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Pancreatic Exocrine Insufficiency and Pancreatic Enzyme Replacement Therapy

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Content

- Pancreatic Exocrine Insufficiency (PEI) – causes, consequences and symptoms
- Pancreatic Enzyme Replacement Therapy (PERT) – what is it, who needs it, contraindications, effective usage and titrations
- PERT trouble shooting and current shortages
- Case study
- Conclusion / take home messages and time for questions

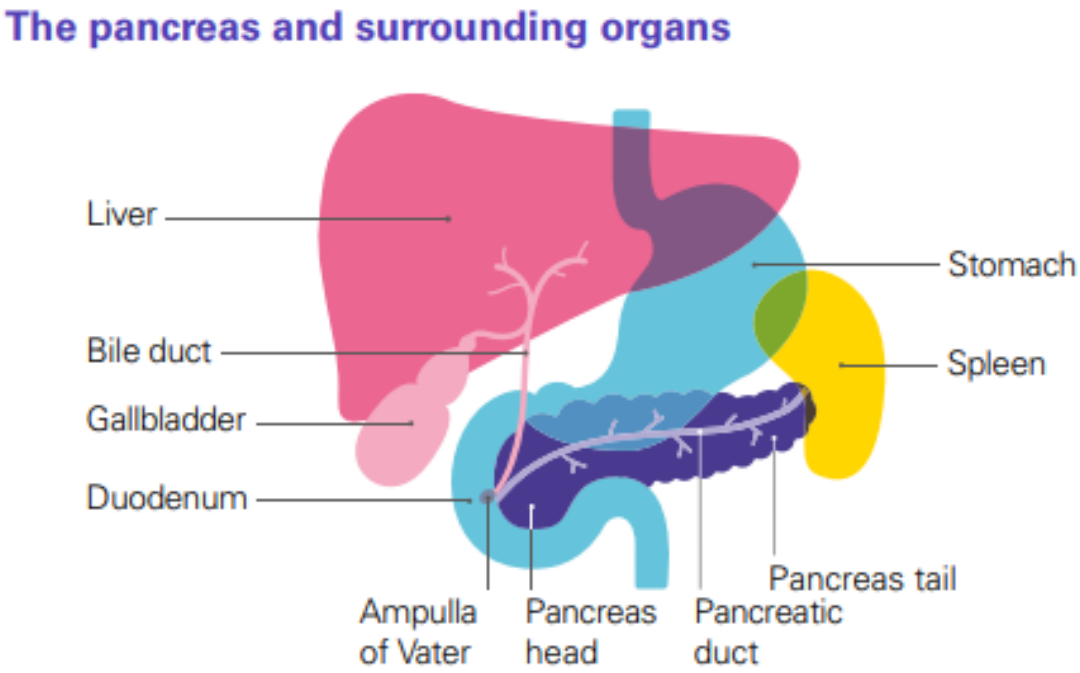
Learning outcomes

- To understand what PEI is and to recognise symptoms
- To understand the medication used in the treatment of PEI
- To understand optimising the use of PERT; considering dosages, timings and dose titration
- Consider how current PERT shortages might impact treatment and patient experience

Causes of PEI

- Primary
  - Insufficient pancreatic tissue to secrete sufficient enzymes
  - Occurs secondary to pancreatic cancer, surgery, pancreatitis

- Secondary
  - Lack of stimulation of the pancreas
  - Occurs secondary to total gastrectomy, duodenal bypass, poor small bowel function (e.g. undiagnosed CD or IBD, potentially also SIBO)



Consequences of PEI

- Weight loss and Malnutrition
- Fatigue
- Micronutrient deficiency
- Abdominal symptoms

Symptoms of PEI

- Nausea / Vomiting
- Steatorrhea (pale/greasy stools)
- Abdominal pain
- Bloating
- Reflux
- Hypoglycaemia
- Increased wind (burping or flatulence)
- Diarrhoea
- Tiredness
- Weight loss / malnutrition / micronutrient deficiency

PERT – What is it?

