

**Examining the WHO and HOW to
investigate for upper GI cancers:
Diagnostic work up for Esophageal,
Gastric and Pancreatic cancer**

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Presenter Disclosure

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Relationships with commercial interests:

– **Investigator: Cook Medical/Endoscopy**

Mitigating Potential Bias

Not applicable

Esophageal cancer:

Increasing squamous cell (less smoking): 3/100,000. NOTE: 3x more common in men, and 6x more common in blacks

Increasing adenocarcinoma (obesity, GERD, other factors?): 3-5/100,000
NOTE: 7-10x more common in men

Gastric cancer: stable or decreasing rates in North America. Increasing and high rates in Asia. Canada: 4-9/100,000/year, less in women (down to 1/100,000 in the 1970's/80's)

Better treatment of H.pylori, and decreased reliance on salt preservation of food? Better hygiene? Refrigeration?

Pancreatic cancer: Slow steady increase in rates over time (aging population) 10/100,000/year or 4-5000 new cases in Canada/year

These cancers are relatively rare, but have very high mortality rates, and are

Esophageal Cancer


Who should we investigate for esophageal cancer?

~~Abdominal pain?~~


~~GERD? Non responsive GERD, long standing GERD, atypical GERD?~~

~~Family history of cancers?~~

~~Alcohol and smoking use/abusers?~~

Dysphagia? 

Unexplained Weight loss? 

Iron deficiency anemia? 

The GERD question

Hypothesis: Longstanding or severe GERD -> Barrett's esophagus -> Gastric Barrett's -> Esophageal adenocarcinoma

Guidelines recommended screening pts. with GERD >10years, for Barrett's

study has ever shown this is effective at reducing cancer or mortality

is expensive, it is stressful for patients and all it does is increase the # of patients with Barrett's that need further testing. With NO benefit.

Guidelines from AGA, ACG, and European GI consortium all explicitly recommend against the routine screening for Barrett's.

Instead patients with a combo of GERD >10 years plus other risk factors (smoking, severe obesity, ETOH abuse, family history, etc) or a concerning symptom (dysphagia, weight loss, anemia etc) should be screened.

Who should we screen in Barrett's esophagus

	Barrett prevalence	Cancer incidence/100,000	Cancer distribution Adeno-Carcinoma	Annual cancer risk with this type	NNT for screen in Barre
10% (n)	1%	4.6	56%	0.32%	316
20% (n)	5%	1.9	24%	0.04%	2421
30% (n)	15%	1.7	20%	0.01%	9008

with Barrett's?

Currently, guidelines in America: short segment Barrett's (<3cm) is recommended for a gastroscopy every 3-5 years (if risk factors?), a long segment every 2 years (or longer if stable for 2 scopes)

Patients with documented LGD: repeat within 1 year and or refer for ablation strategies

Patients with HGD: need either ablation with RFA, endoscopic resection of HGD areas OR surgery.

The main problem is that AGAIN, no study in the Barrett's surveillance population has shown mortality benefit, survival benefit or cost benefit

