

# MEN 1 GEP Tumours

Pancreatico-Nodal (-Duodenal)

Affects 35-80% of MEN1 patients

Functioning or non functioning

Hyperplasia → microadenoma → macrotumours

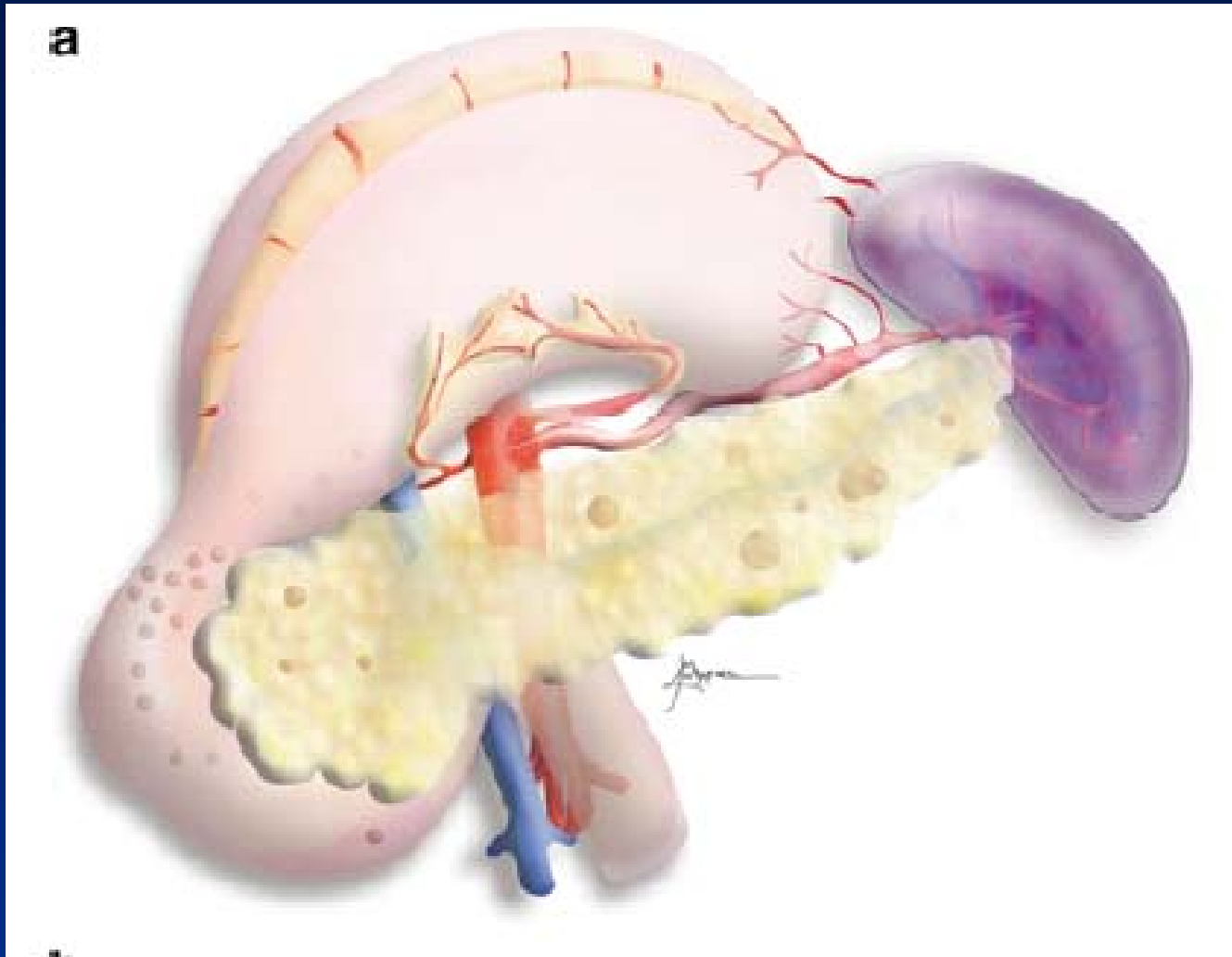
Solid or cystic

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  
 \_\_\_\_\_

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

# 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

1<sup>st</sup> 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

$\leq 1$  cm repeat at 1 year

$>1$  cm ?????

