

MEN 1 GEP Tumours

Pancreatico-Nodal (-Duodenal)

Affects 35-80% of MEN1 patients

Functioning or non functioning

Hyperplasia → microadenoma → macrotumours

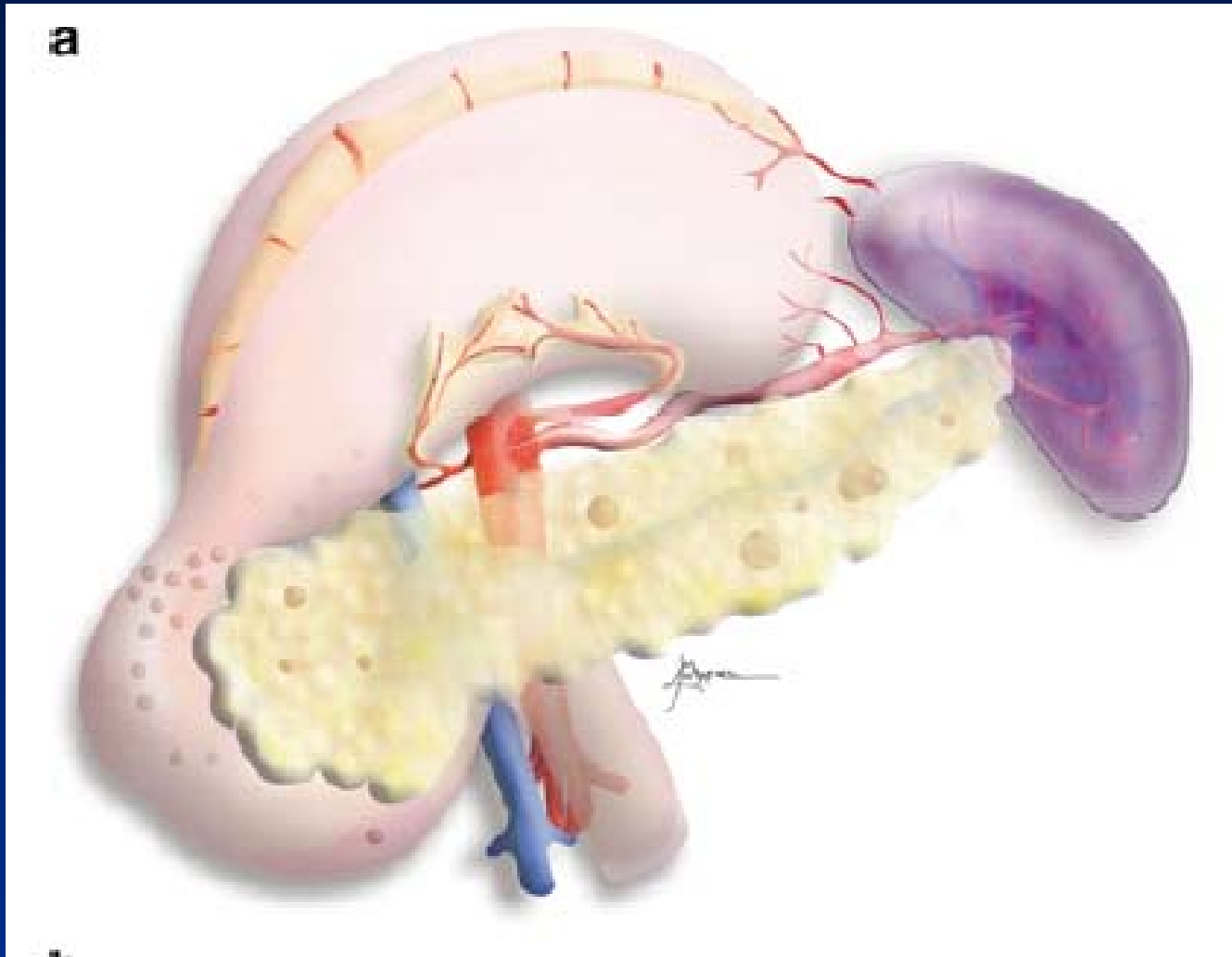
Solid or cystic

50% malignant (well / poorly differentiated)

Progression is slow

Recurrence is common

**Diagnosis – abnormal morphology and /or
abnormal biochemistry**



Treat the hormonal and the tumour syndromes

MEN-1 Monitoring Sheet

Mutation:
 DNA test: YES/NO
 Date:

DATE

P A A R R T H Y R O I D	Corrected calcium (NR 2.20-2.60)		
	PTH (NR 2-63)		
	Bone ALP: Ehos		
	NTX		
P A N C R E A S	Grt Peptides VIP (NR<30)		
	FP <i>(NR < 300)</i>		
	Gastrin <i>(NR=40)</i>		
	Glucagon <i>(NR<50)</i>		
	Somatostatin <i>(NR=250)</i>		
	Neurotensin <i>(NR<100)</i>		
I M A G I N G	Dexaz Score Lumbar Spine and Femoral Neck		
	MRI Ebitary		
	MRI Pancreas and Adrenals		
	Comments and Treatment		

MEN 1 Pancreas

Non Functioning Tumours

> 50% patients on screening

>80% patients on histology

RR of Death 3.6

10 year survival 62%

Rare Functioning Tumours

Glucagonoma (1.5%)/Vipoma (1%)/Somatostatinoma (<1%)

10 year survival 53%

MEN 1 Pancreas

Insulinoma

10-33% of functioning GEP

20% patients on histology

Very rare in head of pancreas

>3cm diameter increased risk of malignancy

10 years survival 90%

MEN 1 GEP

Gastrinoma

60% of functioning GEP

85% in duodenum

Diagnosis by elevated basal gastrin and secretin test

Exclude metastases by CT and SRS

Significance of nodal disease ??

At duodenal surgery - $\leq 0.5\text{cm}$ enucleate

Remember all duodenum is at risk

10 years survival 80%. RR of Death 2.5

PET in MEN Type 1

“...indications for intervention are controversial...”

Pancreatic Endocrine Tumours in
MEN-1. Skogseid *et al* in ‘Surgical
Endocrinology’ (2001) Eds Doherty
& Skogseid. Lippincott

Management of Pancreatic Endocrine Tumours in MEN 1

“...current management ...is very much an art as well
as a science....”

Kouvaraki *et al.* World J Surg 2006;30:643-53

GEP in MEN 1 –Natural History

Lethality of MEN Type I

Doherty GM et al 1998

Are Patients with MEN Type I Prone to Premature Death?

Dean PG et al 2000

Do Patients with MEN Syndrome Type 1 Benefit from Periodical Screening?

Geerdink et al 2003

Nodal disease indicates malignancy not aggressivity

Liver metastases do not necessarily indicate short survival

Screening for GEP in MEN 1

Age at onset?

French GTE Registry > 800 MEN cases

Dalac et al. WorldMEN 2006

15% \leq 20 years of age

23% (29 patients) with PET

1st tumour in 25 pts

Insulinoma >non functioning>gastrinoma

Node +ve or metastases in 4 patients

GEP in MEN 1 - Screening

How?

EUS Detection of PET in Asymptomatic Patients with Type 1 MEN

Wamsteker et al 2003

Prospective Evaluation of Imaging Procedures for the Detection of
PET in Patients with MEN Type 1

Langer et al 2004

Prospective EUS evaluation of the Frequency of Non Functioning
PDET in Patients with MEN Type 1

Thomas-Marques et al 2006

GEP in MEN 1 - Screening

Abnormal morphology

EUS

Resolution 1-2 mm

Good for pancreatic disease (80%)

Good for nodes (60%)

Less for gastrinoma – small duodenal tumours

SRS

<1cm tumours (30%)

Good for metastases

GEP in MEN 1 - Screening

Abnormal morphology

No Tumour identified

Repeat EUS at 3 years

Tumour/s identified

≤ 1 cm repeat at 1 year

>1 cm ?????