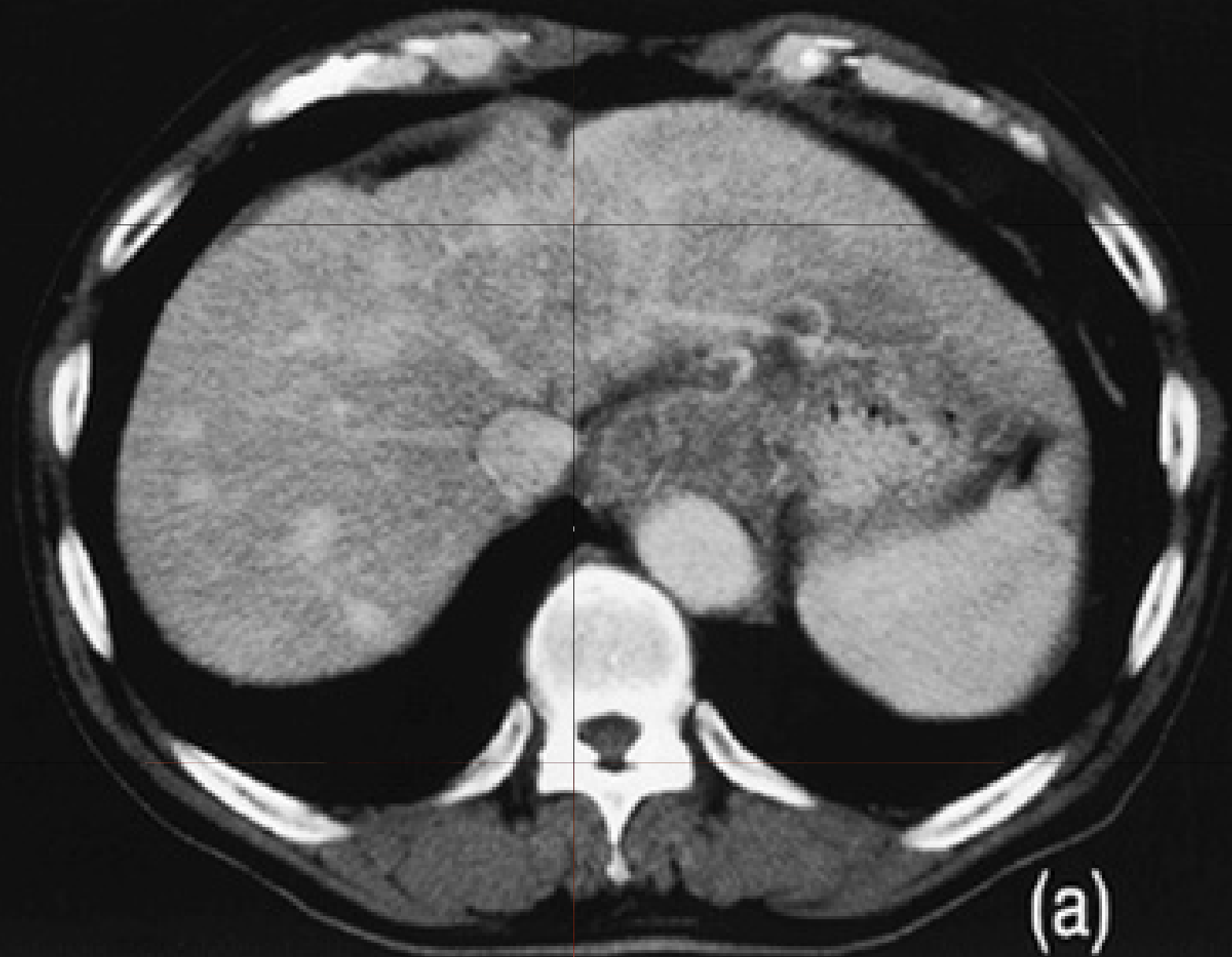
But new data is coming, this year that may show some benefit in targeted screening.

Who should we investigate for esophageal cancer?

Patients with new or progressive dysphagia.

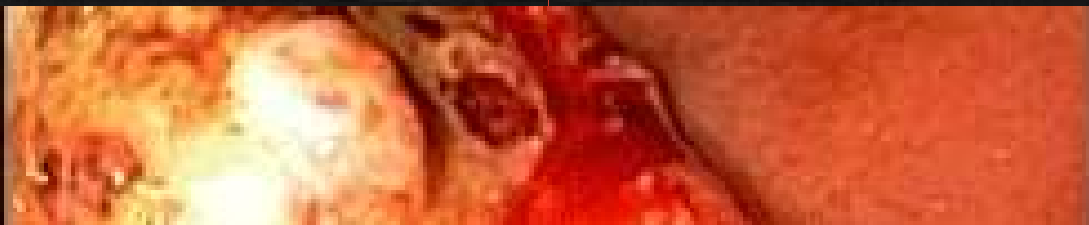
Patients with known Barrett's esophagus AND risk factors (smoking, ETOH use, family history, prior toxic ingestion etc), or Barrett's with dysplasia.

Patients with unexplained weight loss, anorexia and anemia (as part of pan endoscopy).



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Biopsies confirm either SSCa or AdenoCa:

usually takes 4-7 days even if sent rush.

