Nutritional assessment and treatment for patients diagnosed with pancreatic cancer.

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Patients and carers struggle with the lack of dietary information and support.

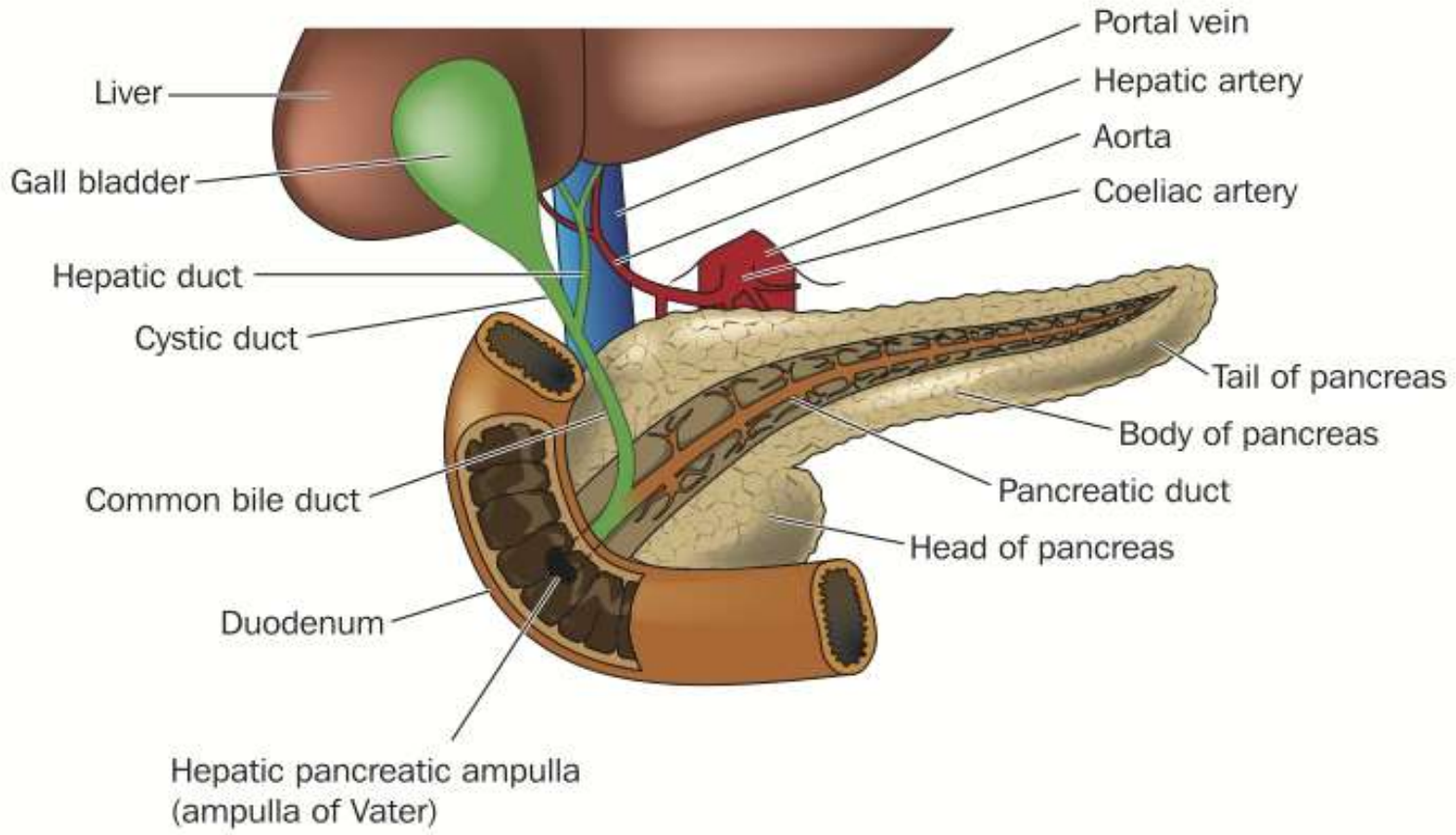
(Gooden and White, 2013)

Bozzetti and Group (2009) recommend early involvement of dietitians and nutritional assessment to guide management due to high nutritional risk in pancreatic cancer

Discussion topics

- Pancreatic anatomy and physiology
- Nutritional assessment
- Pancreatic enzyme replacement therapy (PERT)
- Secondary diabetes (type 3c)
- Psychological therapies
- NICE guidelines (2018)
- Case study and nutritional treatment

Anatomy


Portal vein
Hepatic artery
Aorta
Coeliac artery
Liver
Gall bladder
Hepatic duct
Cystic duct
Tail of pancreas
Body of pancreas
Pancreatic duct
Common bile duct
Head of pancreas
Duodenum
Hepatic pancreatic ampulla
(ampulla of Vater)

Histology and function

- **Endocrine** (Islets of Langerhans)
  Alpha cells – glucagon
  Beta cells - insulin
  Delta Cells - Somatostatin

