Chronic Pancreatitis

Medical Management

DR. MOHAMED BADBESS
CONSULTANT PHYSICIAN & GASTROENTOROLOGIST

Definition - Guideline Consensus

ACG 2020 definition:

- Chronic pancreatitis is a **pathologic fibro-inflammatory syndrome** of the pancreas in individuals with **genetic, environmental, and/or other risk factors**, characterized by **progressive, irreversible structural damage** that leads to **pain and/or loss of endocrine and exocrine function** over time.

IAP–APA 2017 definition:

- CP is a continuing inflammatory disease of the pancreas characterized by **irreversible morphologic changes** typically causing **pain and/or permanent loss of function**.

BSG 2018 Practical Guide:

- A chronic, progressive, fibro-inflammatory process resulting in **fibrosis, calcification, and ductal irregularity** with subsequent **exocrine and endocrine insufficiency**.

Key conceptual points

- **Irreversible** → differentiates from recurrent acute pancreatitis.
- **Multifactorial** → genetic + environmental + metabolic causes.
- **Progressive** → ongoing inflammation and fibrosis → structural + functional failure.
- **Clinical hallmark** → chronic abdominal pain, steatorrhea, diabetes (late).

Risk Factors and Etiologies

The **TIGAR-O** classification (endorsed by ACG and IAP-APA) divides causes into 6 major categories:

Category	Examples	Notes from Guidelines
T – Toxic-Metabolic	Alcohol use (most common worldwide), smoking, hypercalcemia, hypertriglyceridemia, chronic renal failure, certain drugs (valproate, azathioprine)	Alcohol and smoking are independent and synergistic risk factors; cessation is a strong recommendation (ACG).
I – Idiopathic	Early-onset (<20 yrs), late-onset (>50 yrs), often with genetic predisposition (e.g., CFTR, SPINK1 variants)	Genetic testing considered in young or idiopathic cases.
G – Genetic	PRSS1, SPINK1, CFTR, CTRC mutations	PRSS1 (autosomal dominant hereditary pancreatitis) carries high lifetime risk of pancreatic cancer.
A – Autoimmune	Autoimmune pancreatitis (Type 1 or 2)	Distinguish because it's potentially reversible with steroids.
R – Recurrent and Severe Acute Pancreatitis	Recurrent episodes leading to fibrosis and ductal damage	Each acute episode can accelerate progression.
O – Obstructive	Pancreatic duct obstruction (tumor, stricture, pancreas divisum, annular pancreas, sphincter of Oddi dysfunction)	Relieve obstruction if possible (endoscopic or surgical).

Major Modifiable Risk Factors (ACG 2020)

- **Alcohol:** Most significant risk factor in many regions. No safe threshold; lifetime consumption >5 drinks/day for >5 years markedly increases risk.
- **Smoking:** Independently increases risk and progression even without alcohol.
- **High triglycerides, hypercalcemia:** Secondary causes to identify and correct.
- **Medications:** Rare but reported (azathioprine, valproate, thiazides).
- **Genetics:** Important in early-onset or idiopathic cases.

Investigations

1. Laboratory evaluation

Used mainly to **exclude other causes** and assess **exocrine/endocrine function**, not to confirm CP directly.

Purpose	Recommended Tests	Notes / Guideline Context
Screen for acute flare or alternative diagnoses	Serum amylase & lipase	Often normal or mildly elevated in chronic disease (not diagnostic).
Assess exocrine function	Faecal elastase-1 (preferred, non-invasive)	<200 µg/g = pancreatic exocrine insufficiency. Used for diagnosis and monitoring (ACG conditional recommendation).
	72-hour faecal fat test (gold standard but rarely done)	Used when precise quantification needed.
Assess endocrine function	Fasting glucose, HbA1c	Screen for pancreatogenic (Type 3c) diabetes.
Etiologic assessment	Calcium, triglycerides, genetic panel (PRSS1, SPINK1, CFTR, CTRC), autoimmune markers (IgG4)	Based on patient age, presentation, and family history.
Nutritional status	Albumin, vitamin levels (A, D, E, K), prealbumin	Routine in established CP.

Investigations

2. Imaging — cornerstone of diagnosis

A. First-line: Contrast-enhanced CT scan (ACG strong recommendation):
Detects calcifications, ductal dilatation, atrophy, and complications (pseudocysts, stones, strictures).
→ Best initial test for **moderate/late-stage CP**.

B. If CT is inconclusive (early disease)

- **MRI/MRCP (with secretin stimulation if available):**
  Detects subtle ductal irregularities, side-branch changes, and early fibrosis.
  Recommended when CT is non-diagnostic but suspicion remains high.