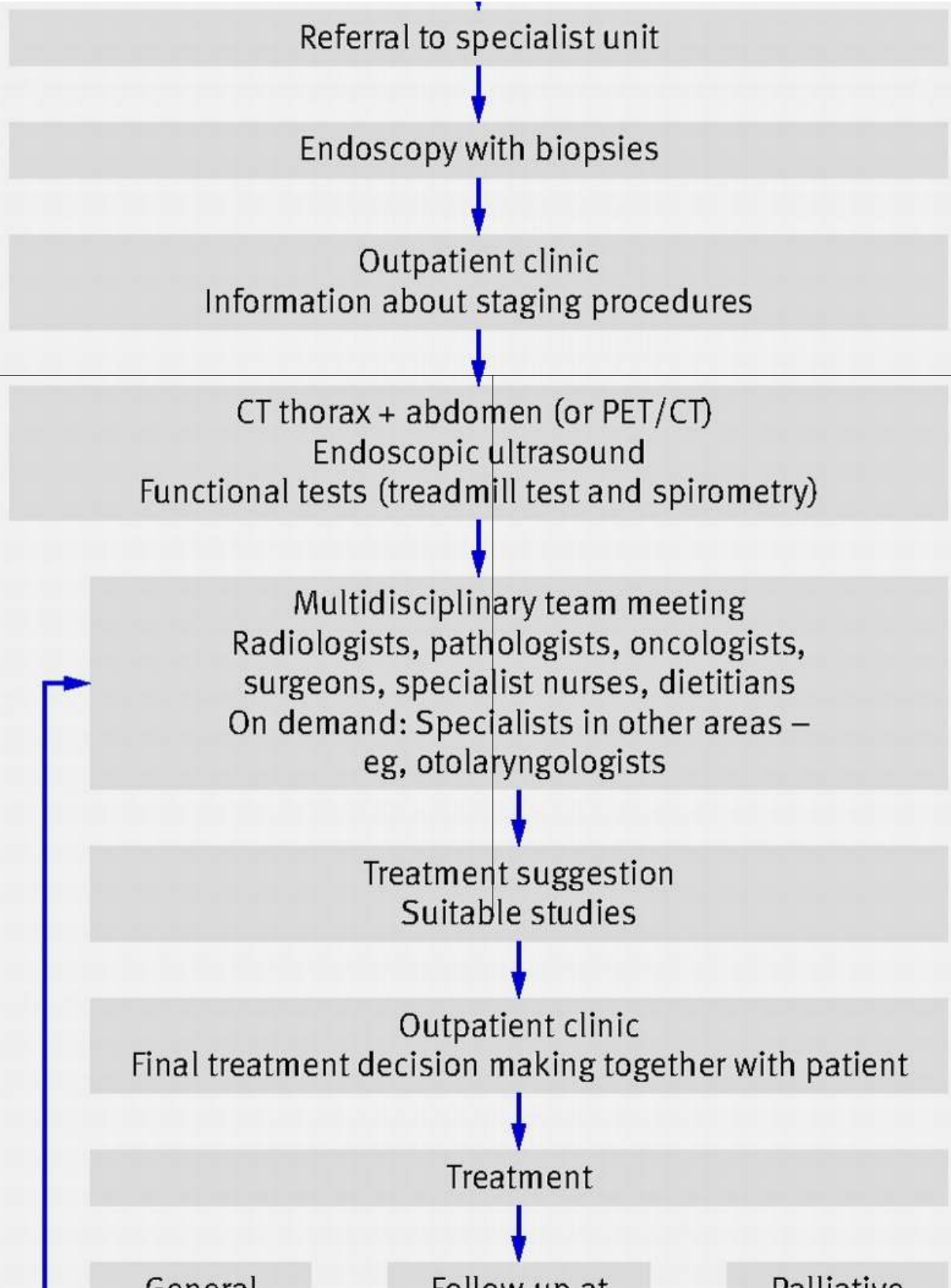
CT scan of the chest/abdomen for staging is standard of care:

Assess local and distant nodes, and metastasis.

NOTE: Endoscopic ultrasound has good evidence for staging local lymph nodes (95% accuracy vs. 45% CT for celiac nodes), and is far superior for determining T2-T4 lesions, except post radiation therapy.

PET/CT often required, to differentiate malignant liver cysts and/or lung nodules. Very high sensitivity and accuracy for distant mets.

PET activity ALSO can be used to predict response to chemo and radiation AND has been shown to predict overall survival.