- Pancreatic Enzyme Replacement Therapy
- Medication to replace the exocrine job of the pancreas
- Different brands are available in the UK
  - Creon (10,000 unit and 25,000 unit capsules)
  - Nutrizym (22,000 unit capsules)
  - Pancrex V (powder)

PERT – Side effects

- Constipation
- Nausea/vomiting
- Abdominal distension
- Less common: skin reactions and fibrosing colonopathy
- First line treatment is generally to trial an alternative preparation (for example changing creon dose to equivalent nutrizym)

PERT – who needs it?

PEI is highly likely with high benefit from PERT: no further test required as significant benefit from treatments and the negative predictive value of FEL-1 is not strong enough to prevent starting treatment

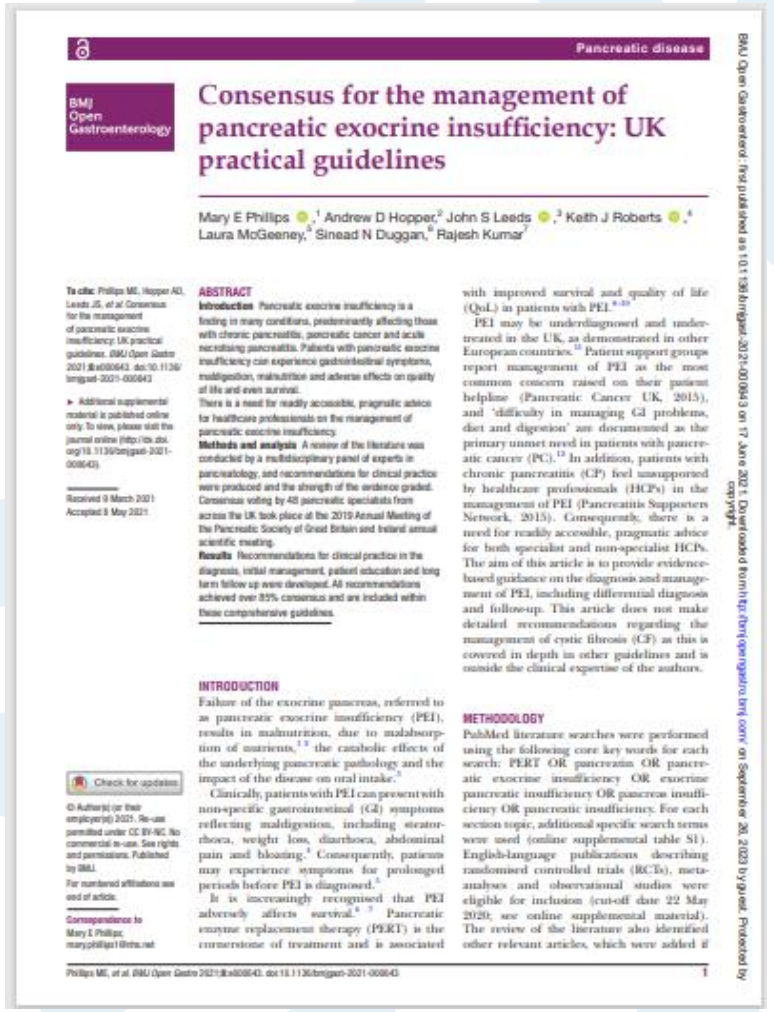
- Head of pancreas cancer
- Pre-surgery and post-surgery for head of pancreas cancer with or without pylorus preserving operation
- Total pancreatectomy
- Steatorrhoea or malabsorption symptoms in patients with CP with dilated pancreatic duct or severe pancreatic calcification
- Severe necrotising pancreatitis

Patients that require initial investigation with FEL-1

- GI symptoms of maldigestion in secondary care with or without known associated conditions
- Maldigestion symptoms: steatorrhoea, weight loss, diarrhoea, abdominal pain or bloating
- Associated conditions: patients with coeliac disease, IBS-D, HIV, type 1 diabetes and acute severe pancreatitis after initial phase

Following a positive FEL-1 test

- A positive FEL-1 requires up-to-date cross-sectional imaging to exclude developing obstructive tumour or lesion as the cause
- If subsequent investigation cannot find a morphological pancreatic cause of PEI, FEL-1 should be repeated even if patient has already started PERT



Pancreatic disease

BMJ Open Gastroenterology

Consensus for the management of pancreatic exocrine insufficiency: UK practical guidelines

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ABSTRACT

Introduction Pancreatic exocrine insufficiency is a finding in many conditions, predominantly affecting those with chronic pancreatitis, pancreatic cancer and acute necrotising pancreatitis. Patients with pancreatic exocrine insufficiency can experience gastrointestinal symptoms, maldigestion, malnutrition and adverse effects on quality of life and even survival.

