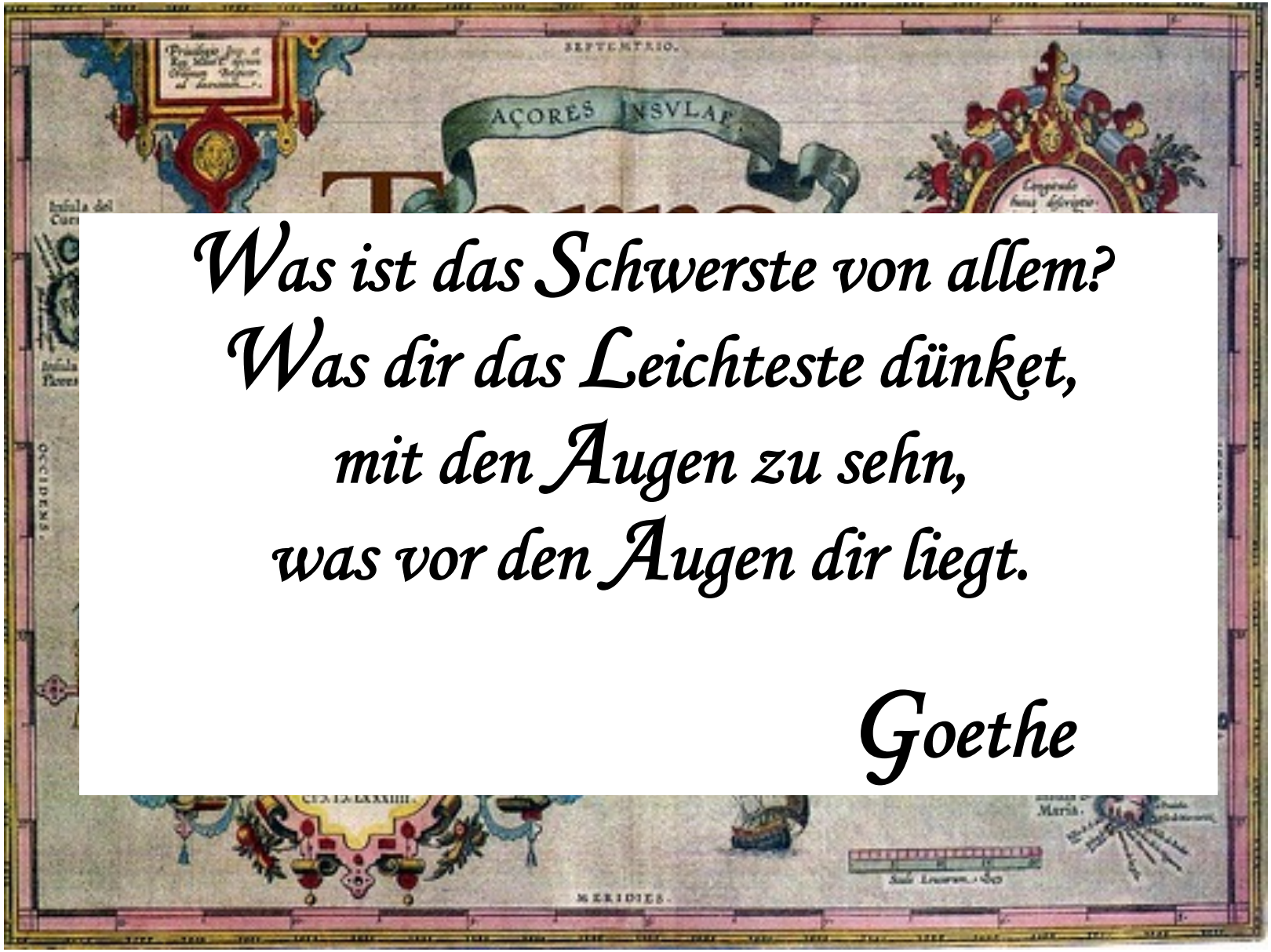
Authors
Muhammad Ali Khan[1], Todd H. Baron[2], Faisal Kamal[1], Bilal Ali[1], Richard Nollan[3], Mohammad Kashif Ismail[1], Claudio Tombazzi[1], Everson L. A. Artifon[4], Alessandro Repici[5], Mouen A. Khashab[6]

Conclusions:

FCSEMS appear to have excellent efficacy in benign biliary stricture Managment. They are as effective as multiple plastic stenting but require fewer ERCPs to achieve clinical success

Endoscopy 2017

If recurrence then surgery .....



Was ist das Schwerste von allem?
Was dir das Leichteste dünket,
mit den Augen zu sehn,
was vor den Augen dir liegt.

Goethe