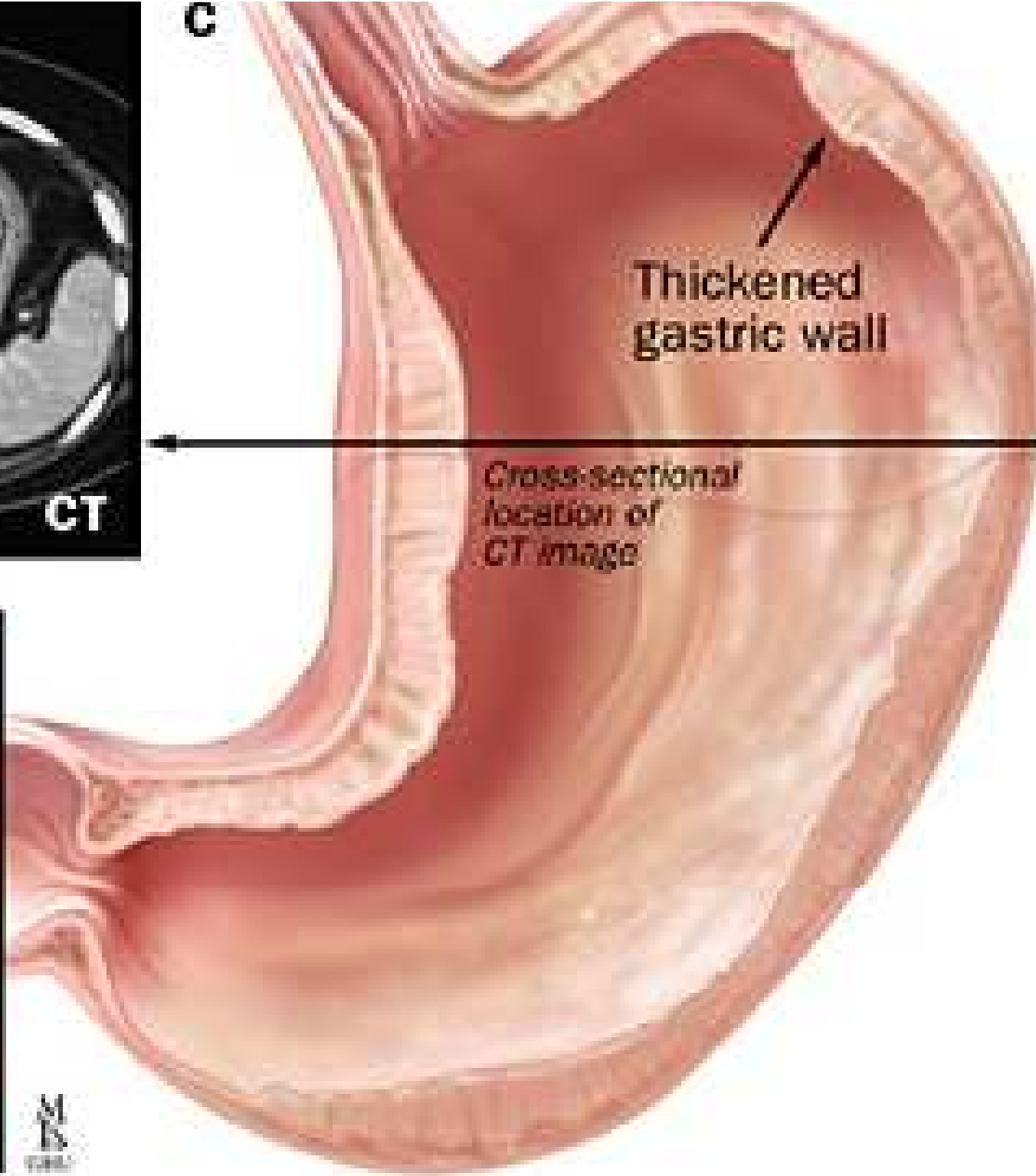
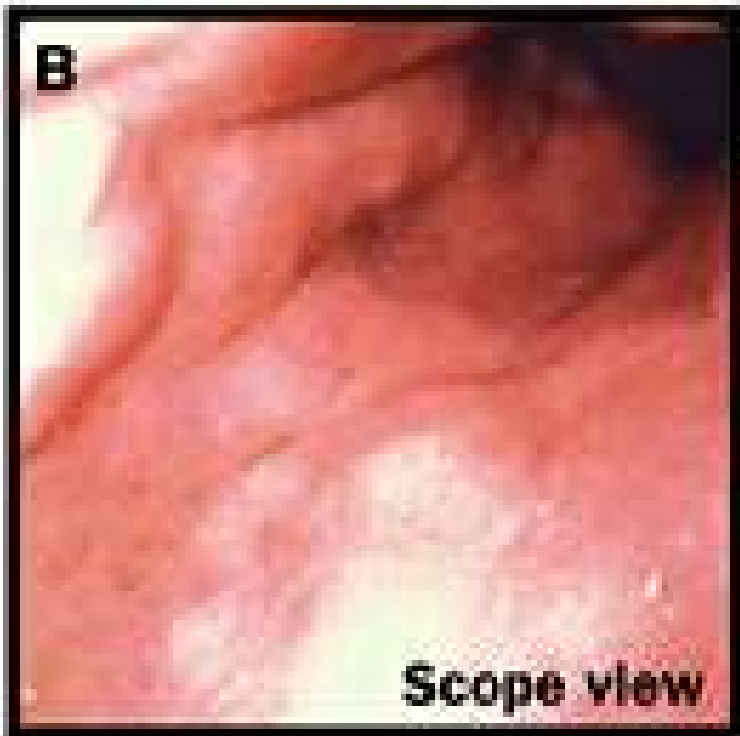
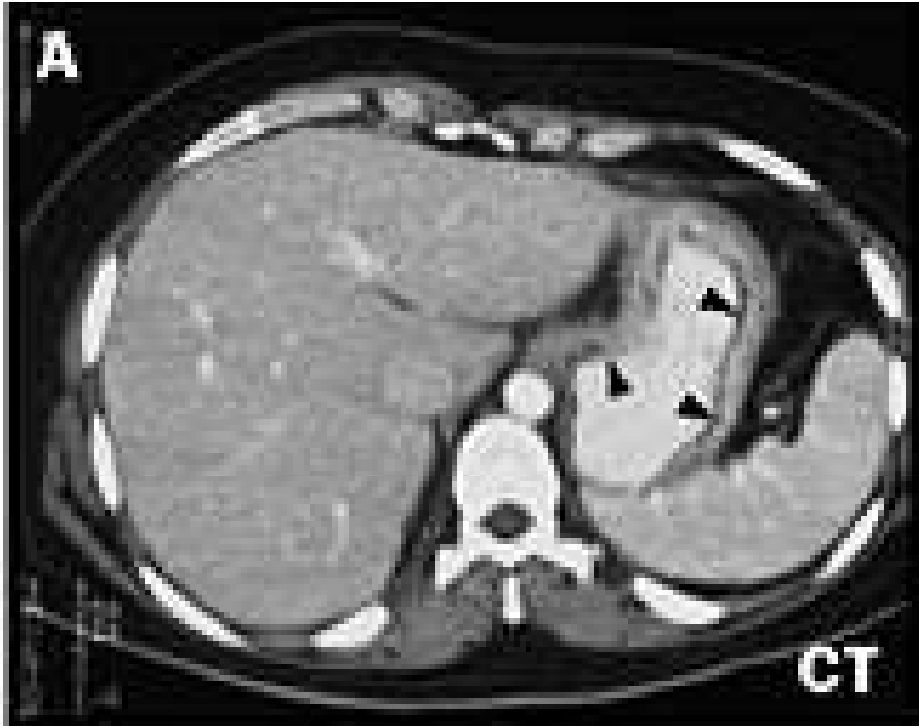
Gastric Cancer

