



# Fibrous Dysplasia/McCune-Albright Syndrome

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# Fibrous Dysplasia/McCune-Albright Syndrome

- **Phosphate problems in FD**
- **Gastrointestinal disease in FD/MAS**
- **Cancer and FD/MAS**

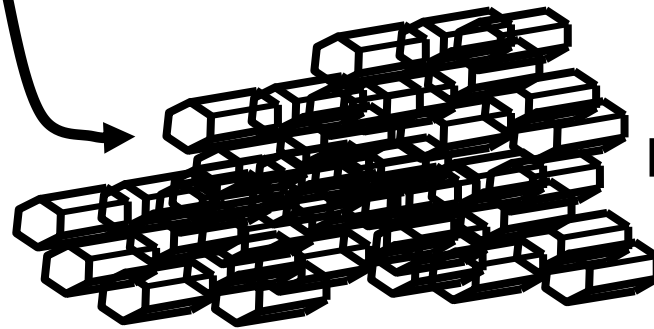
# Why do we care about Phosphate?

**Phosphate**

**Calcium**



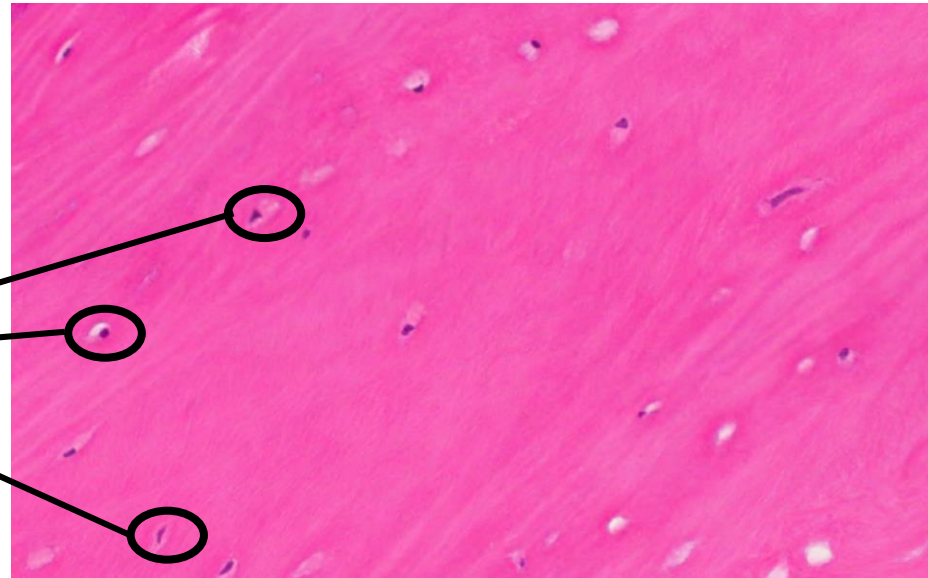
mineralization; the hard stuff the makes up bone



