

Pancreatic Carcinoma

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Types of Pancreatic Neoplasms

- Broadly speaking, there are three basic types:
- **Ductal adenocarcinoma** >90% of pancreatic cancers with a 4% 5-year survival (worst of any cancer)
- Neuroendocrine tumors aka islet-cell tumors, rare
- Cystic neoplasms account for <1% of pancreatic cancers

Overview

- Carcinoma of the pancreas 4th most common cause of cancer related deaths in US (5th in women)
- Incidence of tripled in last 50 years in US (2005)



Epidemiology

- Increasing incidence over the past few decades in the US
- 4th leading cause of cancer death in US
- Estimated new cases and deaths in 2008:
 - Cases 37,680
- Deaths 34,290 (2008)
- 28 000 new cases per year of whom only 1000 expected to survive 5 years after diagnosis



Pathogenesis & Genetics

- Little is known about causes
- Greatest link is with smoking
- Other factors implicated:
 - Chronic alcohol use
 - High protein diet
 - High fat diet
- Chronic pancreatitis – greater frequency in pts with chronic pancreatitis
- Diabetes mellitus – but DM may develop as a consequence of chronic pancreatitis

Pathogenesis & Genetics

- Familial clustering of pancreatic cancer have been reported but no genetic abnormality has been described
- A rare form of pancreatitis – **familial relapsing pancreatitis** is significantly associated with pancreatic cancer
- Point mutations at codon 12 of K-ras found in over 90% of pancreatic cancers
 - Maybe an early event in pathogenesis since this mutation is found in chronic pancreatitis
- 60-80% of patients with pancreatic carcinoma exhibit mutations in p53

Risk Factors

- Smoking
- Advanced age (>50)
- Male sex (M:F 1.3:1)
- Chronic pancreatitis
- Diabetes mellitus
- ?Obesity (BMI>30 compared w/ <23)
 - total physical activity was **inversely** associated with risk among individuals with a BMI of at least 25 kg/m²



Risk Factors

Familial Syndromes associated w/ increased risk:

- familial atypical multiple-mole melanoma
- familial breast cancer (BRCA-2)
- Peutz-Jeghers syndrome: multiple hamartomatous polyps in GIT
- hereditary non-polyposis colorectal cancer
- hereditary chronic pancreatitis (familial relapsing pancreatitis)
 - mutation in cationic trypsinogen gene & is transmitted as autosomal dominant with high penetrance.
 - Acute attacks of abdominal pain early in life, often progresses to chronic pancreatitis.
 - Cumulative increase in risk of pancreatic ca in affected family members



Morphology

- Site: head of the pancreas common site (60%).
Sometimes originating from body (15%) or tail (5%)
- Entire gland involvement in 20% of cases
- Carcinoma involving tail can destroy islets cells can cause DM