Changing demographics all over the world.

Significant decrease in the last 60 years, due to less H.pylori, better food preservation, and less smoking?

Paradoxical increase in younger patients in the last 15 years?





What symptoms/signs predict gastric cancer?

Abdominal pain?

Early satiety?

Weight loss?

Vomiting?

Dysphagia?

Abdominal mass?

Iron def. anemia?

Lymph node abnormalities?

Gastric ulcers?

Gastric Cancer

ptoms experienced by patients newly diagnosed with Gastric CA
type:

dominal pain: 30-67%

arly satiety: 45%

eight loss: 60-75%

miting: 7-17%

spagia: 5-25%

n def. anemia: 20-39%

stic ulcers: <15%

dominal mass: 7% (always advanced disease)

mph node abnormalities: <5% (always advanced disease)

st pretest probability: Anemia + weight loss + early satiety: PPV =

Screening

0% of cases, are diagnosed with advanced disease, and are incurable

Screening is beneficial in HIGH risk populations.

Data from Japan/Korea/China, shows decrease in advanced cancer mortality by 30% with biannual gastroscopy

Costs of \$28,000/life year saved

Screening is not beneficial and is extremely costly in low risk groups (e.g. North Americans)

Costs of >\$240,000/life year saved (best case scenario from data!)

Targeted approach to screen at risk individuals and those with concerning symptoms is recommended in North America

Helicobacter pylori (HP) infection	Odds ratio (OR): 2.3	High risk area - mass screening Low risk area - mass screening
Atrophic gastritis	1. Hazard ratio 7.13 (compared with no HP)	See above
Intestinal metaplasia	2. Hazard ratio 14.5	HP eradication
HP and extensive intestinal metaplasia	3. Hazard ratio 61.9	HP eradication
Colorectal cancer	Standardized incidence ratio: 5	Screening by upper endoscopy (UE)
Gastric cancer	15-24 years, RR = 9.4	Screening by UE recommended
	25-46 years, RR = 55.6	
Family history	Not available	Surveillance post polypectomy
Adenomatous polyposis	Not available	Screening by UE recommended
Adenomatous polyposis colorectal cancer	Not available	Screening by UE recommended
Family history of gastric cancer	OR: 2.5-5.1	HP eradication +/- UE screening

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OR 1.22

OR 1.55

Group A: OR 1.2

Alcohol intake: OR 1.15

Smoking intake: OR 1.4

Other more rare signs of Gastric Cancer

- a) DVT/thrombophlebitis (Trousseau sign)
- b) Eruptive seborrheic keratosis on the trunk and back (Sign of Leser-Trélat)
- c) Membranous nephropathy

