ACUTE PANCREATITIS

*Classification by severity ie **organ** failure and **complications** (Atlanta 2012):*
Mild: (i)no organ failure (ii)no local/systemic complications
Moderately severe: (i)organ failure resolves <48hrs (ii)local/systemic complications without persistent organ failure
Severe: persistent organ failure >48hrs **most often pancreatic necrosis**

Aetiology (after first three, no fucking attempt at ordering by prevalence):
1. Gallstones: block ampulla of Vater → CBD bile reflux into PD under pressure
2. Alcohol: SoO hypotonia/acinar cell hypersensitivity to CCK/cytotoxic to acinar cells
3. Iatrogenic + Drugs: ERCP/Surgery/DXT/Drugs(steroids, valproate, thiazides, E2, morphine, cytotoxics, azathioprine
4. Idiopathic
5. Infection: coxsackie B, mumps
6. Autoimmune: IgG4 autoimmune disease spectrum (periductal lymphoplasmocystic infiltrate)
7. Trauma: crush against vertebral column
8. Obstructive: tumour of panc head or ampulla/benign PD stricture/sphincter dysmotility
9. Toxins: scorpion bite
10. Vascular
11. Hyperlipidaemia: triglycerides > 1000/dL
12. **Hypercalcaemia**: hyperPTH
13. **Congenital:** cystic fibrosis, haemochromatosis, cysts, pancreas divisum

Pathogenesis:
1. Sphincter damaged/blocked→ (i)**duodenopancreatic reflux** (ii)**PD HTN** → enterokinase + pressure activate pro-enzymes (i)**Trypsin**→ autodigestion + activates PLA (ii)**Lipase+PLA** → FFA+Ca^{2+} → fat necrosis (insoluble soaps) (iii)**Amylase**
2. **Gland oedema/haemorrhage**→ blood-stained/enzyme-rich (retro)peritoneal **effusion** as paracrine enzyme leak
3. **Necrosis:** perilobular: ischaemic necrosis at watershed areas complicated by A+V thromboses and enzymes
periductal: damage to endothelium in duct at centre of lobule -> enzymes escape (esp EtOH/gallstones)
4. **SIRS/MOF**

Progression:
1.Interstitial oedematous pancreatitis
2. Necrotizing pancreatitis

Clinical features

General: Symptoms= **Pain:** epigastric/upper abdo → back; sudden onset/constant; severe; sit forwards/worse if supine
Vomiting (early and profuse ?ileus)
Signs: I= posture/SIRS signs/jaundice/distension from ileus+ascities
Pa= tenderness/rebound/guarding, epigastric mass/pseudocyst(overlies stomach, can't get above, moves with resp)
Pe=pseudocyst hyperresonant to percuss (stomach), ascities (shifting dullness), pleural effusion
Ausc= ileus/pleural effusion

Complications: Fluid-related (dehydration/pleural effusion and pulmonary oedema/ascites)
Necrotizing pancreatitis: (i)Cullen's sign(falciform) (ii)Grey-Turner's sign(retroperitoneal extravasation)
SIRS features

Other: jaundice due to (i)gallstone (ii)swollen pancreatic head compresses CBD (iii)tumour (iv)PD stricture

Investigations

Diagnosis: 2 of (i)Pain (ii)3x amylase/lipase (iii)CT diagnosis

Blood: (i)Routine FBC/U&E/LFT/CS (ii)CBG (iii)Amylase/lipase (iv)CRP
ABG: (i)severity scoring (ii)lactate in dehydration
Urine: amylase/lipase
CXR: pleural effusion/oedema + rule out PU perf
AXR: ileus (sentinel loop sign, colonic cut-off sign, halo sign)

US: on admission in all! (biliary tree for stones)
EUS: (i)better for stones/microlithiasis in idiopathic pancreatitis (ii)drainage of peripancreatic collections
MRCP: (i)retained stones (ii)distinguishing pseudocyst from WON

CT: can't identify necrotizing pancreatitis first few days (intrapanc fluid→ heterogeneous enhancement)
Early: uncertain diagnosis Later: identifying/monitoring complications

Amylase: Normal if very early/delayed presentation + atrophied pancreas
CRP: prognostication/severity

Differential dx:

Severity scoring (Glasgow)

Admission: (i)AGE >55 (ii)WCC >15 (iii)PO_2 <8 (iv)Urea >16 (v)CBG > 10
Within 48 hours: (vi)Ca^{2+} <2 (vii)Albumin <32 (viii)LDH >600 (ix)AST >200
3+= severe acute pancreatitis (25% mortality)
CRP>150 also indicates severe pancreatitis