Investigations

C. Endoscopic Ultrasound (EUS):

- **Most sensitive for early CP**.
  Allows tissue sampling and can detect parenchymal/ductal changes before CT/MRI abnormalities.
  ACG suggests EUS when CT/MRI are non-diagnostic and clinical suspicion persists.
  Avoid over-diagnosis: minor EUS features alone are not diagnostic — use Rosemont criteria (IAP-APA).

D. ERCP:

- No longer recommended for diagnosis — reserved for **therapeutic purposes** (duct drainage, stone extraction, stenting).
  (ACG and ESGE: strong recommendation against diagnostic ERCP due to risk of iatrogenic pancreatitis)

Diagnostic Criteria (IAP–APA, ACG)

Diagnosis requires **combination of**:

- **Typical clinical features:**
  - recurrent/continuous upper abdominal pain, malabsorption, steatorrhea, diabetes
- **Imaging findings:**
  - calcifications, ductal dilatation, parenchymal atrophy
- **Functional impairment:**
  - evidence of exocrine or endocrine insufficiency
- *In early disease, rely on **EUS/MRCP** and **risk factors** (genetic, metabolic) to support diagnosis.*

Management: Key principles & initial steps

1. Identify & modify risk factors / etiologic triggers
2. Stratify key clinical problems to manage
3. Set realistic goals

Identify & modify risk factors / etiologic triggers

Abstinence from alcohol is strongly recommended

The ACG guideline gives a strong recommendation that patients with CP stop alcohol use

Smoking cessation is likewise strongly recommended

ACG: “We recommend smoking cessation in patients with CP.”

Nutritional assessment

Many patients with CP have malnutrition, weight loss, malabsorption (exocrine insufficiency). Early recognition is key

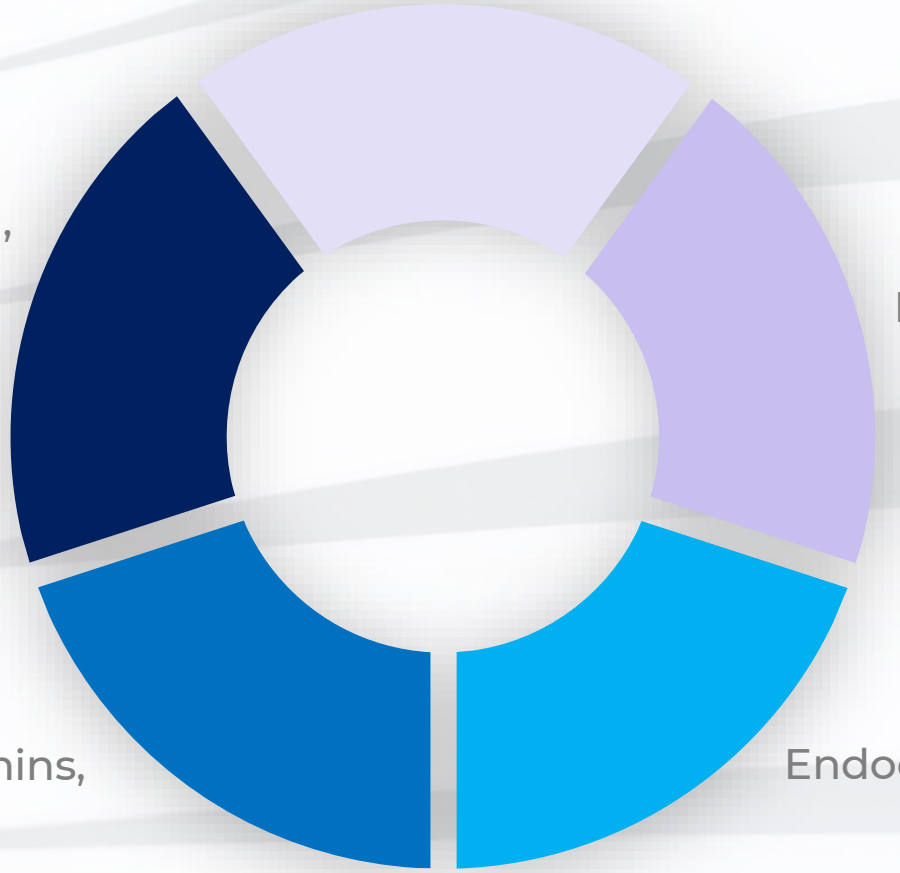
Multidisciplinary care

A team approach (gastroenterologist, dietician, pain specialist, endocrinologist)

Stratify key clinical problems to manage

Pain (the dominant symptom in many)

Monitoring and preventing complications (ductal obstruction, pseudocysts, malignancy risk)