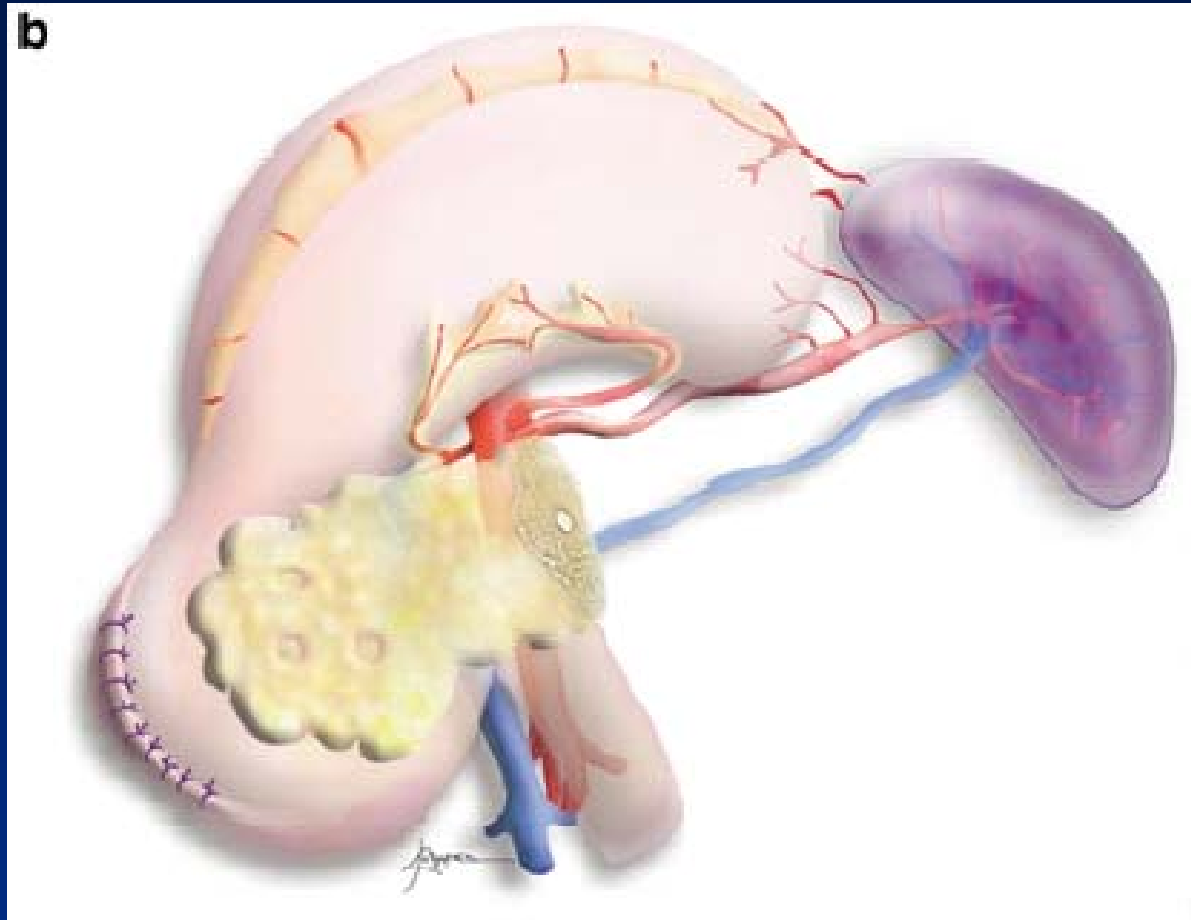
# GEP in MEN 1 - Operation

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 ( $\leq 2$ 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<sup>+</sup>/hr (<5)

GTT normal

Timing of surgery

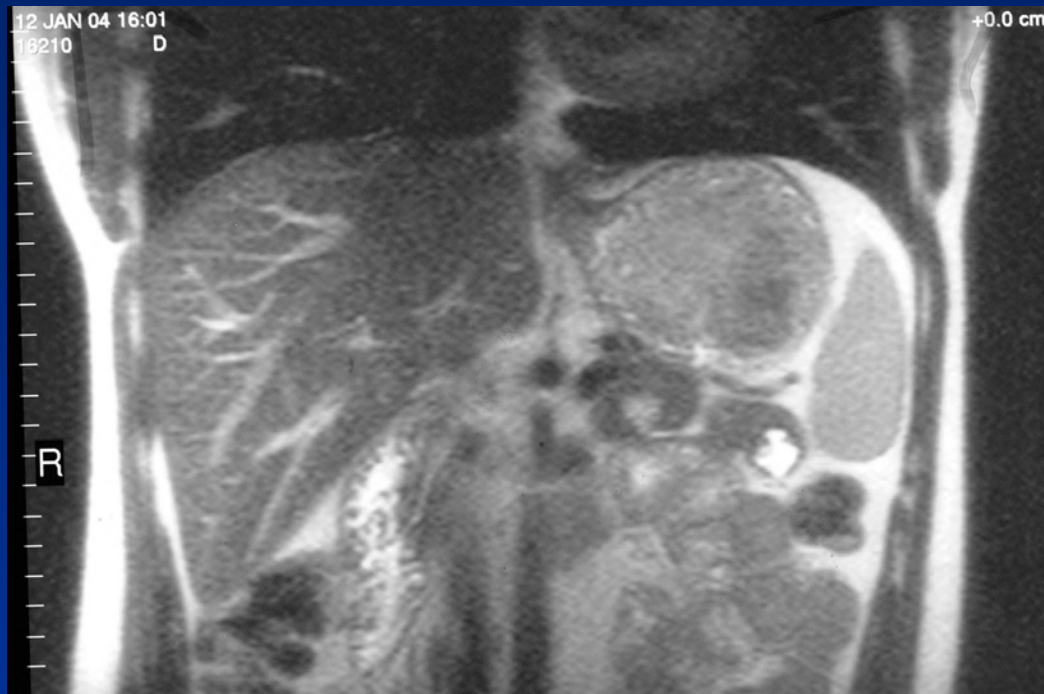
'Cure' is possible



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

4<sup>th</sup> 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