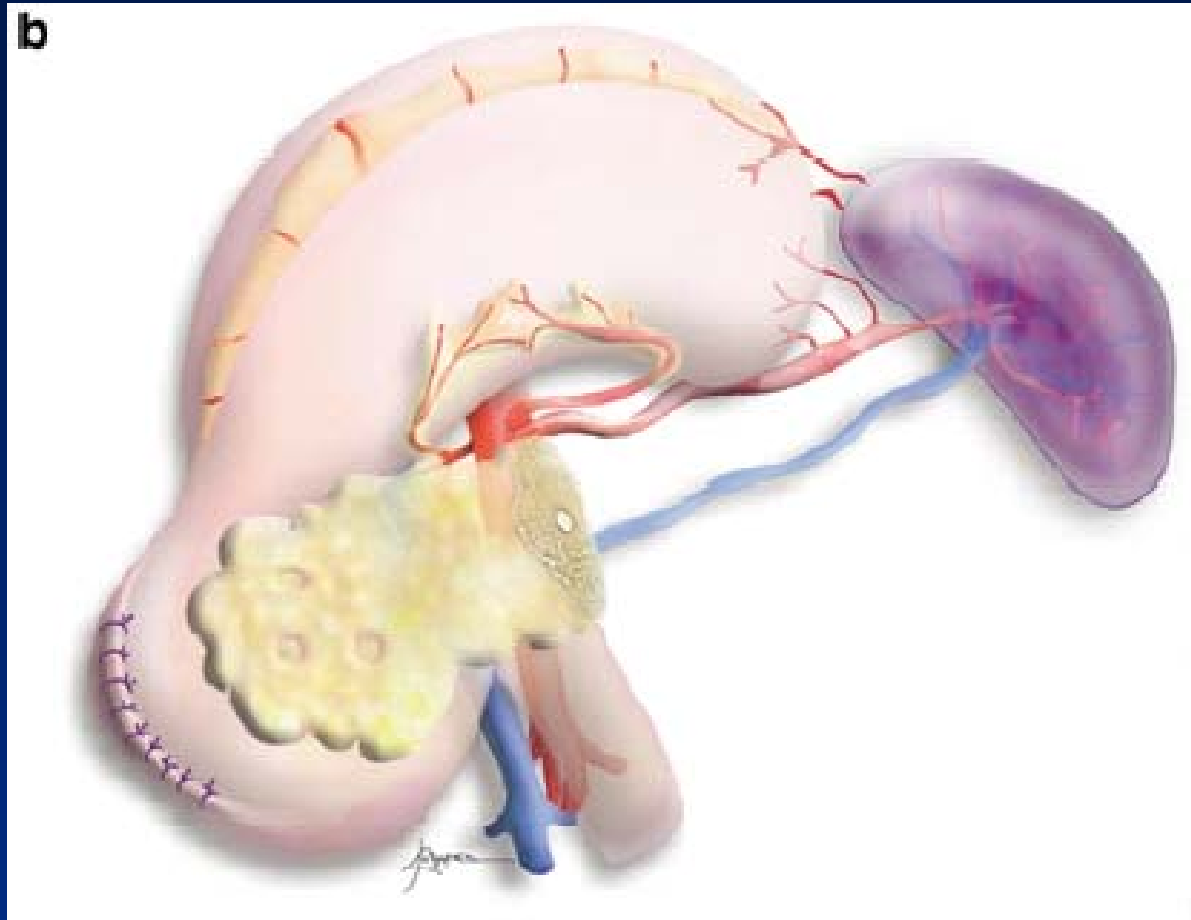
GEP in MEN 1 - Operation

Comparison of surgical results in patients with advanced and limited disease with MEN Type 1 and ZES

Norton et al 2001

The surgical management of MEN-1 pancreatoduodenal neuroendocrine disease.

Hausman et al 2004



Gastrin normal – duodenotomy not required
Intraoperative endoscopy
Intra operative USS

GEP in MEN 1 – Outcome

Management of Pancreatic Endocrine Tumours in MEN 1

Kouvaraki et al 2006

Is Surgery Beneficial for MEN 1 Patients With Small (≤ 2 cm) Nonfunctioning PET?

Triponez et al 2006

GEP in MEN 1 – Outcome

Prognosis

Mean age at death is 51 years

80% of patients will live 10 years

Survival better in young/functioning/no distant metastases

Distant metastases are rare in the absence of liver metastases

♀ 09/1974 Gene +ve MEN 1

- @ 25 y HPT surgery
- @ 27 y MRI pancreas - normal
- @ 29 y rising glucagon 55-83 (<50)
- @ 30 y MRI – mass in pancreatic tail

Distal pancreatectomy

Multifocal NET: 5 lesions showing ‘invasion’

Gut hormones normal

GTT normal

Don't leave it too long

Glucagonoma

♀ 05/1964 Gene +ve Z-E syndrome

@ 22 y Prolactinoma surgery and DXT

@ 30 y HPT surgery

@ 40 y MRI lesion in pancreatic tail and 1.2 cm lesion in head of pancreas

Spleen preserving distal pancreatectomy

Pancreas: multifocal NET: 4 tumours 2-14mm diameter

Duodenum: 3 NET

Nodes: positive

BAO 3.1 mm H⁺/hr (<5)