hydroxyapatite

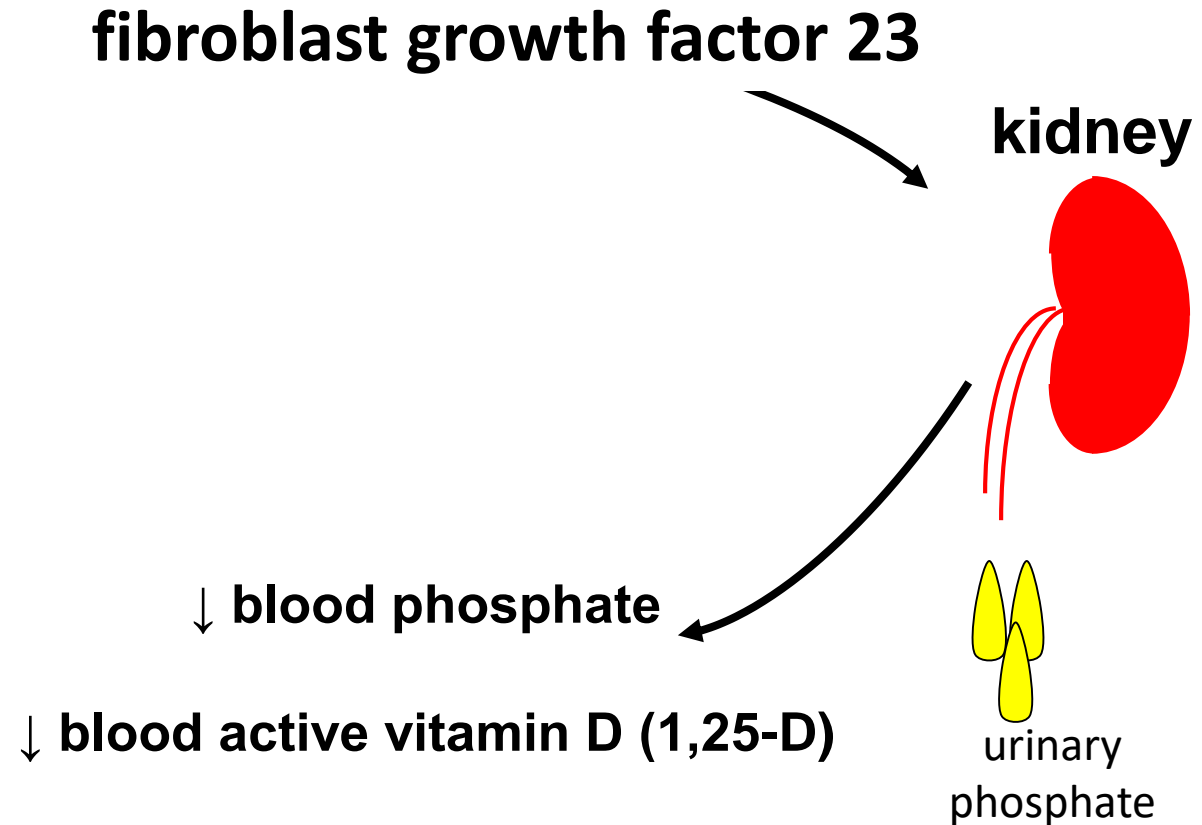
bone is mostly hard stuff

with a few cells

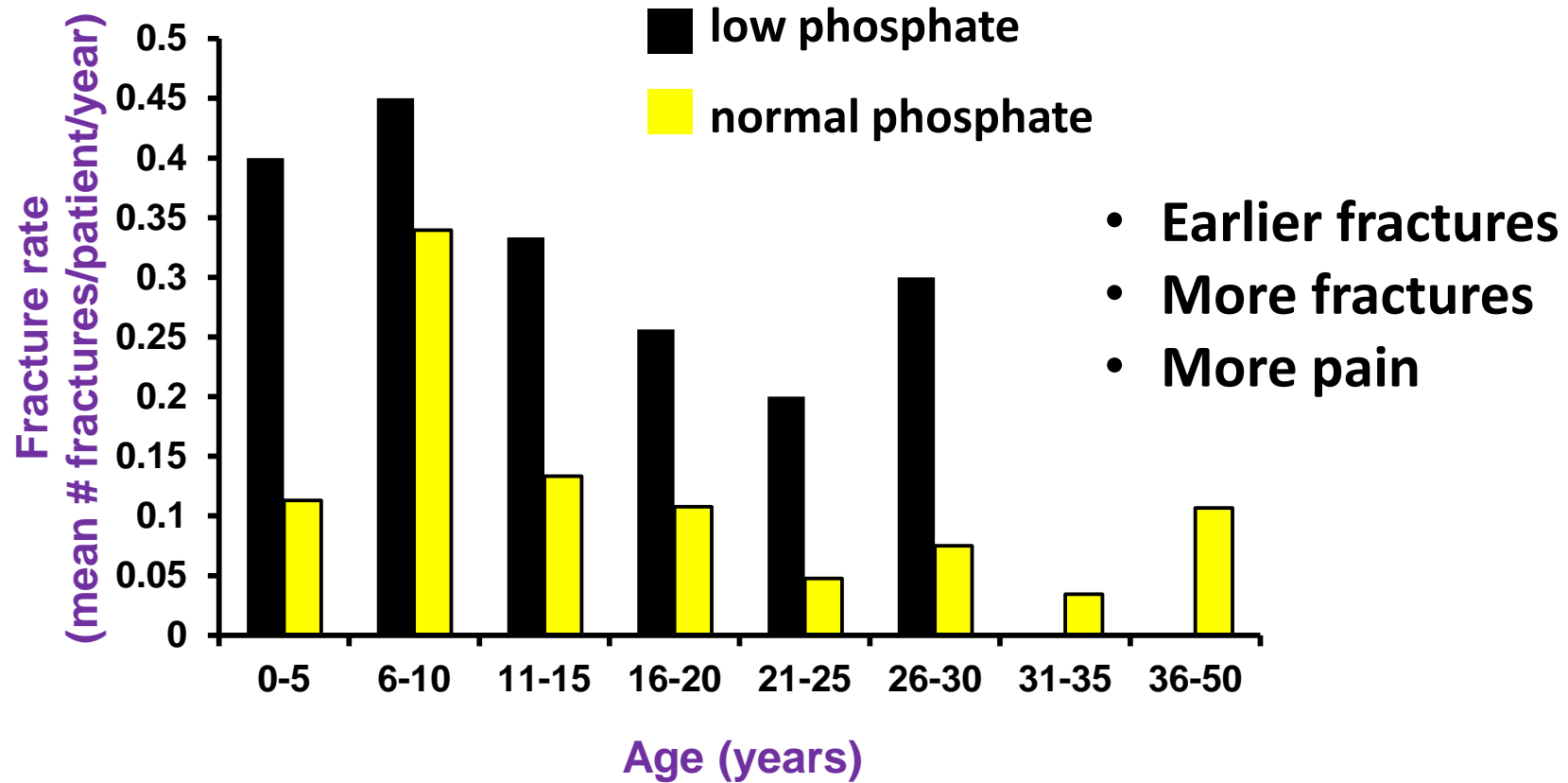


# FD overproduces FGF23

FGF23 made by FD, acts at the kidney to regulate blood phosphate and active vitamin D levels