Morphology

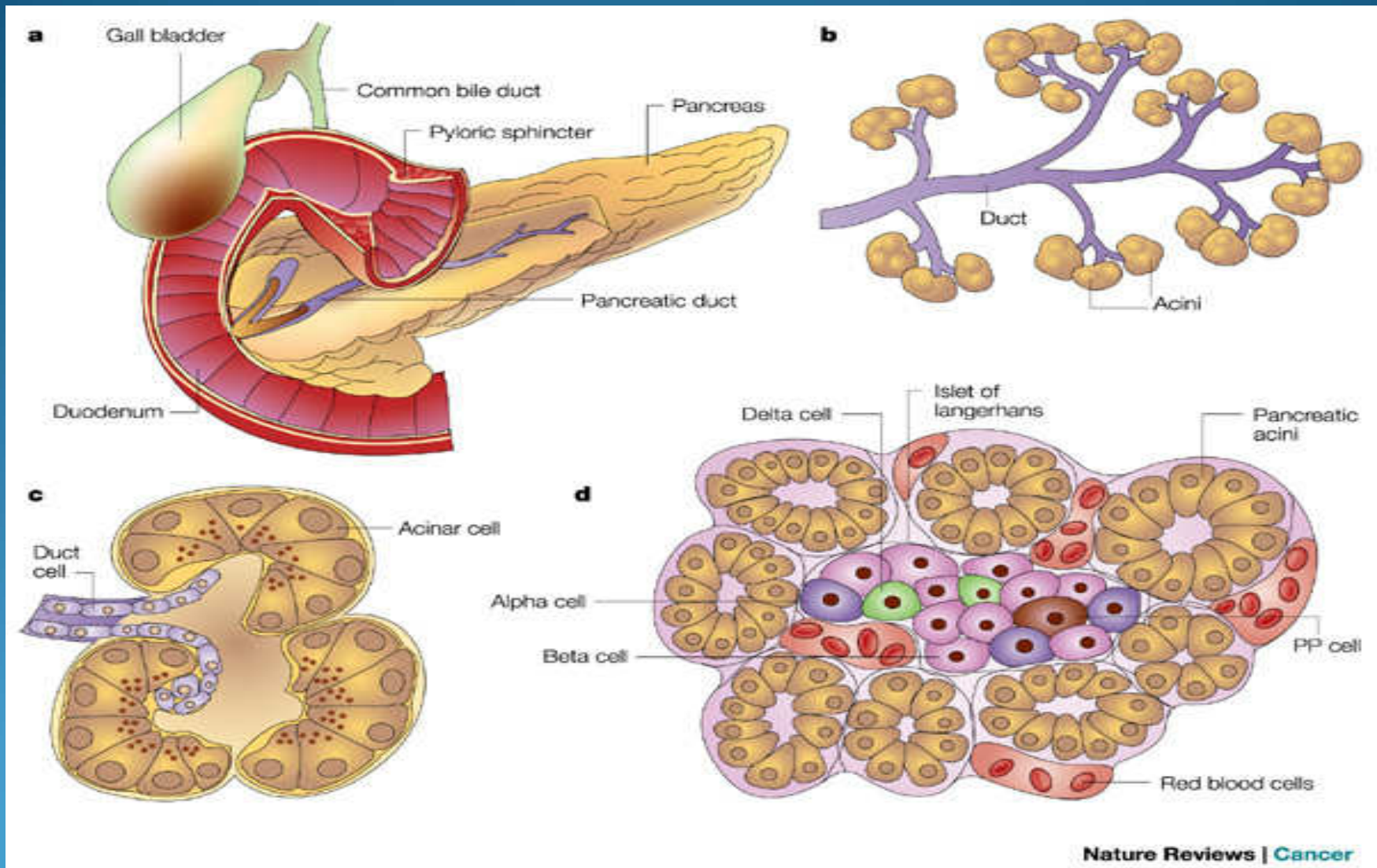
- Virtually all are adenocarcinoma and originate from ductal epithelium
- Some may secrete mucin and have abundant stroma
- These appear gritty grey-white hard masses.
- Early stage the tumour spreads locally and infiltrates adjacent structures
- With head of pancreas involvement of ampullary region is invaded and blocks outflow of bile resulting in obstructive jaundice
 - Marked distension of biliary tree occur on 50% of cases