There is a need for readily accessible, pragmatic advice for healthcare professionals on the management of pancreatic exocrine insufficiency.

Methods and analysis A review of the literature was conducted by a multidisciplinary panel of experts in pancreatology, and recommendations for clinical practice were produced and the strength of the evidence graded. Consensus voting by 48 pancreatic specialists from across the UK took place at the 2019 Annual Meeting of the Pancreatic Society of Great Britain and Ireland annual scientific meeting.

Results Recommendations for clinical practice in the diagnosis, initial management, patient education and long term follow up were developed. All recommendations achieved over 85% consensus and are included within these comprehensive guidelines.

INTRODUCTION

Failure of the exocrine pancreas, referred to as pancreatic exocrine insufficiency (PEI), results in malnutrition, due to malabsorption of nutrients,[1 2] the catabolic effects of the underlying pancreatic pathology and the impact of the disease on oral intake.[3]

Clinically, patients with PEI can present with non-specific gastrointestinal (GI) symptoms reflecting maldigestion, including steatorrhoea, weight loss, diarrhoea, abdominal pain and bloating.[4] Consequently, patients may experience symptoms for prolonged periods before PEI is diagnosed.[5]

It is increasingly recognised that PEI adversely affects survival.[6 7] Pancreatic enzyme replacement therapy (PERT) is the cornerstone of treatment and is associated with improved survival and quality of life (QoL) in patients with PEI.[8–10]

PEI may be underdiagnosed and undertreated in the UK, as demonstrated in other European countries.[11] Patient support groups report management of PEI as the most common concern raised on their patient helpline (Pancreatic Cancer UK, 2015), and 'difficulty in managing GI problems, diet and digestion' are documented as the primary unmet need in patients with pancreatic cancer (PC).[12] In addition, patients with chronic pancreatitis (CP) feel unsupported by healthcare professionals (HCPs) in the management of PEI (Pancreatitis Supporters Network, 2015). Consequently, there is a need for readily accessible, pragmatic advice for both specialist and non-specialist HCPs. The aim of this article is to provide evidence-based guidance on the diagnosis and management of PEI, including differential diagnosis and follow-up. This article does not make detailed recommendations regarding the management of cystic fibrosis (CF) as this is covered in depth in other guidelines and is outside the clinical expertise of the authors.

METHODOLOGY

PubMed literature searches were performed using the following core key words for each search: PERT OR pancreatin OR pancreatic exocrine insufficiency OR exocrine pancreatic insufficiency OR pancreas insufficiency OR pancreatic insufficiency. For each section topic, additional specific search terms were used (online supplemental table S1). English-language publications describing randomised controlled trials (RCTs), meta-analyses and observational studies were eligible for inclusion (cut-off date 22 May 2020; see online supplemental material). The review of the literature also identified other relevant articles, which were added if

Porcine origin

- All pancreatin products have a porcine origin
- There is currently no available alternative although this is in development stages
- All patients should be made aware of this before commencing the medication
- Jewish and Muslim faith leaders consent to the use of PERT. Encourage patients to discuss with their local religious support networks if they are unsure.

Pregnancy and creon

Use in pregnancy and breastfeeding

Statement 8.1: Further work is required to confirm the efficacy and safety of PERT during pregnancy and breastfeeding; although the authors have experience of successful use in pregnancy, the numbers are small and there are no published data. Malabsorption should be avoided in pregnancy (GPP; 93% agreement)

The systematic literature search did not identify any articles concerning the use of PERT in pregnancy or breast feeding. Essential fatty acids are required for brain and retinol development in the first 8 weeks of gestation.[159] Thus, it is important that adequate PERT is maintained in pregnancy.