# What are the effects of too much FGF23 on FD ?



- the more FD, the more FGF23
- probably need  $>1/2$  if the skeleton to be FD to get  $\uparrow$  FGF23

# Treatment of low phosphate

- **Oral phosphate + active vitamin D**
  - 3-5 times per day
  - diarrhea common
  - risk of kidney stones
- **May go get better/go away with time**
- **New drug just approved – may be beneficial**
  - Burosumab – blocks the action of FGF23

# Prevalence of findings in NIH cohort

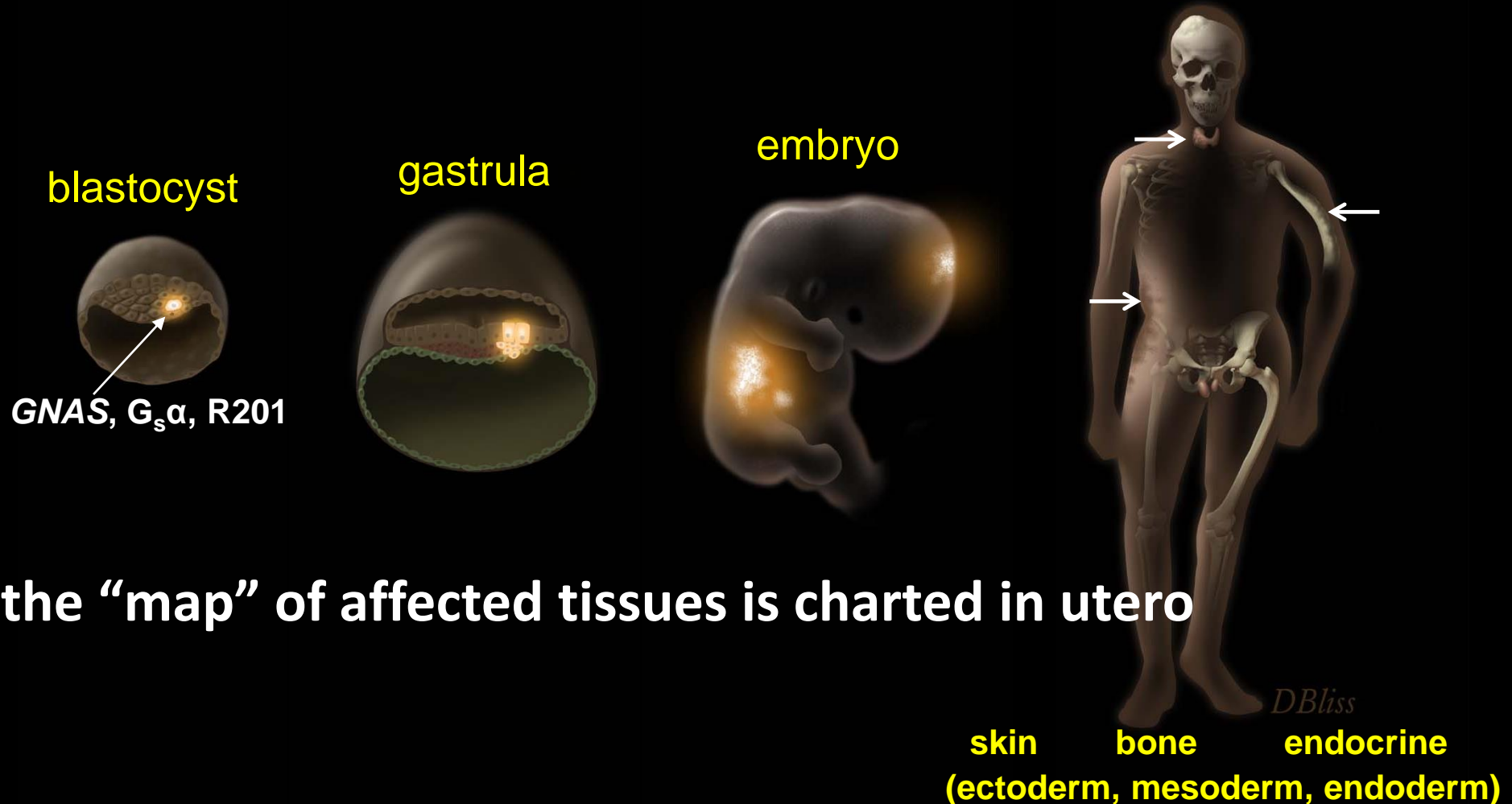
<u>Findings</u>	<u>Prevalence (%)</u>
Fibrous dysplasia	99
Café-au-lait	89
Gonads	
male (U/S or PP)	77
female (PP)	78
Thyroid	69
Phosphate wasting	48
requiring treatment	17
Growth hormone excess	18
Cushing's	7