Exocrine pancreatic insufficiency (EPI) / malabsorption

Nutritional deficits (vitamins, minerals, bone)

Endocrine insufficiency (pancreatic-diabetes)

Set realistic goals

Guidelines emphasize that often complete pain-freedom may not be achievable

The goals are:

Specific management domains

1. Pain Management

Pain Management

Pain control is central, often the hardest part of medical management in CP

Non-pharmacologic measures

- Ensure abstinence from alcohol & cessation of smoking
  - These accelerate progression and worsen pain and complications

- Dietary / nutritional support: small frequent meals, low to moderate fat intake, avoid aggravating foods etc. (though evidence is limited)

- Psychological/behavioural support: given chronic pain may have neuropathic or central sensitisation features. Some guidelines (IAP-APA) stress behavioural interventions

Pain Management

Analgesic/Pharmacologic therapy

- First line: non-opioid analgesics (NSAIDs, acetaminophen) if no contraindications. Then escalate (e.g., weak opioids) if needed. The 2017 IAP-APA-JPS guideline: "simple step-wise escalation of analgesic drugs with increasing potency until pain relief is obtained."
- Use of pancreatic enzyme therapy (PERT) solely for pain relief **is not recommended** by ACG:
  - "We do not suggest the use of pancreatic enzyme supplements to improve pain in CP."
- **Antioxidants:** ACG suggests *considering* antioxidant therapy for pain (conditional recommendation, moderate evidence) but benefit is modest
- **Interventional pain control:** If pain is refractory, guidelines suggest considering **celiac plexus block** (conditional)
- Importantly: Before escalating, consider whether structural complications (ductal obstruction, pseudocysts) may account for pain and refer appropriately for endoscopic/surgical options

Pain Management

Endoscopic/Surgical management for pain

- The ACG guideline strongly recommends **surgery over endoscopic therapy for long-term pain relief** in obstructive CP when first-line endoscopy fails

- The IAP-APA guideline emphasises:
  - "Endoscopic treatment can be used in patients with evidence of ductal obstruction …
  - "Surgery should be considered early … after a maximum of five endoscopic interventions."

Specific management domains

2. Exocrine Pancreatic Insufficiency (EPI)

Exocrine Pancreatic Insufficiency (EPI)

Necessary when disease has progressed to the point where exocrine function is reduced:

- malabsorption, steatorrhoea, weight loss, nutrient deficiencies may occur

Key recommendations

The ACG guideline:

- "We suggest pancreatic enzyme replacement therapy (PERT) in patients with CP and exocrine pancreatic insufficiency to improve the complications of malnutrition." (conditional recommendation, low quality evidence)

The Medscape summary:

- "Pancreatic enzyme replacement therapy is essential … to improve fat and protein maldigestion."
- Alongside PERT, address diet: ensure adequate caloric intake, moderate fat but not too restrictive, replacement of fat-soluble vitamins, calcium, bone protection

Exocrine Pancreatic Insufficiency (EPI)

Practical considerations

- Start PERT at **adequate** doses and **titrate** based on:
  - Symptoms
  - weight gain/loss
  - stool quality
  - nutritional markers
- Ensure correct timing (with meals/snacks)
- Monitor for malnutrition (albumin, pre-albumin, weight, BMI) and complications (osteoporosis, vitamin deficiencies)
- In patients with CP who are diabetics, coordinate between gastroenterology and endocrinology/dietician to ensure nutritional needs are balanced

3. Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Many patients with CP eventually develop diabetes (estimates ~30-40% in some series)

Diagnosis:

- Insulin deficiency (relative or absolute)
- Presence of pancreatic exocrine insufficiency
- Evidence of pathological pancreatic imaging
- Absence of antibodies for T1DM

NB: Measure C-peptide to assess phenotype

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Pancreatic endocrine function – islet cells (of Langerhans)

- Beta cells: produce **insulin** to lower blood glucose
- Alpha cells: produce **glucagon** to raise blood glucose
- Delta cells: produces somatostatin which regulates other hormones
- Gamma cells: produce pancreatic polypeptide

Pathophysiology of endocrine dysfunction:

- Decreased insulin secretion → glucose intolerance
- Decreased glucagon secretion → propensity for low blood glucose

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Treatment goals:

- Patients share **similar risk** for diabetes complications (compared to T1DM & T2DM)
  - Microvascular complications: neuropathy, nephropathy, retinopathy
  - Macrovascular complications: heart disease, stroke, peripheral vascular disease
  - Other complications: infections, poor wound healing
- **Individualized** glucose targets and HBA1c
- Maintaining nutritional status

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Lifestyle modifications:

- Reducing toxic and modifiable contributors to chronic pancreatitis
  - Smoking cessation, avoiding alcohol
- Medical nutrition therapy
- Improving insulin sensitivity
  - Avoiding sedentary time, staying active
- **Don’t** necessarily need a low carbohydrate diet

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Pharmacological therapy:

1. Insulin

- If insulin deficiency is present (low/absent C-peptide) → start insulin (most robust evidence for use in Type 3c diabetes)
- Use lower starting dose → 0.2U/kg
- Titrate cautiously
- Frequent self monitoring of blood glucose / CGM

2. Metformin

- If mild hyperglycemia and features of insulin resistance → use metformin if no contraindications
- Monitor tolerance and GI side effects

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Pharmacological therapy:

3. Secretagogues

- Avoid where possible due to risk of hypoglycemia
- Only use cautiously if there is preserved beta cell function
- If needed, prefer short acting meglitinides, with close monitoring

4. DPP4 inhibitors

- Limited efficacy in insulin deficiency patients
- Historical signals show concern about pancreatitis/pancreatic cancer
- Avoid in active pancreatic disease

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Pharmacological therapy:

5. SGLT2 inhibitors

- Avoid in insulin deficient patients → risk of euglycemic DKA
- Dehydration, weight loss may be detrimental to malnourished patients

6. GLP1 receptor agonists

- Weight loss and significant GI side effects → undesirable in malnourished patients
- Safety signal from observational data → pancreatitis/pancreatic cancer
- Avoid use where possible, especially in active pancreatic disease

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Challenges:

- Unpredictable absorption and digestion
- Higher risk of hypoglycemia
- Lack of endogenous insulin production
- Maintaining nutritional status
- Lack of awareness and information

Future directions:

- Automated insulin delivery
- Pancreatic transplant
- Islet cell transplant
- Stem cell therapy

Endocrine Insufficiency – Pancreatogenic Diabetes (Type 3c)

Guideline points

- Key points include: recognizing that diabetes in CP (pancreatogenic) often has **both insulin and glucagon deficiency** and may be **brittle**
- Management should follow standard diabetes care but with awareness of **hypoglycaemia risk**
- IAP-APA notes:
  - "In patients with diabetes, lifestyle changes are recommended …
  - For patients with suspected insulin resistance, metformin is the first choice if there is no contraindication
  - Other oral hypoglycemic drugs have limited evidence for use and may have significant adverse events
  - When oral drugs are ineffective, insulin should be used."

Specific management domains

4. Nutritional & bone health support

Nutritional & bone health support

- Given malabsorption and altered nutrient metabolism in CP, nutrition is vital
- Ensure patients maintain adequate energy intake
- Monitor weight/BMI, consider dietician referral
- Small frequent meals, moderate fat (not ultra-low as may worsen weight loss)
- Replace **fat-soluble vitamins** (A, D, E, K) if EPI present
- Monitor bone health (osteopenia/osteoporosis) given malabsorption + endocrine diabetes risk
- For anaemia, osteoporosis and micronutrient deficiencies monitor and treat as appropriate

Algorithmic summary of management

At diagnosis of CP (or when following a known CP patient)

Confirm structural/functional diagnosis (imaging, labs)

Evaluate risk factors: alcohol, smoking, genetics, idiopathic

Baseline: pain history, nutritional status (weight/BMI/albumin), exocrine markers (steatorrhea, stool fat if available), endocrine status (glucose, HbA1c)

Initiate lifestyle modifications: alcohol cessation, smoking cessation, dietician referral

Algorithmic summary of management

Pain control strategy

Start first-line analgesics (NSAIDs/acetaminophen) + lifestyle

If pain persists: consider weak opioids

Consider antioxidants (optional)

Always assess for structural complications (ductal stones/strictures, pseudocysts) and referral for gastro endoscopy/surgery if indicated

Algorithmic summary of management

Concurrently manage exocrine insufficiency

If steatorrhea, weight loss, nutritional deficits → initiate PERT

Ensure timing and adequate dosing of enzymes

Optimise diet

Monitor nutritional markers and bone health

Algorithmic summary of management

Monitor for endocrine dysfunction

Screen periodically for diabetes (e.g., annually or sooner if risk factors)

If diabetes present: manage with insulin/metformin as per type 3c guidelines

Be cautious of hypoglycemia

Coordinate with GI for malabsorption issues

Algorithmic summary of management

ONGOING Surveillance & Support

Nutritional follow-up (weight, BMI, micronutrients, bone)

Pain and quality-of-life reassessment

Evaluate for complications (e.g., pancreatic cancer risk, ductal hypertension, pseudocysts) and refer accordingly

Multidisciplinary follow-up (GI, endocrinology, nutrition, pain management)

THANK YOU!!!