How to take PERT effectively

- Current guidance is to commence on 50,000 units per meal and 25,000 units per snack at least
- Spread out dose throughout meals and snacks
- Take with a cold drink
- There is no maximum dose of PERT but consider comorbidities if dose exceeds 100,000 units per meal

Dose titration

Table 2 Evaluation of the need for PERT dose escalation: nutritional and symptom assessments

Anthropometric	Biochemical	Clinical	Dietary
► Weight changes in relation to nutritional intake (unexplained weight loss / failure to gain weight) ► Functional changes (grip strength, sit-to-stand times, 6 min walk)	► Micronutrient status (iron, ferritin, B_{12} and folate, fat-soluble vitamins, selenium, zinc, magnesium, copper, clotting) ► Glycaemic control (HbA1c and random glucose) ► Inflammatory markers for assessment of accuracy of micronutrients (CRP)	► Stool frequency, texture, colour, appearance, presence of oil, floating/ difficult to flush, ► Flatulence, bloating, abdominal pain ► Medication that may mask symptoms (opioids, ondansetron, iron supplements, etc)	► 24-hour dietary recall with relevant PERT dose to assess adherence and ratio of PERT with nutrition ► Food avoidance due to abdominal symptoms ► Avoidance of fat-containing products ► Nutritional adequacy of diet

CRP, C reactive protein; HbA1c, haemoglobin A1c; PERT, pancreatic enzyme replacement therapy.

PERT and enteral feeding

- Peptide based feeds is first line for those with PEI
- Peptide feed preparations will reduce, but not necessarily remove, the need for PERT
- Lower feed rates over long periods may also decrease the risk of overwhelming patients digestive capacity
- Literature recommends 2 hourly enzyme administration. This is difficult to achieve and there is no evidence base for this recommendation either
- Adding PERT directly to the feed bottle is easiest, starting dose is 2g Pancrex V powder per 500ml (equivalent to 50,000 units lipase).
- Current recommendations for hanging time are 4 hourly in hospital and 8 hourly in the community to minimise risk of tube blockages

PERT trouble shooting

- Are all diagnoses definite? Can you read any of the scans?
- Is it progressive disease? E.g. new duodenal stricture due to extrinsic pressure
- Are they on a PPI to aid PERT effectiveness?
- Are they prescribed PERT properly? Have they been educated on PERT dosing, timings and titration based on symptoms

- Have other investigations happened
  - It could just be an infection – get a stool sample!
  - Could it be other medications causing symptoms?
  - Could it be undiagnosed CD, SIBO or BAM?
  - Could it be recurrent cancer?

Differential diagnoses – case study

Mr A Non has been diagnosed with stage 3 pancreatic cancer four months ago. He presents in your clinic complaining of urgency to go and regular diarrhoea. What further questions might you ask? What differential diagnoses may be present and what tests might you ask for?

[word cloud for participation]

Differential diagnoses – case study

On discussion, Mr Non also reveals he has regular abdominal pain. What might you ask about? What differential diagnoses may be present and what tests would you suggest for this?

