One organ plays two tunes - how is your pancreas today?

Dr HJ Bodansky
Associate Professor University of Leeds,
Consultant Physician Leeds Teaching Hospitals
Declaration of interests

Received honoraria for attending meetings and presenting on behalf of:

- Mylan
The pancreas...

...an organ which plays 2 tunes
endocrine & exocrine
Poll...

How many people in the room are aware of pancreatic exocrine insufficiency?
Learning Outcomes

➢ The relationship between the endocrine & exocrine pancreas

➢ Types of diabetes

➢ Pancreatic exocrine insufficiency (PEI)
  • What is it
  • How to diagnose
  • How to manage
Importance of diagnosis

➢ The **right** diagnosis = the **right** treatment

➢ The **wrong** diagnosis = the **wrong** treatment

➢ **No** diagnosis = **no** treatment
Diagnosis

➢ You can only diagnose a condition that you have heard of

➢ You can only diagnose a condition you have heard of and considered as possible

➢ Consider all possibilities...
 Depends on the type of diabetes

Which types of diabetes do you know?
Types of diabetes

- Type 1 insulin dependent
- LADA latent autoimmune diabetes in adults
- Type 2
- Pancreatic disorders
- Drug induced
- Endocrine disorders
- Ethnic variants of diabetes
- Monogenic: MODY
- Genetic syndromes
Diabetes secondary to pancreatic disorders

- Chronic or acute pancreatitis
- Calcific tropical pancreatitis
- Pancreatectomy
- Pancreatic cancer
- Cystic fibrosis
- Haemochromatosis
Pancreatic disease: History

- Previous pancreatitis
- Pancreatic surgery
- Alcohol excess
- Family history: pancreatitis or pancreatic disorder, haemochromatosis
- Related conditions: hypogonadism, liver disorder
- Steatorrhoea
Pancreatic disease: Examination

- Nutrition, BMI
- Features of liver disease
- Hypogonadism
Pancreatic disease: Investigation

- Plain x-ray of the abdomen for pancreatic calcification
- CT scan of the abdomen for pancreatitis / liver disease
- Faecal elastase test
- Ferritin, genetic testing for haemochromatosis
Pancreatic Calcification
Raised Ferritin Level

- Acute phase reactant
- Alcohol excess
- Liver disease
- Uncontrolled diabetes
- Hemochromatosis
One organ, two tunes

Compound gland with distinct exocrine and endocrine functions

- Exocrine tissue: 80% to 85% of the pancreas
- Exocrine acini secrete digestive enzymes and bicarbonate
- Endocrine pancreas: Islets of Langerhans secrete insulin and glucagon
Pancreatic exocrine insufficiency

Condition in which quantity of activated enzymes secreted in response to a meal are insufficient for maintaining normal digestion

- Reduced availability of pancreatic enzymes
  - Loss of parenchyma
  - Pancreatic duct obstruction
  - Inadequate stimulation of enzyme production due to postprandial asynchrony, coeliac disease


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Better Health for a Better World
**Using faecal elastase 1 (FE-1) screening. All studies used a threshold <200 μg/g FE-1 to indicate potential PEI


Why might patients T1 & T2 diabetes have PEI?

They can develop chronic changes in their pancreas

- Lack of trophic insulin effect
- Activation of stellate cells by hyperglycaemia
- Dysregulation of islet cell hormones
- Diabetic neuropathy
- Diabetic microangiopathy
- Recurring subclinical pancreatitis, due to diabetic acidosis
- Simultaneous autoimmune against endocrine and exocrine

Pancreatic exocrine insufficiency
PEI symptoms

- PEI causes malabsorption and maldigestion, resulting in symptoms of:
  - Steatorrhoea is the most common symptom of PEI and is characterized by loose, greasy, foul-smelling voluminous stools that are difficult to flush
    - Steatorrhoea may not appear until PEI is advanced


PEI signs

- Low BMI
- Low insulin dose
- Insulin sensitivity
- Falling insulin requirements
- Features of haemochromatosis, stigmata of liver disease
Symptoms are often missed because...