# Prevalence of findings in NIH cohort

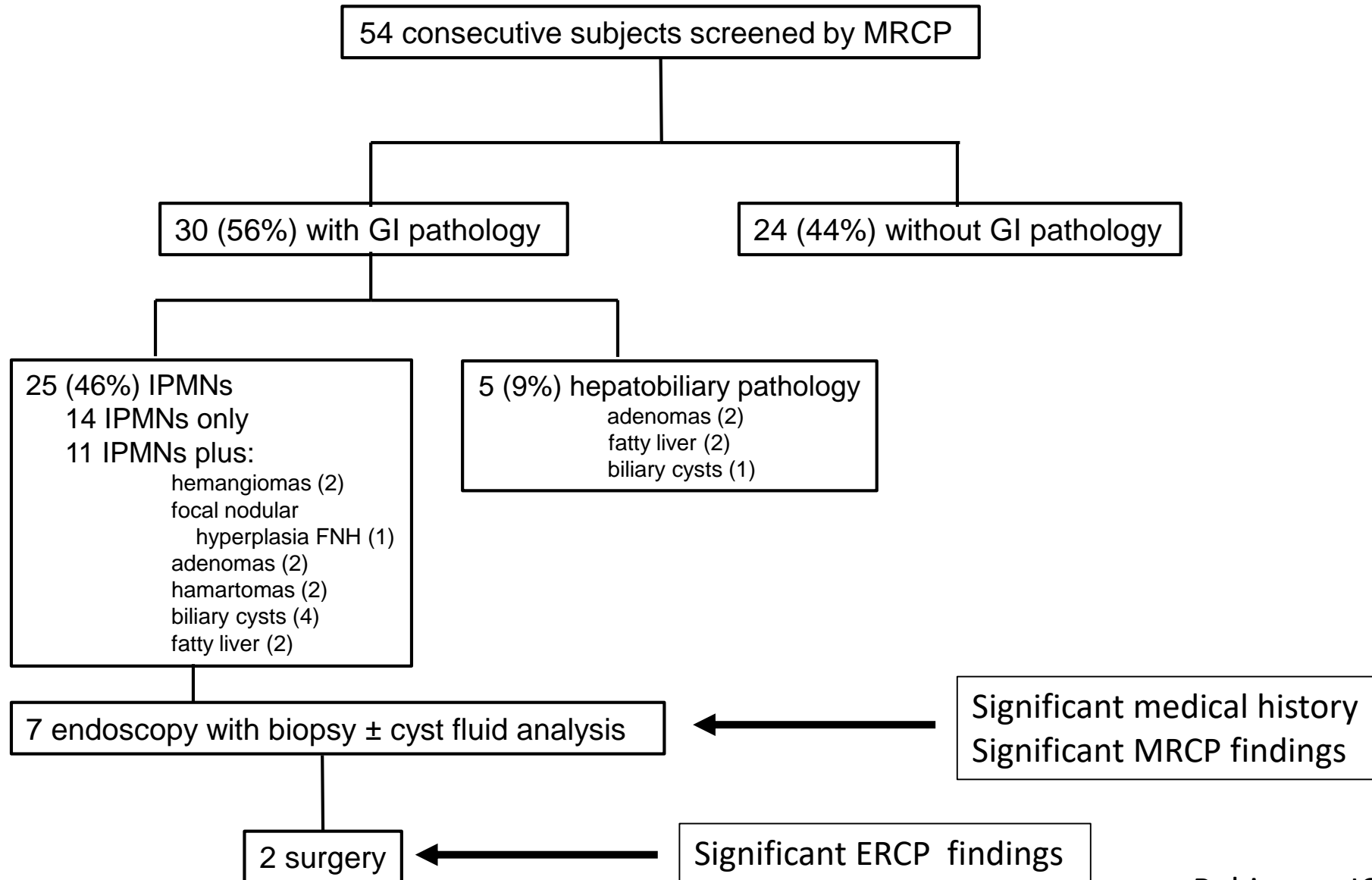
<u>Other Clinical Findings</u>	<u>% Patients</u>
<b>Gastrointestinal</b>	<b>50 (?)</b>
Hepatitis, Reflux, Pancreatitis, Polyps	
<b>Cardiac</b>	<b>6</b>
Tachycardia	<b>4</b>
Aortic root dilatation (GH excess)	<b>2</b>
<b>Cancer</b>	<b>4</b>
Thyroid	<b>2</b>
Breast	<b>2</b>
Bone	<b>1</b>
Testicular	<b>1</b>
<b>Hyperparathyroid (?G<sub>s</sub>-mediated)</b>	<b>1</b>
<b>Neuropsychiatric</b>	<b>20 (?)</b>
<b>Marrow failure</b>	<b>1</b>