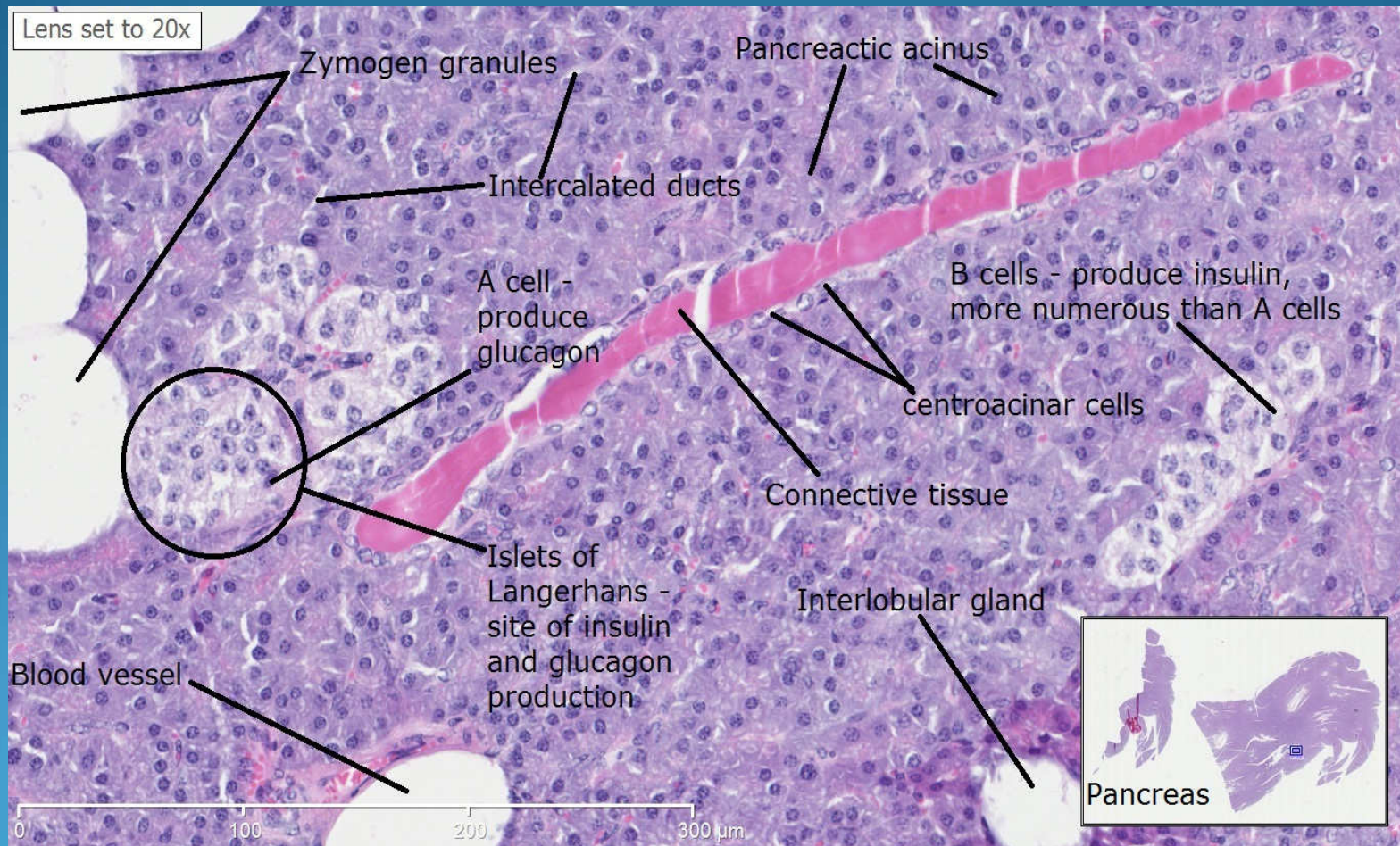
Morphology

- In marked contrast carcinoma from body or tail is clinically silent and may present very late with distant metastasis
- Ulceration of tumour into duodenal mucosa may occur