INITIAL MANAGEMENT

1.Aim: supportive

NBM + iv fluids (monitor urine output) + PPI
Analgesia: oral/PCA/block
Nutrition: (i)early feeding (low-fat) (ii)enteral>parenteral (infection/organ failure/mortality; Kalfarentzos et al 1996) but may need to TPN if ileus
Antibiotics: only for **cholangitis**; no supportive evidence in ANC

2.Identify and Treat Cause:

Gallstones → obstructive jaundice → cholangitis → (i)**ERCP** within 24hrs (ii)**lap chole** during admission
Hyperlipidaemia: fibrates first line; niacin/omega3 second line
Hypercalcaemia: treat underlying cause
Autoimmune: steroids (pred 40mg/d 4 weeks then taper)
Sphincter dysmotility: sphincterotomy but 30% PEP

Mild: most don't require imaging and resolve by 3-5days
Moderate: require extended hospitalization
Severe: most have pancreatic necrosis → 30% mortality (doubles if infected necrosis)

3. Managing systemic complications

Indications for HDU/ITU: organ dysfunction not responsive to supportive therapy (resp/renal/cardiac)

LOCAL COMPLICATIONS (ATLANTA 2012)

A. INTERSTITIAL PANCREATITIS

1. Acute peripancreatic fluid collections: Homogenous without well-defined wall (<4wks)

2**. Pancreatic pseudocyst:** Heterogenous peripanc fluid in well-defined granulation (not epith) tissue-lined sac (>4wks)

(i)Duct disruption (ii)non-disrupted but effusion → MRCP to identify if communicates with PD

If symptomatic (obstruction) → radiological drainage/**EUS-endoscopic** (most effective)/laparoscopic/open cystgastrostomy

B. NECROTIZING PANCREATITIS

1. Acute necrotic collections: necrosis of parenchyma/peripancreatic tissues (<4 wks)

2. Walled-off pancreatic necrosis (WON) necrotic debris and fluid in well-defined sac (>4wks)

Avoid EUS-endoscopic drainage (infection risk)

Management of fluid/necorizing collections:

1. ***Characterise fluid collection****: CT fails to identify necrotic debris so* ***MRCP (WON vs PP)***
2. ***Step-up approach****: only intervene if clinical course attributable to necrosis (****pain/gastric outlet obstruction/sepsis****)*
3. *(i)WON: radiological drain with culture to prove infection → nephroscopic necrosectomy or VARD + closed drain*
   (ii)PP: EUS-endoscopy +/- step-up

C. OTHER LOCAL COMPLICATIONS

Ductal disruption: pleural effusion/ascites/enlarging collection; MRCP → ERCP+stent

Fistula: esp if instrumentation; amylase-rich opalescent fluid; MRCP → ERCP+stent

Vascular: (i)splenic vein thrombosis →GO varices (ii)pseudoaneurysms(4-10%)→ angioembolize

GOO:

PD Stricture

SYSTEMIC COMPLICATIONS (TERTIARY UNIT)

Biochemical derangement: (i)hypoalbuminaemia/hypocalcaemia (ii)**diabetes** (iii)**malabsorption**

SIRS/MOF : **resp/renal/cardiac** failure

Other: peptic **ulcers**

FOLLOW-UP

BILIARY DISEASE: cholecystectomy during same admission/within 4 weeks

NON-BILIARY:autoimmune screen/Ca2+/LFTs/lipids; consider CT/MRI/EUS to absolutely rule out stones

CHRONIC PANCREATITIS

*Definition: **Progresssive, irreversible** destruction of functional pancreas by **inflammation** and **fibrosis***
*Consequences: **Exocrine** then **endocrine** insufficiency*

Aetiology:

TIGAR-O-HAM = Toxic-Metabolic, Idiopathic, Genetic, Autoimmune, Recurrent pancreatitis, Obstructive
Toxic-Metabolic (70%): alcohol/smoking cause + accelerate chronic pancreatitis and increase cancer risk
Idiopathic (20%)
Genetics (*PRSS1/SPINK1*)
Autoimmune (IgG4)
Obstructive: cholelithiasis/tumour in panc or duo/stricture of PD or SoO/CF
Anatomical: pancreas divisum/annular pancreas
Malnutrition
HyperCa2+

PATHOLOGY

Pathogenesis

Protein plugs in finer ductules → **dilatation** of ductules and acini
Acinar epithelium becomes **cuboidal** then **atrophic**; ductile epithelium **necrosis**
Necrosis → perilobular fibrosis → intralobular fibrosis → ductal obstruction/periductal inflammation
Parenchyma replaced by **calcification** + **fibrosis** with **exo/endocrine** resultant (islet tissue usually survives)
Duct ecastia + strictures → **chain of lakes** (sacculations with intervening stricutures) → **occlude** (debris/stones)