# Affected tissues in FD/MAS a somatic, mosaic condition



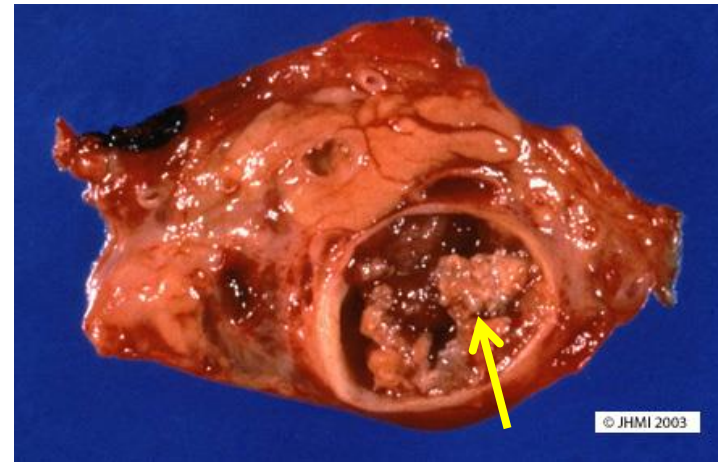
# MAS-Associated GI Pathology in NIH Cohort as of 2018



# Sporadic Intraductal Papillary Mucinous Neoplasms (IPMNs)

- Arise from the main pancreatic duct or its branches
- More common older men
- ↑ Risk of invasive cancer

Cross-section of main pancreatic duct

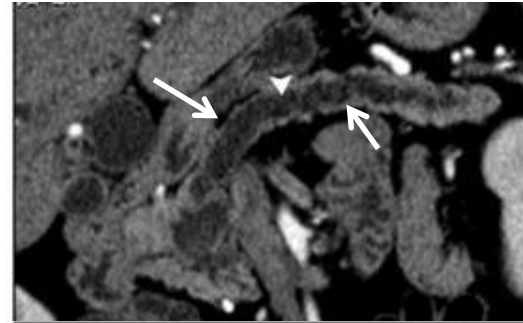
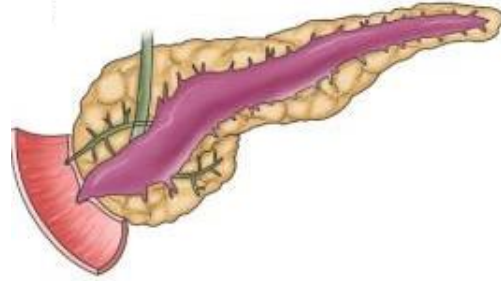


IPMNs

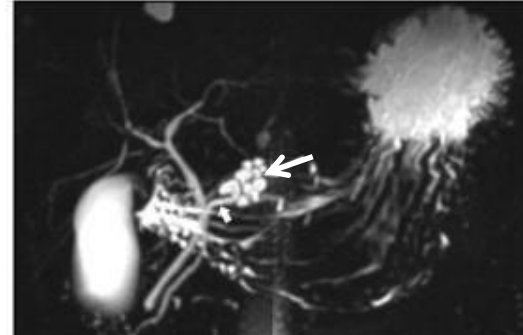
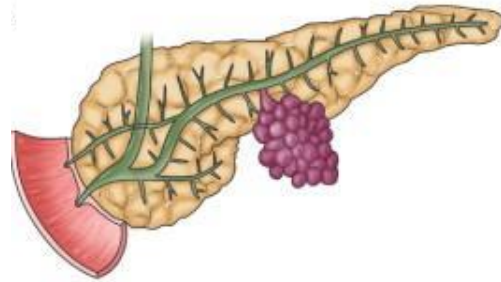
# Types of IPMNs

## IPMN type

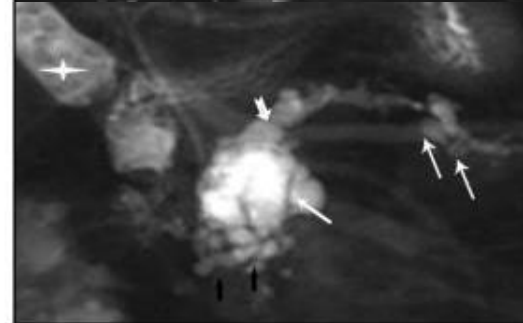
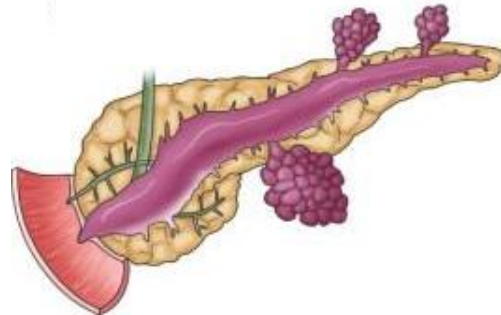
Main duct