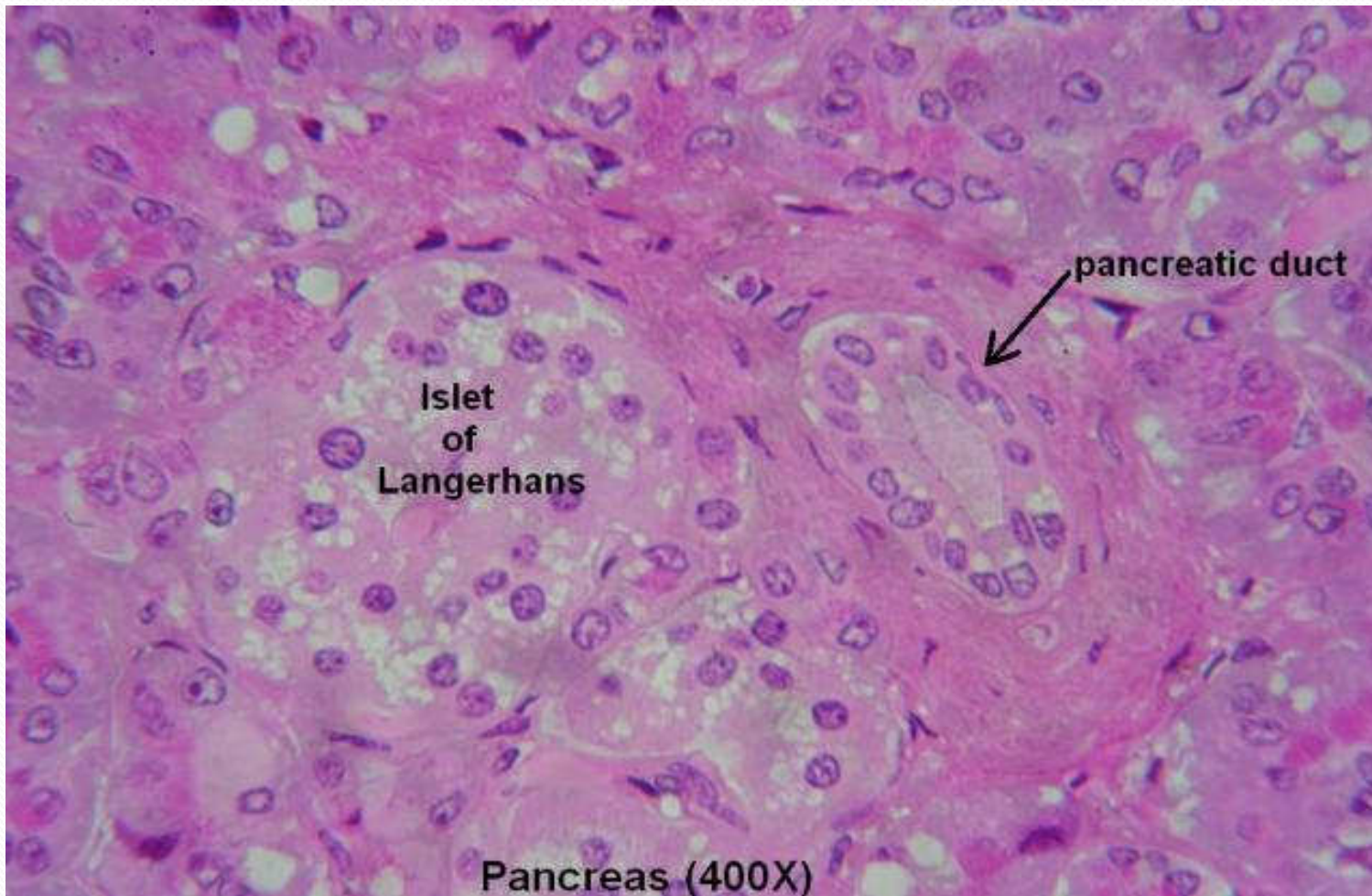
Histology



Normal histology



Normal histology – High Power





Histopathology

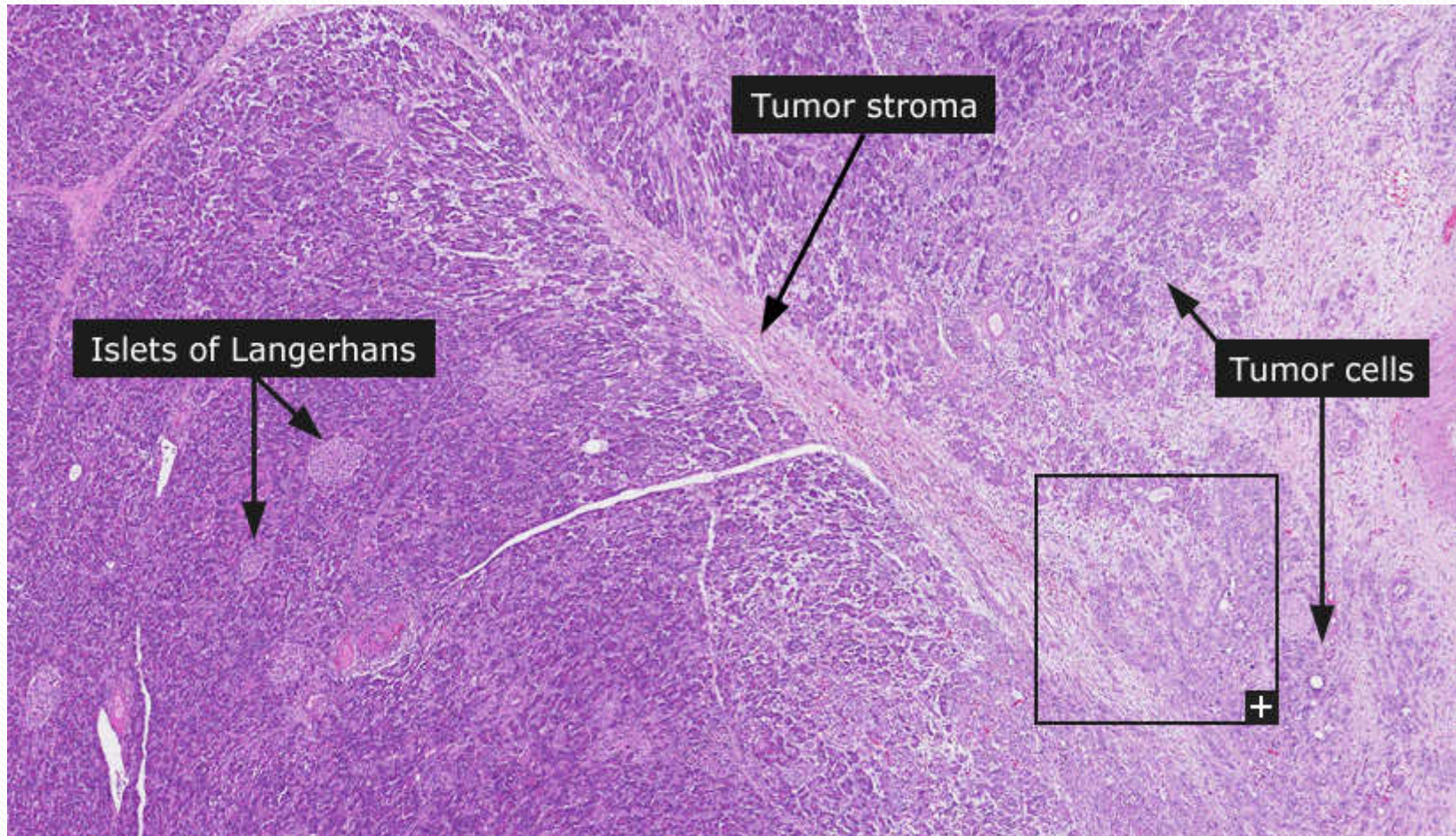
- No difference microscopically between carcinoma of the head, body or tail
- Moderately – poorly differentiated adenocarcinoma forming tubular structures or cell clusters
- Exhibit an aggressive deeply infiltrative growth pattern
- Dense stromal fibrosis accompanies tumour invasion
- Tendency for perineural invasion within organ & beyond
- Malignant glands atypical, irregular, small & bizarre and lined by anaplastic cuboidal to columnar epithelial cells