- Gastrointestinal symptoms are commonly attributed to side-effects of diabetes medications, particularly:
  - metformin
  - glucagon-like peptide-1 receptor agonists
  - dipeptidyl peptidase-4 inhibitors
- Autonomic neuropathy
- Small intestinal bacterial overgrowth
- Coeliac disease
- Irritable bowel syndrome / inflammatory bowel disease
- Bowel cancer
What should I do if I suspect PEI?

- Faecal elastase test (FE1) – a non-invasive pancreatic function test
- Faecal elastase is an enzyme produced in the pancreas; the measurement of this correlates to the overall pancreatic secretion

<table>
<thead>
<tr>
<th>&gt;200ug/g of stool</th>
<th>Normal Value</th>
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<tbody>
<tr>
<td>100-200ug/g of stool</td>
<td>Suggests mild pancreatic insufficiency</td>
</tr>
<tr>
<td>&lt;100ug/g of stool</td>
<td>Suggests severe pancreatic insufficiency</td>
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Should we routinely ask about GI symptoms?

- During DM clinic, routinely asked about GI symptoms, including diarrhoea (Type 5, 6 and 7 were considered abnormal), steatorrhoea or unexplained weight loss
- Faecal elastase was performed

Cummings M et al. Practical Diabetes 2015; 32(2): 54-58

25 patients did not provide a FE1 sample

- 220/288 (76%) had no symptoms
- 68/288 (24%) had 1 symptom
- 25/43 (58%) had low FE1
- 18/43 (42%) had normal FE1
- 6/18 (33%) had moderate PEI
- 12/18 (67%) had severe PEI

Who should we screen?

PEI may be more likely in people with:

• History of pancreatic disease of surgery

• History of high alcohol intake

• Recurrent unexplained hypoglycaemia, decreasing insulin requirements, or particularly erratic blood glucose control

• Long duration of T1DM
Why should we treat?

It’s important to treat PEI to avoid complications

- PEI leads to maldigestion and malabsorption which results in:
  - Low bone mineral density
  - Vitamin Deficiencies
  - Malnutrition
How to treat PEI

- Pancreatic Enzyme Replacement Therapy (PERT) is the main treatment for PEI in adults, children and infants
- Orally-administered PERT provides the extra digestive enzymes needed to maintain healthy digestion

How PERT works

1. PERT capsules, tablets, granules or powder taken with each meal
2. Capsules/tablets dissolve in the stomach releasing enteric-coated pancreatic enzyme complexes that mix with food
3. Enteric coating prevents digestion of the complexes in the stomach. Not all preparations are enteric coated
4. Enteric coating dissolves in the duodenum releasing the enzymes to digest the nutrients
5. Complexes must be small enough to pass through the pylorus

References:
Recommended initial doses of PERT:

- **Main Meal**: 50,000 units lipase/meal
- **Snacks**: 25,000 units lipase/snack

PERT should be taken *with* food
Gastrointestinal disorders in diabetes—could it be pancreatic exocrine insufficiency?

- Algorithm developed by a multidisciplinary expert panel
- Supported via an educational grant from Mylan
- To raise awareness of PEI in diabetes
- To give a clear and concise management algorithm
- To ultimately give better care to people with diabetes who may have PEI but who have not been diagnosed
Summary

✓ PEI pancreatic exocrine insufficiency
✓ More common than we may think
✓ Can be diagnosed if it is considered
✓ Suspect in diabetes, alcohol, pancreatic disorders
✓ Look out for steatorrhoea, diarrhoea, weight loss
✓ Order a faecal elastase test
✓ Easy to treat with enzyme supplements
To find out more about PEI including its diagnosis, treatment and management, and the conditions underlying it, visit the new website resource for HCPs:
Thank you for your attention!

Any questions?