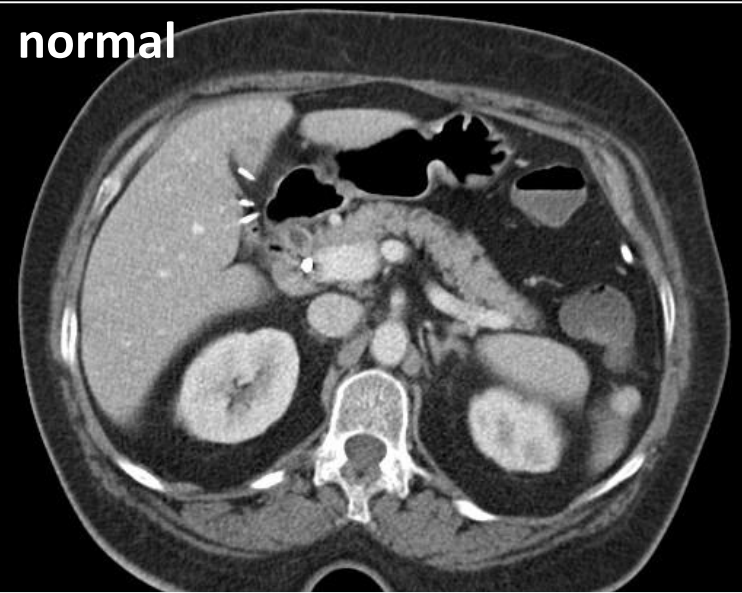
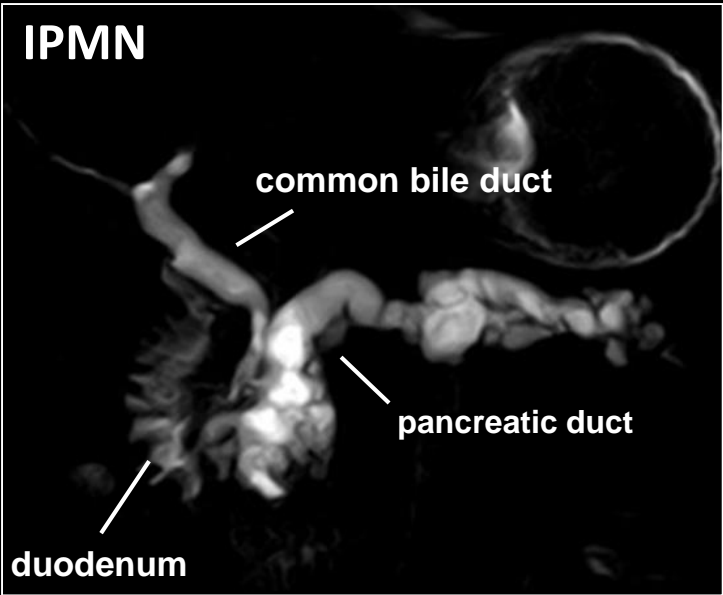
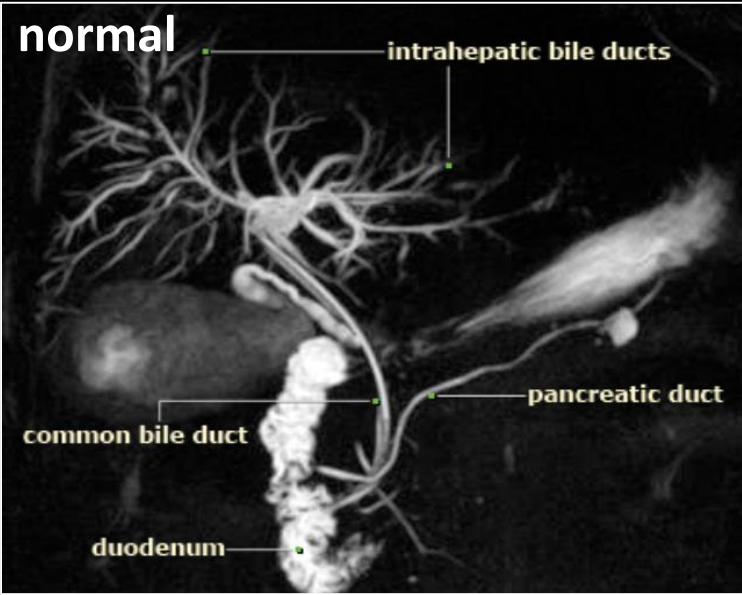
Branch duct