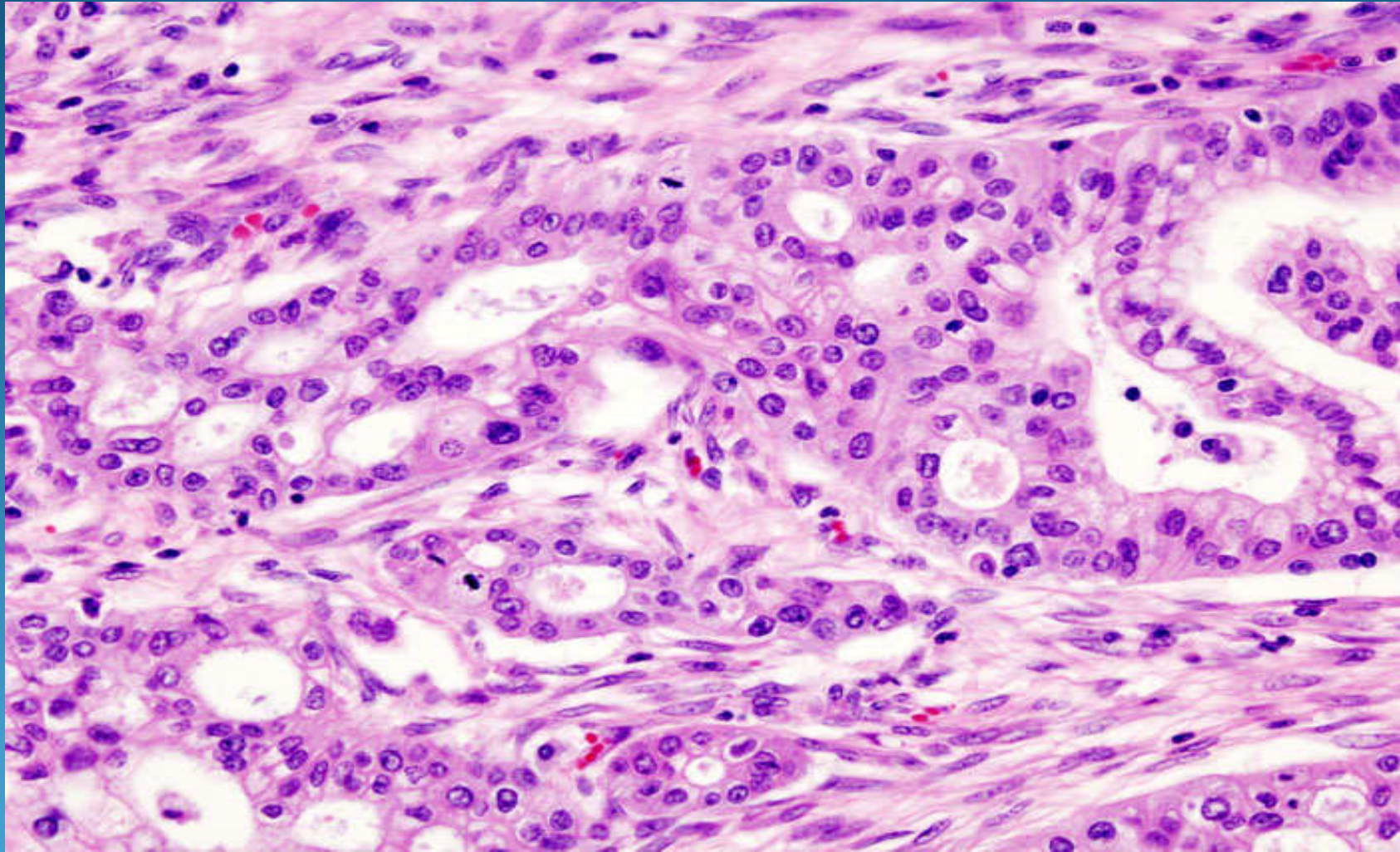
Histopathology

- Well differentiated tumor does occur
- Dysplasia and intraductal tumour growth in keeping with ductal origin of these tumours
- 10% show adenosquamous pattern or extreme dysplasia with giant cell formation or a sarcomatoid histologic appearance
- Rarely arise from acinar cells:
 - acinar cell carcinoma which are distinguished by the plump, polygonal eosinophilic appearance of tumour cells