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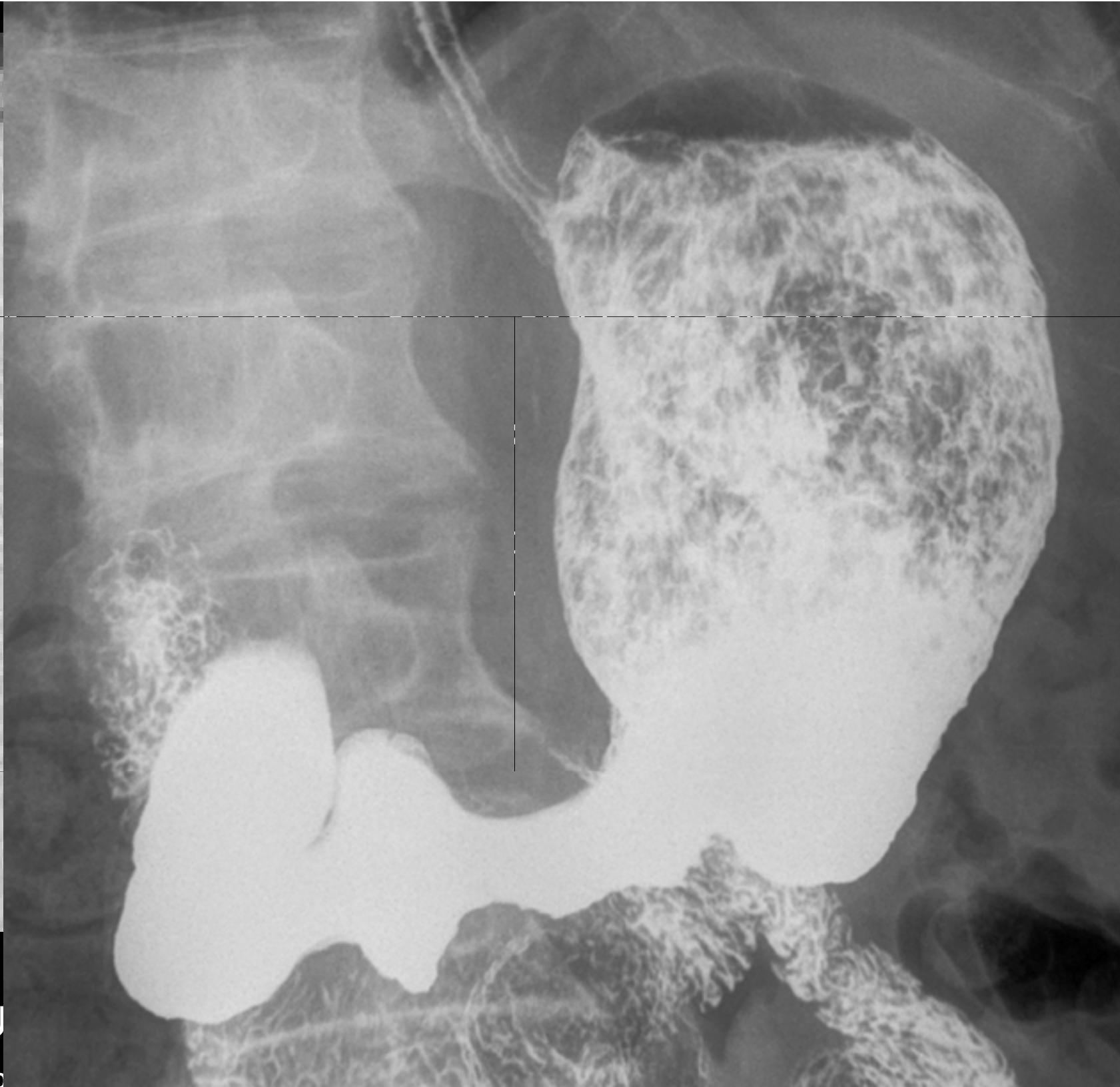
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Work up for established gastric cancer

CT scan (chest/abd/pelvis) with IV contrast: Looks for local, and widespread metastasis.

EUS: most effective staging for depth of invasion, and can sample possible nodal spread with FNA.

T stage Accuracy compared to CT scanning 95% vs. 73% $p < 0.0001$.

N stage accuracy compared to CT: 80% vs. 65% $p < 0.05$

PET/CT: Most sensitive for distant mets, in one study post EUS and CT, PET/CT upstaged disease state in 10% of cases... used very frequently to complete the staging, pre chemotherapy and surgery.

Staging laparoscopy: still the gold standard for N staging...

Pancreatic cancer

pancreatic cancer: signs and symptoms

Symptoms	%
Weight loss	85
Abdominal Pain	79
Anorexia	76
Cholestasis (dark urine/pale stool)	50-59
Back pain	49
Diarrhea	44
Vomiting	33
Steatorrhea	25
Thrombophlebitis	3

Signs	%
Jaundice	55
Hepatomegally	39
RUQ mass	15
malnutrition	13
Courvosier' s sign	13
Ascites	5
Lymph nodes	5

no individual symptom or sign if can effectively screen for Panc Ca.

incidence of jaundice ≥ 50 yo is 20-33%

Other symptoms/signs

Idiopathic pancreatitis in those > 50 yo: follow up CT is warranted. New pancreatic lesions found in ~10-12% of individuals.

New onset diabetes >50 years old: Association has been seen in several cohort studies.

Not cost effective to screen all diabetics, but if they are losing weight, have no family history, or have symptoms of steatorrhea -> consider a CT scan.