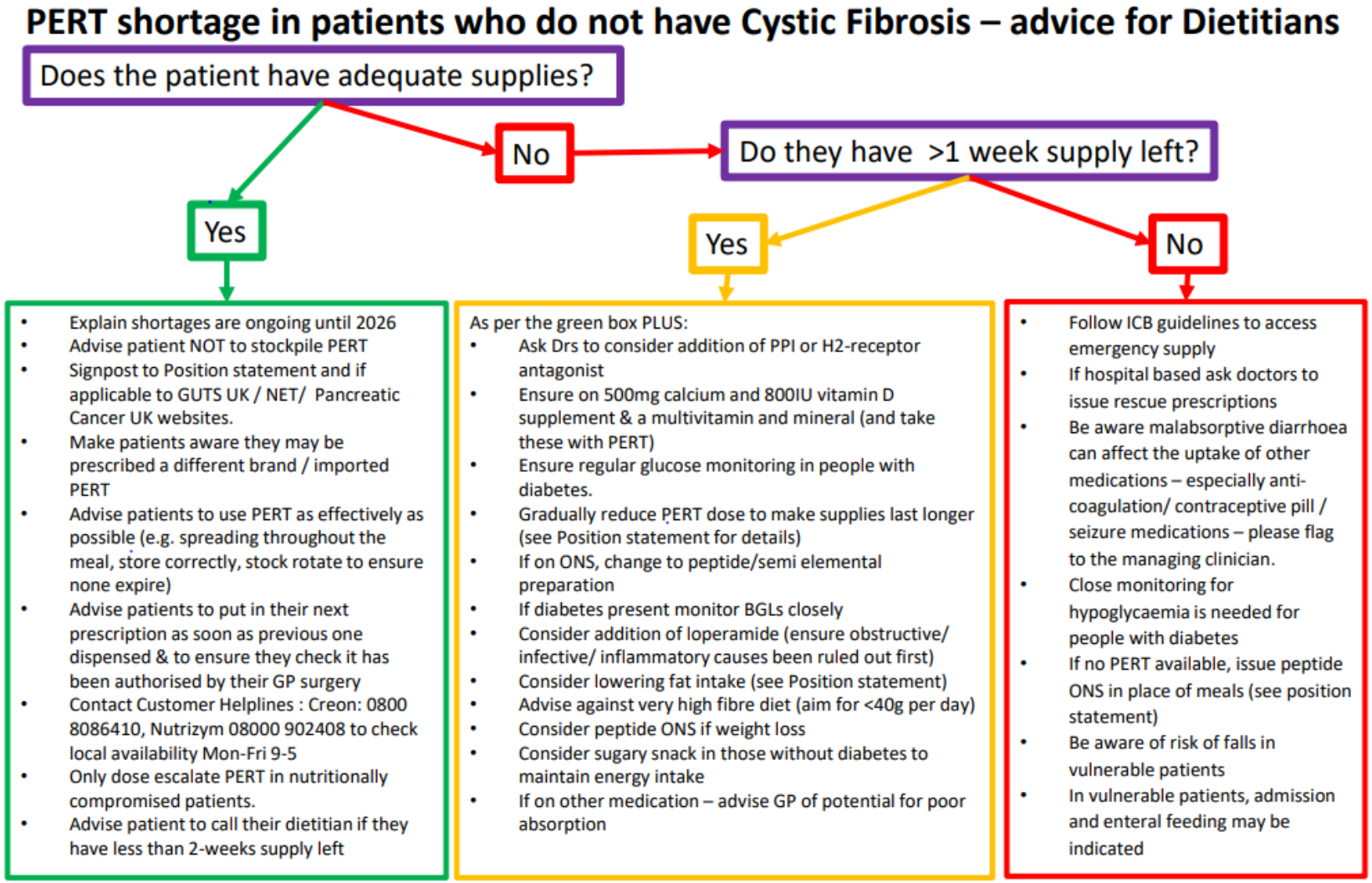
[word cloud for participation]

Position Statement: Pancreatic enzyme replacement therapy (PERT) shortage – advice for clinicians on the management of adults with pancreatic exocrine insufficiency

Phillips M.E[1,3], McGeeney L.M[1], Watson K-L[2], Lowdon J[2].

Position statement and advice for prescribers from the [1]Nutrition Interest Group of the Pancreatic Society of Great Britain and Ireland (NIGPS), [2] Cystic Fibrosis Specialist Group and [3] Gastroenterology Specialist Group, British Dietetic Association.

Main takeaways from position statement



Link to Position statements: Position Statement: Pert Shortage | Pancreatic Society of Great Britain and Ireland (psgbi.org).

Thank you to Emily Button, Cambridge University Hospitals for developing this flowchart.

Main takeaways from position statement

- Use logistics guidelines
  - Do not encourage patients stockpiling PERT
  - Hospital “rescue prescriptions” for those who have run out of PERT completely
  - Focus on patients dosing and storing PERT correctly
- Only dose escalate when patients are nutritionally compromised
- Prescribe peptide based or fat free ONS
- Ensure those patients on insulin are regularly monitoring blood sugars
- Admission for invasive nutrition may be needed for those with poorly controlled malabsorption

PERT shortages further advice

- Pancreatic Cancer UK webinar from September
- Be aware - patients can get enzymes or herbal enzymes from Amazon and Holland & Barrett. However, these are unlicenced for use and not recommended as alternatives.
- NIGPS currently exploring importing medications from Europe and the US. However, these are also unlicenced for use in the UK currently. Discuss with your local ICBs

Thank you

Any questions?

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