Adenocarcinoma – low power



Adenocarcinoma – High Power



Adenosquamous Pattern

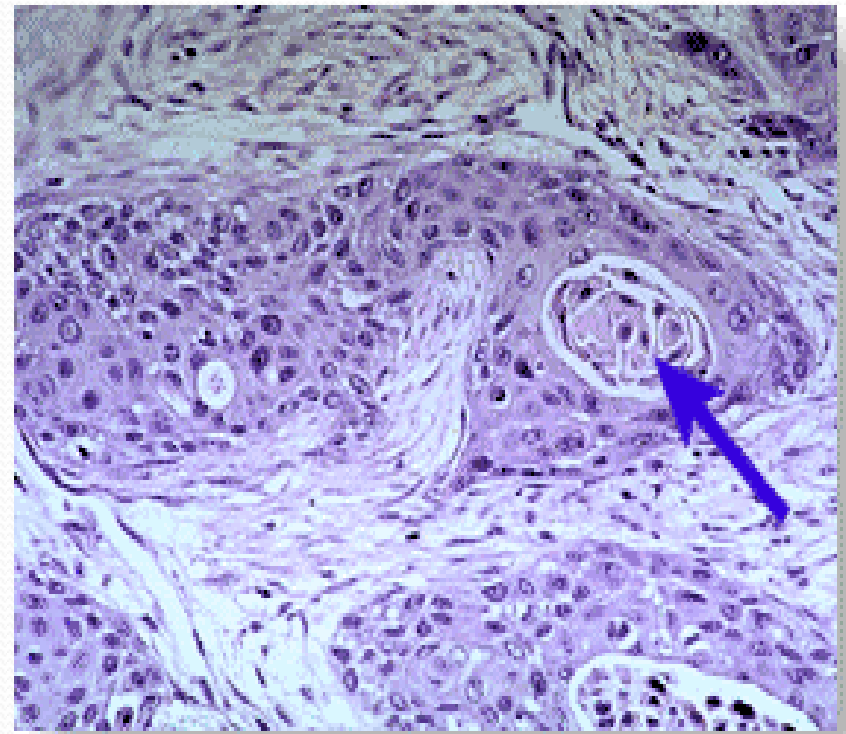
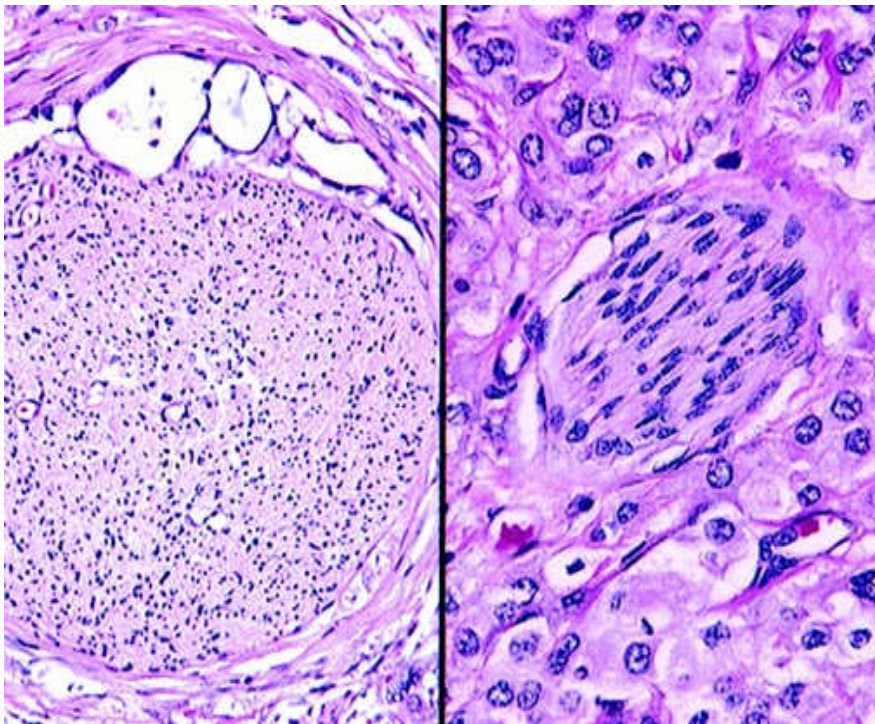
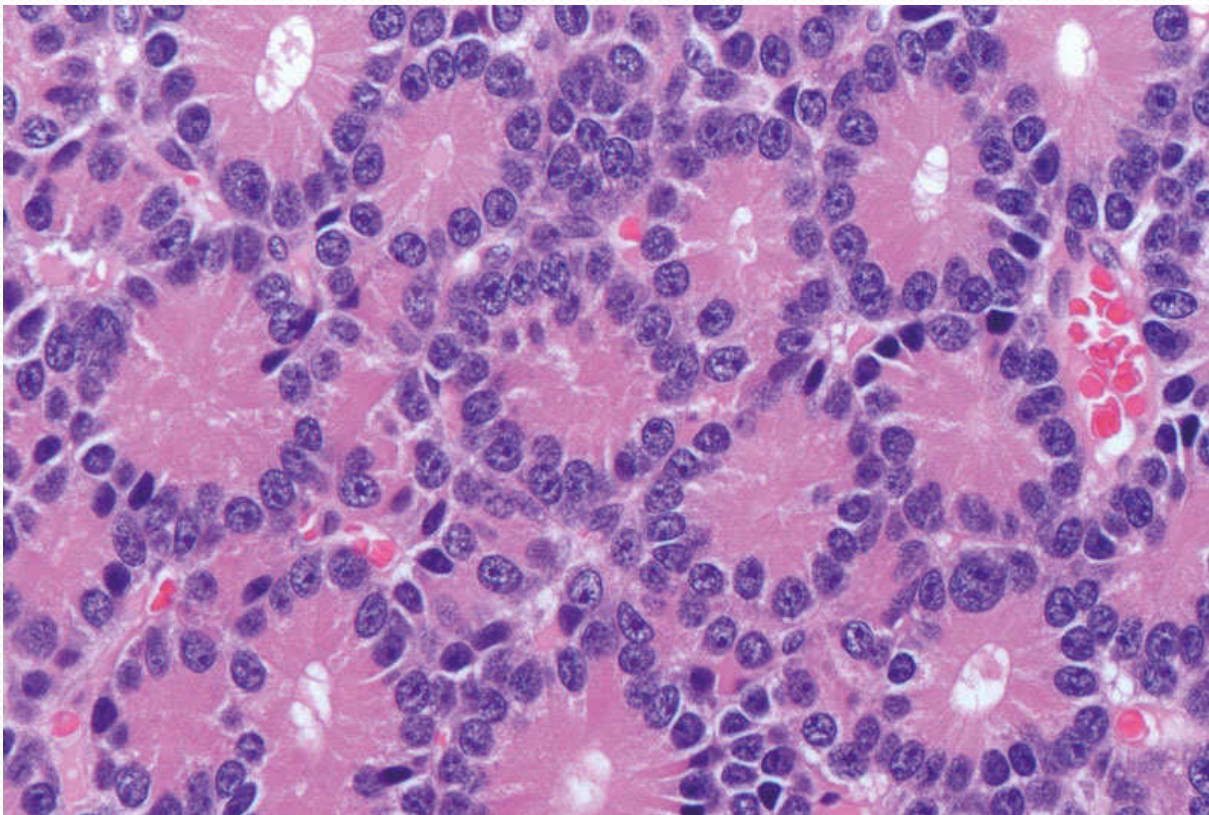