Mixed-type



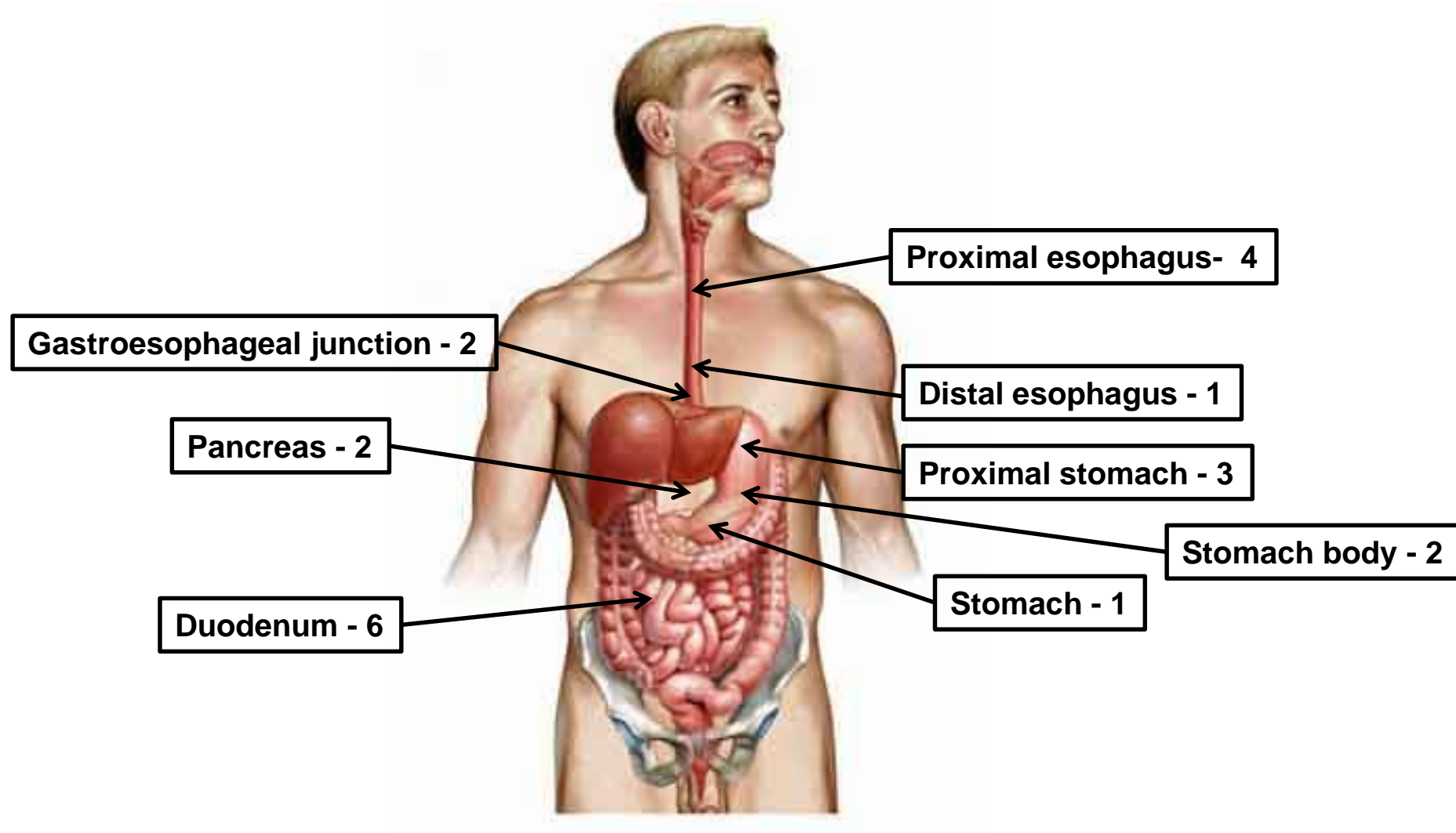
# IPMNs - MRCP



# Recommendations: Pancreas in FD/MAS

- Baseline screening with MRCP
- If negative – you're done
- If abnormal → referral to a center with experience in complicated pancreas disease
- This is an evolving story...