Initial testing for pancreatic Ca

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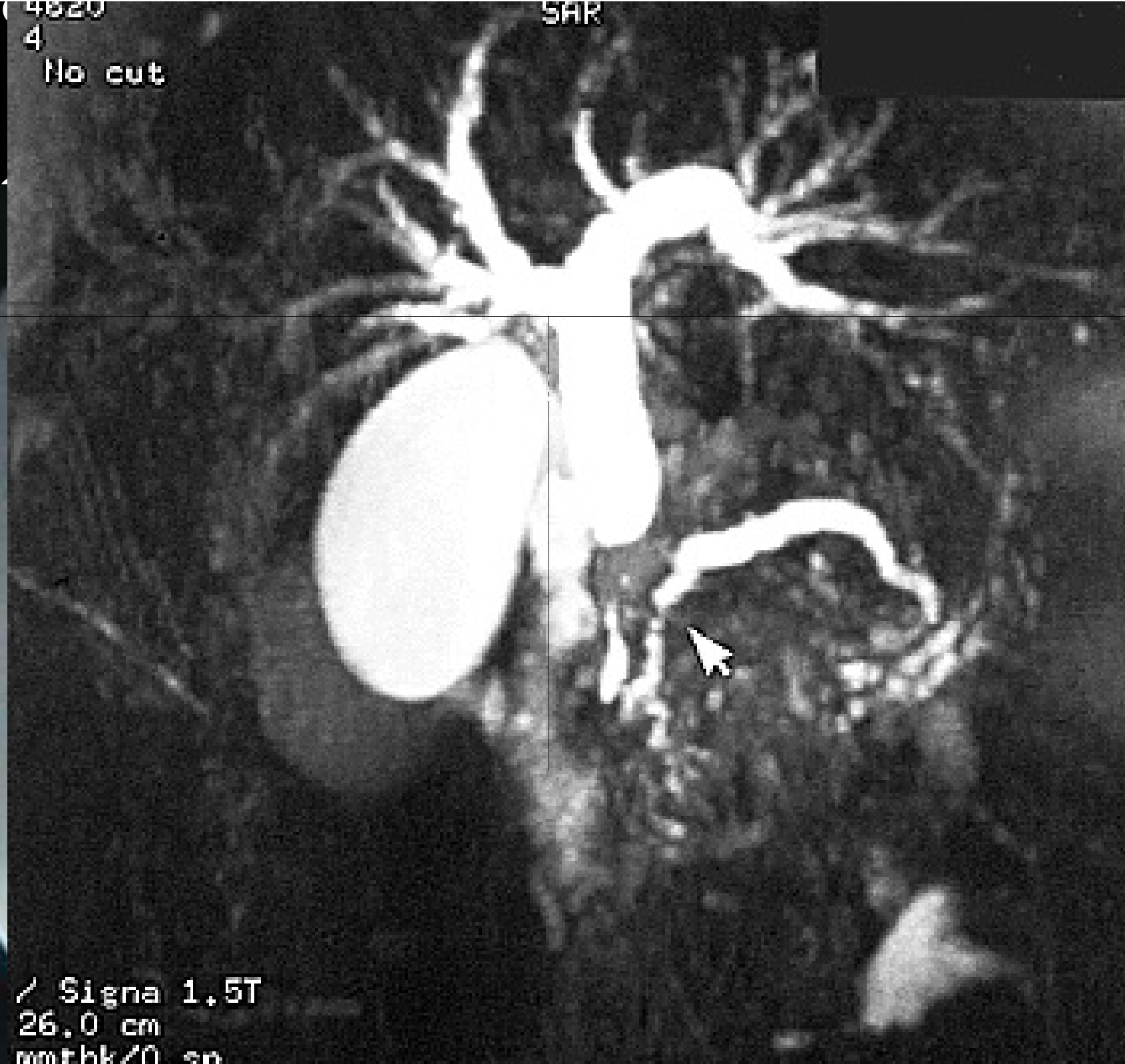
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SMA,

pancreas protocol CT is 100% for tumors >2cm

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Tumor markers

optimal serologic marker doesn't exist.

9-9 is the best option, but still has limited sensitivity (70-90%) and specificity (68-80%)

limited by needing + Lewis blood group antigen (90 of the population)