fig. 2-4

Acinar Cell Pattern



- Granular eosinophilic cytoplasm & single prominent nucleoli. Resembles normal pancreas



■ **Spread of pancreatic tumours:**

A. Local Invasion

B. Lymphatic

C. Blood

D. Via peritoneal & omental causing ascites

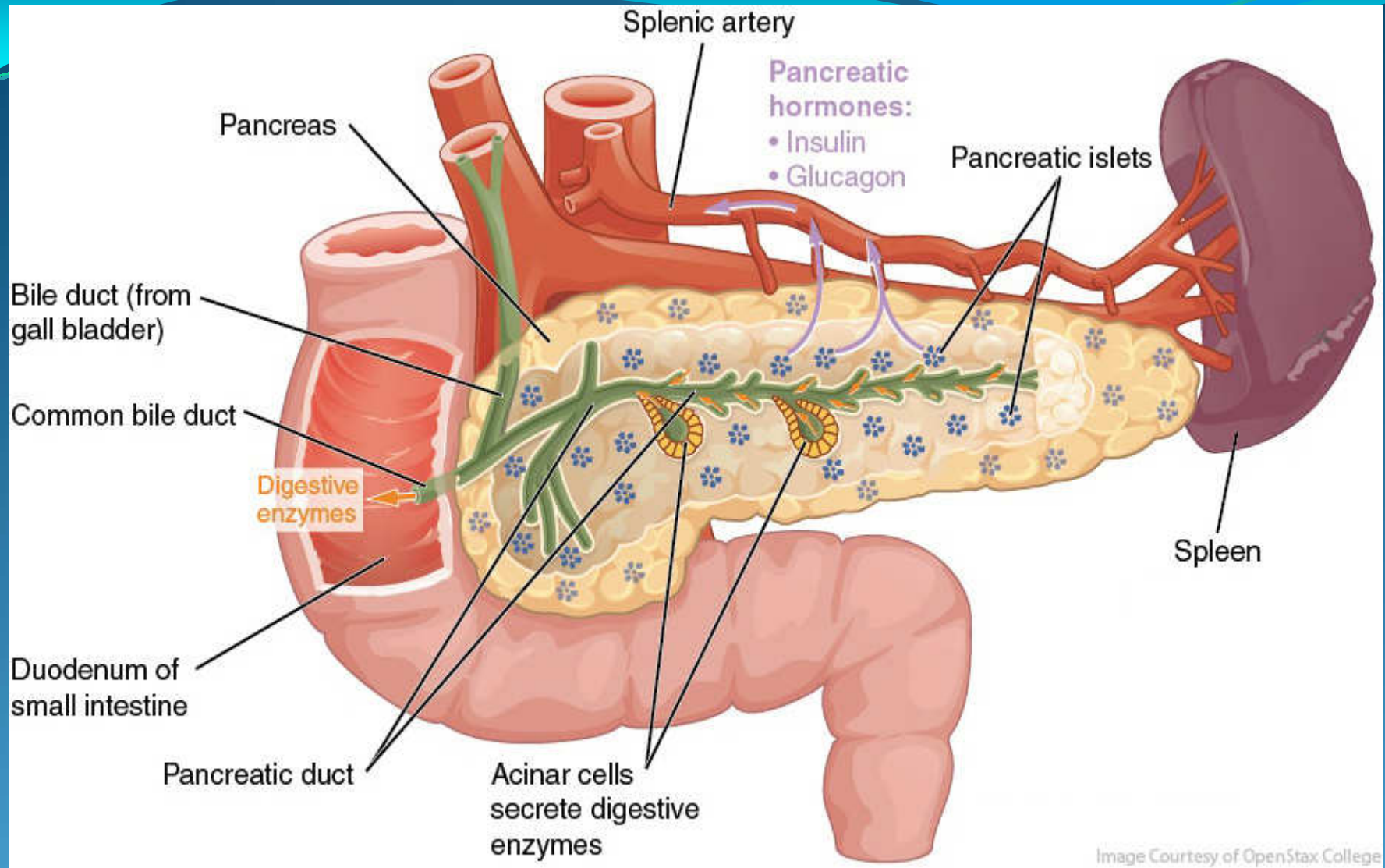


Image Courtesy of OpenStax College



Common sites of metastasis

- Local invasion
 - Extend through retroperitoneal spaces and impinge on nerves
 - Invade spleen occasionally
 - Adrenals
 - Vertebral column
 - Transverse colon
 - Stomach
- Local lymph nodes: peripancreatic, gastric, mesenteric, omental and portahepatic nodes
- Liver involvement can cause hepatomegally
- Distant metastasis commonly to bone and lung

Clinical Presentation

- Abdominal pain that radiates to back – erosion to posterior abdominal wall and affecting nerves
- Abdominal mass
- Wt loss
- Jaundice in 50% (obstruction or compression of bile duct)
- Paraneoplastic syndromes (e.g. **Trousseau syndrome** characterised by migrating thrombophlebitis attributable to plt-aggregating factors and procoagulants from tumor or its necrotic products)
- Anorexia
- Bloating
- Steatorrhea or diarrhea

Diagnosis

- Abdominal Ultrasound
- CT Abdomen
- Biopsy (Percutaneous or Endoscopic)
- Serum CA 19-9
 - Elevated in 80% of pancreatic ca cases
 - Low specificity
 - Can be a useful gauge of treatment



Pancreatic Cancer: Serum Markers

- Is there a role for serum markers? If so, what?
 - CA 19-9 is a sialylated Lewis A blood group antigen commonly expressed and shed in pancreatic and hepatobiliary disease, not tumor specific
 - This antigen, when significantly increased, can assist in differentiating between pancreatic adenocarcinoma and inflammatory pancreatic disease
 - decrease in serial CA 19-9 correlates with survival of pancreatic patients after surgery or chemotherapy
 - Debatable as to whether this is useful as early treatment of recurrences have not been shown to improve outcomes

Prognosis

- Overall survival rate 4%
- For patients with small cancers (<2cm) with no extension beyond capsule of pancreas, complete surgical resection has a 5 year survival rate of 18-24%
- For patients with advanced cancers, survival at 5 years is 1%, with most patients dying within a year

END

References: Robins Pathological Basis of Diseases

Download seminar notes: www.pathologyatsmhs.wordpress.com

The screenshot shows a web browser window with the following content:

- Browser Tabs:** UPNG SMHS User Portal, Gastrointestinal Pathology, Useful Websites | UPNG SMHS
- Address Bar:** pathologyatsmhs.wordpress.com/notice/
- Page Title:** UPNG SMHS Pathology Seminar Notes
- Text:** Dr Rodney Itaki's Seminar Presentations
- Image:** Logo of the Division of Pathology, School of Medicine & Health Sciences, University of Papua New Guinea. The logo features a stylized book and a flame within a circular emblem.
- Navigation Menu:** Home, About, Case Studies, Journals, Useful Websites
- Section: Useful Websites**
 - Text:** A list of useful websites is provided below:
 - Text:** Collection of images of microscopic and macroscopic pathology. My personal recommendation. Hosted by university of Utah.
 - Link:** <http://library.med.utah.edu/WebPath/webpath.html#MENU>
 - Text:** Website with normal histology, University of Wisconsin, Department of Anatomy.
- Search Bar:** A search box with a "Search" button.
- Blog Stats:** 3,091 hits
- Recent Posts:**
 - Adrenal Gland Insufficiency Seminar: MBBS 3
 - Breast Cancer: MBBS 2 Seminar Notes
 - Bone & Soft Tissue Healing: MBBS 2 Seminar Notes
 - Neoplasia: MBBS 2 Seminar Notes
 - MBBS 2 Seminar
- Footer:** Waiting for 1.gravatar.com... and a Windows taskbar showing the Start button, open applications (Pepti..., MEDI..., Robbi..., Usefu...), search bar, and system tray (8:10 AM).