# EGD findings in 7 subjects – GI polyps



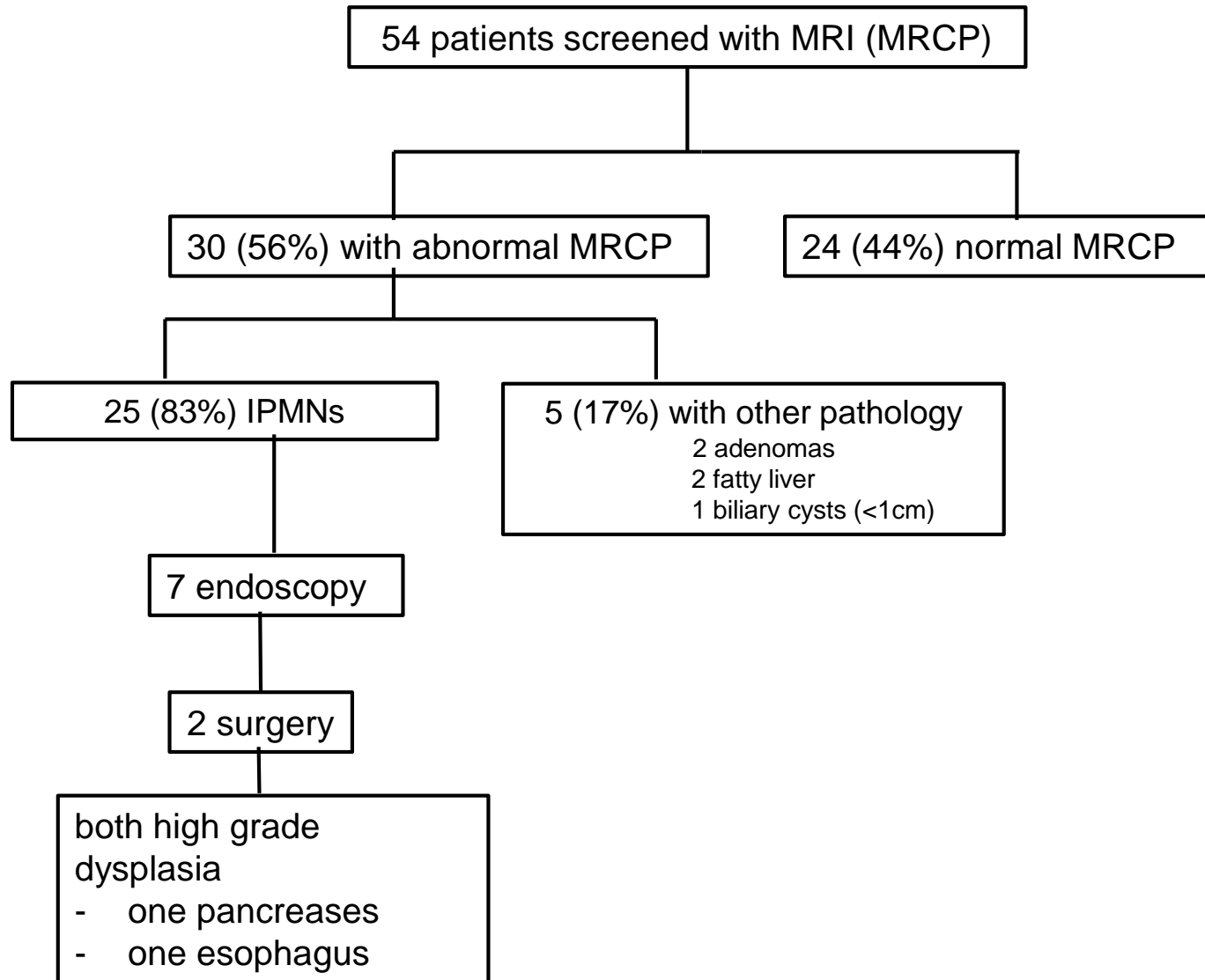


# Conclusions

- **GI manifestations are common in FD/MAS,**
  - **IPMNs**
  - **hepatic adenomas**
  - **risk for pancreatic and hepatic neoplasia**
- **IPMNs occur at a younger age**
- **Appropriate history indicates need for GI screening**
- **Optimal care for GI findings is evolving**



# Pancreatic disease in MAS



# Cancer in MAS

- The gene mutation that causes FD/MAS,  $G\alpha_s$ , is a weak “oncogene” (a gene mutation that promotes tumor growth); the *gsp* oncogene
- It is NOT sufficient to cause cancer
- Cancer only occurs after several to dozens of mutations occur in a cell/tissue

# Cancers that have been seen in association with FD/MAS

- Bone
  - An increase noted following a period when FD was treated with high dose, radiation
  - Very low risk outside of excess radiation
- Thyroid
  - Only 2 cases reported ever
- Testicular
  - Only one case reported
- Pancreas
  - 2 cases reported
- Breast

# Breast Cancer in MAS

- Study of breast cancer in 2 large groups of women with FD/MAS
  - Leiden University Medical Center, Netherlands (134 women)
  - NIH (121 women)
- 15 cases of breast cancer identified
- 3.4-3.9-fold increase compared to the general population

# Breast Cancer in MAS

- Average age 41 years (range 27-54)
- *GNAS* mutation found in only 4/9 cancers
- Risk factors:
  - Precocious puberty
  - FD in the thorax (chest region)

# Breast Cancer in MAS

- Treatment: surgery, chemo, radiation
- 100% survival, 0 metastases
  - average 8.5 years follow-up, range 2-15
- Conclusions:
  - Women with MAS may be at increased risk of breast cancer
  - Compared to the general population, occurred at a younger age, less aggressive, with excellent long-term outcomes
  - Recommend: regular self-exams, and screening mammograms starting at age 40