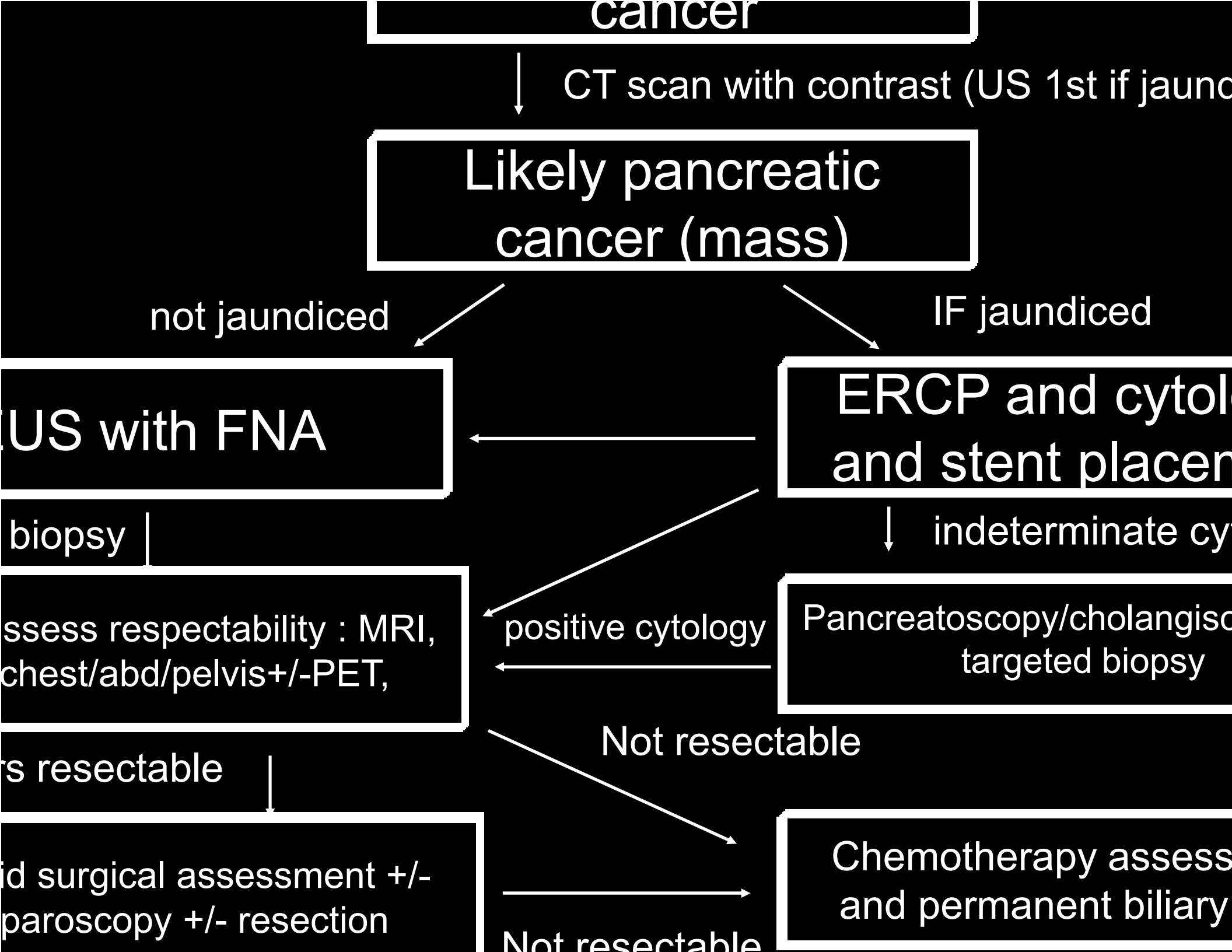
limited by tumor size (levels increase with tumor size)

also positive in any kind of biliary obstruction, or biliary infection.

The magnitude of elevation is associated with long term survival, operability, and respectability, and CAN be followed for signs of recurrence post-surgery... so useful to have a baseline value.

work up for established pancreatic cancer

- 1) CT chest, abdomen/pelvis: for staging
- 2) MRI liver: to accurately assess for mets and help with respectability staging
- 3) PET/CT: useful in some cases, but not routinely ordered
- 4) Baseline CA-19-9.



cancer

CT scan with contrast (US 1st if jaundiced)

Likely pancreatic cancer (mass)

not jaundiced

IF jaundiced

US with FNA

ERCP and cytology and stent placement

biopsy

indeterminate cytology

Assess resectability: MRI, chest/abd/pelvis +/- PET,

positive cytology

Pancreatoscopy/cholangioscopy targeted biopsy

resectable

Not resectable

Obtain surgical assessment +/- laparoscopy +/- resection

Chemotherapy assessment and permanent biliary

Not resectable

Esophageal cancer: Investigate patients with new/progressive dysphagia, longstanding GERD with risk factors (smoking, ETOH, family history, Barrett's esophagus). Endoscopy is the test of choice. No serologic markers.

Gastric cancer: Difficult disease to screen for in North America. Patients with early satiety, anemia and weight loss OR one symptom AND a family history of gastric CA OR H.pylori infection.

Endoscopy is the test of choice. No reliable tumor markers. Barium swallow can be supportive but not definitive.

Colorectal cancer: Investigate for painless jaundice, or weight loss + hematochezia or melena. Note idiopathic pancreatitis in >50yo and late onset diabetes.

Endoscopy is best test US, but CT of the pancreas is superior for diagnosis and staging. EUS is best for diagnosis and biopsy.

ERCP can biopsy but is best for palliation of obstructive symptoms. Serologic markers with CA19.9 +/- CEA can be supportive.