GTT normal

Timing of surgery

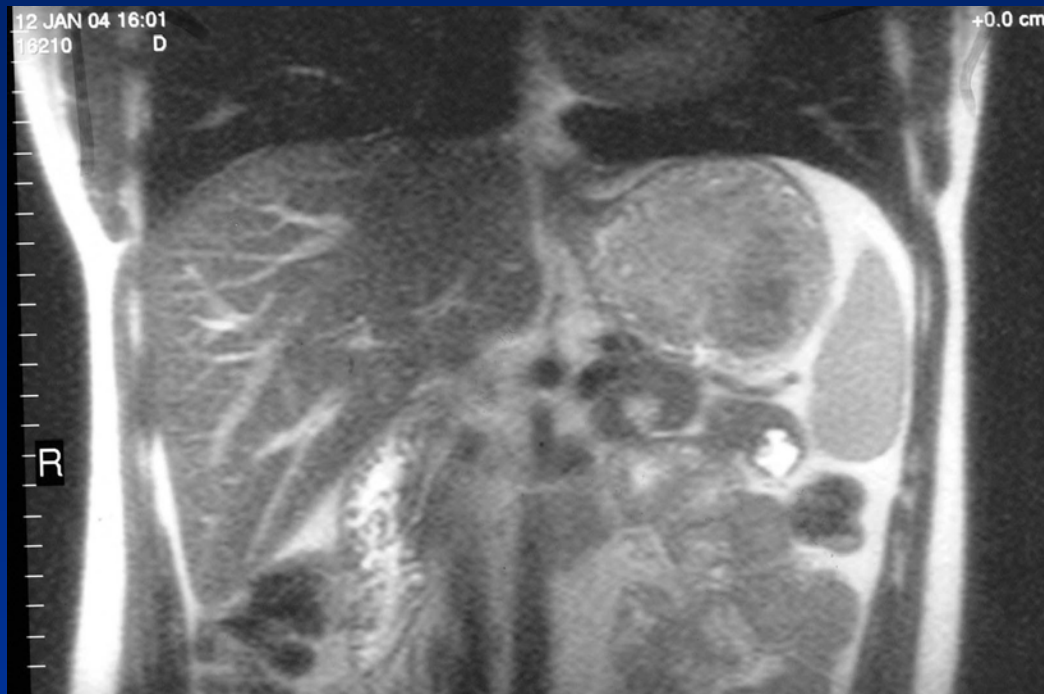
'Cure' is possible



09/1984 Gene +ve MEN 1

@ 14 y HPT surgery

@ 18 y MRI – mass in tail of pancreas
Gut hormones - normal



♂ 09/1984 Gene +ve MEN 1

@ 14 y HPT surgery

@ 18 y MRI – mass in tail of pancreas

Gut hormones - normal

Family History

@ 20 y Spleen preserving distal pancreatectomy

Pancreas: head – 9mm NET enucleated

body/tail - 3 lesions 7-19 mm

- micro tumours 1- 4 mm

@ 22 y GTT normal

Talk to the patient

Does age at onset influence surgical advice?



10/1957 Gene +ve Z-E syndrome

@ 39

4th operation for HPT

@40

MRI lesion in pancreatic tail
lesion in head of pancreas

@49

Spleen preserving distal pan
Pancreas: multifocal NET:
4 tumours 2-14mm diameter
Duodenum: 3 NET. Nodes



Multiple complications. Discharged 4 months post op

♀ 07/1948 Gene +ve Z-E syndrome

@ 56 y Abnormal MRI 2cm lesion in pancreatic head
1cm lesion uncinata process

Spleen preserving distal pancreatectomy

Enucleation head and uncinata tumours

Excision gastric tumour and node metastases

Nil in duodenum

8 months post op – multiple hepatic metastases

Don't leave it too late





Surgery for GEP in MEN 1

Screen early in gene positive individuals

Intervene if abnormal imaging and abnormal biochemistry

or

increasingly abnormal imaging

or

increasingly abnormal biochemistry

and

no metastases (excluding lymph nodes)

25% of patients will have liver metastases
by the time they are symptomatic