Differential: acinar atrophy/interlobular fibrosis/ductal hyperplasia/metaplasia → mimics cancer

Histomorphological variants:

(i)**CALCIFYING CP:** intraductal/parenchymal Ca^{2+} → PD stenosis with periduct inflamm/parenchymal atrophy/necrosis/fibrosis
(ii)**OBSTRUCTIVE CP:** painless **blockage of PD** by tumour/post-pancreatitis/CF → **atrophy/fibrosis without epith changes**
(ii)**AI CP:** lymphoplasmacytic infiltration **IgG4**/macrophages/eosinophils/neutrophils (assoc'd w/ UC/CD/PSC/Sj/thyroiditis/PBC)
(iii)**HEREDETARY CP**: irregular **sclerosis** with parenchymal destruction (*PRSS1* gene)

DIAGNOSIS

Clinical features

1.**PAIN:** (i)PD obstructn$_{(stricture/stone)}$ (ii)inflamm infilt.(iii)enlarged nociceptors (iv)spinal neurons: hyperalgesia/allodynia (v) trypsin
2. **VOMITING:** pseudocyst → gastric outlet obstruction
3. **EXOCRINE FAILURE**: *Malabsorption/steatorrhoea/malnutrition* (i)PD obstn (ii)gland destruction→ Enzymes/ADEK
4. **ENDOCRINE FAILURE**: diabetes in 50%; increases risk of cancer
Other: peptic erosions/ulcers
EVENTUAL BURN-OUT → (i)RESOLUTION OF PAIN (ii)ONGOING EXO/ENDOCRINE DYSFUNCTION

Investigations

(**a)Bloods:** (i)Cause: IgG4 and autoimmune screen (ii)Effects: malabsorption/malnutrition
(b)Pancreatic function$^{(advanced)}$: (i)faecal elastase: <200ug$_{/g}$ (ii)secretin stim: analyse juice for HCO_3^-||(iii)serum trypsin: <20mg/dL
(c)Imaging: (i)**differentials** of severe epigastric pain (ii)exclude **other pancreatic pathology**: cancer/cysts/IPMN

Characteristic features: (i)parenchymal: atrophy/fibrosis/calcification (ii)duct: strictured/dilated/stone
1. CT: parenchyma and calcifications; less ductal detail than MRI
2. MRCP-secretin: ductal details; cannot visualise calcification
3. EUS: duct and parenchyma
4. ERCP: most detailed ductal imaging

MANAGEMENT

(a)Treat cause:
Autoimmune: corticosteroids
Alcohol: abstinence

(b)Symptomatic
Pain: medical therapy/endoscopic therapy/nerve block or neurolysis/surgery
Erosions/ulcers: PPI
ExocrineL enzymes/ADEK vitamins
Endocrine: diabeeeetus
Vomiting: ESU cysto-gastrostomy for pseudocysts

(c)Ductal obstruction
(a)Endoscopic: ERCP + stone trawl/lithotripsy/sphincterotomy(SoOD or stenosis)/stenting PD (>50% pain relief)
(b)Surgery if (i)pain not responsive to other modalities (ii)obstruction (iii)cannot rule out cancer

Drainage: relieves pressure in pancreatic duct
Puestow:lateral pancreaticojejeunostomy
Partington-Rochelle: longitudinal pancreaticojejeunostomy

Resection: inflammatory mass>4cm
(a)Duodenum-preserving pancreatic head resection (DPPHR)
(i)Frey (distal pancjej + head resection not in front of PV)
(ii)Beger (subtotal head resection above PV + roux pancjej)
(iii)Berne (larger head resection not in front of PV; no drainage)
(iv)Hamburg: (subtot head resectn not in front of PV; lat drainage)
(b)Whipple's: pylorus-persevering pancreatico-duodenectomy
(c)Total pancreatectomy: after multiple other radical procedures failed as → brittle diabetes BUT 66% pain relief
Islet cell transplant into portal vein → implant in liver and lessen diabetes

OTHER COMPLICATIONS
Fluid: (i)pancreatic ascites: ERCP and stent (ii)Pseudocyst: leave for 6 wks; transgastric/percutaneous drainage/surgery
Biliary: CBD stricture
Vascular: (i)Splenic vein thrombosis → variceal UGIB (ii)Pseudoaneurysm → UGIB
Pancreatic cancer: 4% (increasesed by smoking and diabetes)
Fistula (pancreatico-pleural/bronchial or mediastinal pseudocyst) → conservative first and if fails, ERCP and stent