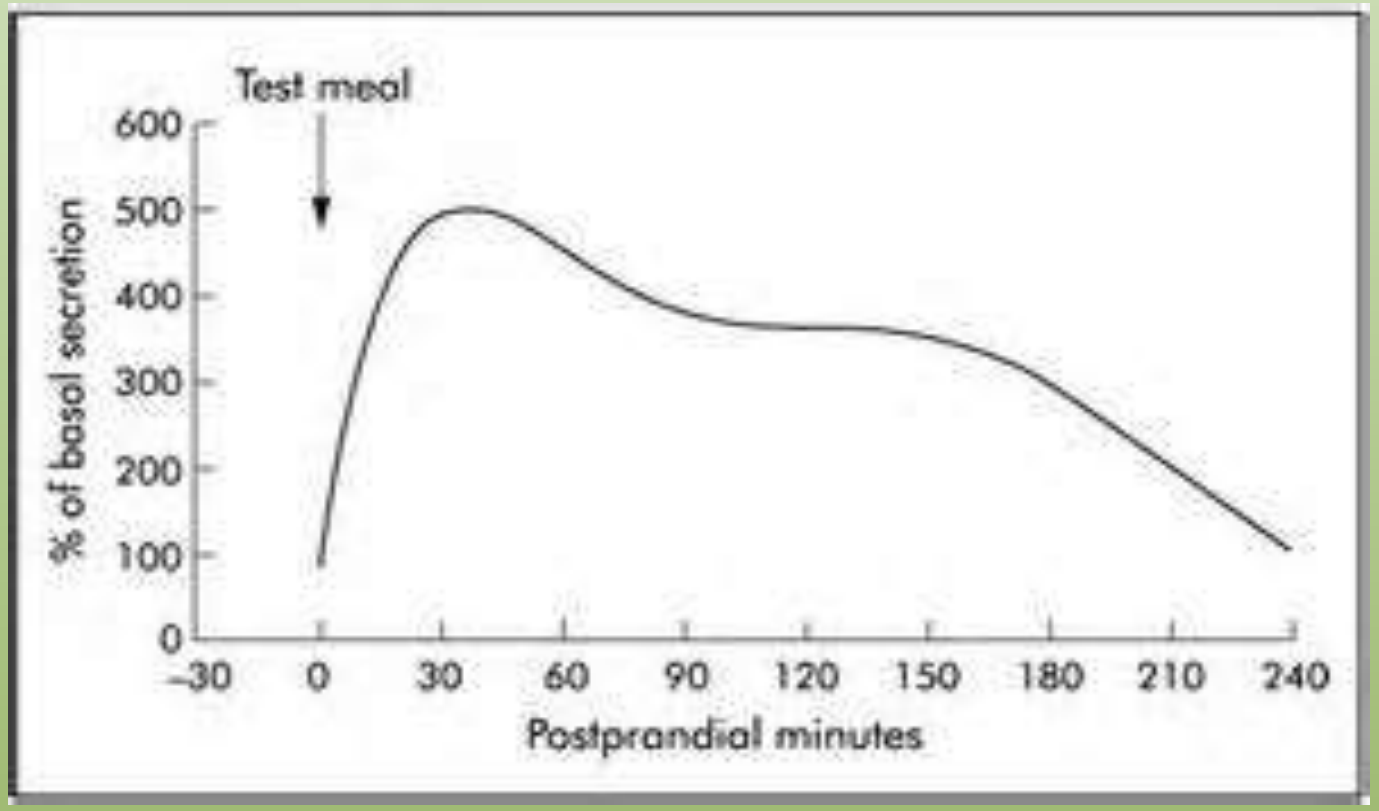
- **Exocrine** (Acinar cells and ducts)
  Trypsinogen and chymotrypsinogen - protein
  Lipase
  Amylase carbohydrates
  Bicarbonate alkaline ph 7-8

- **Controlled by:** gastrin, CCK, Secretin, incretins (Glucagon-like peptide-1 (GLP-1), Glucose dependent insulinotrophic polypeptide (GIP)

Pancreatic enzyme response to a meal

Lipase, amylase, trypsin and chymotrypsin

(Taken from Keller and Layer, 2005)



Lipase secretion rates

(Adapted from keller and Layer 2005)

	Interdigestive	Maximal	2 hours postprandial
U/min	1000	3000 – 6000	2000 – 4000
U/hour	60 000	180 000 – 360 000	120 000 – 240 000

Exocrine tumours – adenocarcinoma (95%)
65 - 75% in the head of the pancreas

Presenting symptoms affecting nutritional status

- **Abdominal pain**
- **Jaundice**
- **Weight loss**
- **Poor appetite**
- **Nausea**
- **Vomiting – duodenal/gastric obstruction**
- **Indigestion**
- **Diarrhoea**
- **Steatorrhoea**
- **Constipation**
- **Taste changes**
- **Lethargy**
- **Feeling full**
- **Depression (33 – 70%) Torgerson and Wiebe 2013, Gooden et al 2016**
- **Physical activity**
- **Diabetes (Misdiagnosed/undiagnosed Ewald et al 2013)**

1 Physical

2 Endocrine insufficiency

3 Exocrine insufficiency –

Pancreatic enzyme insufficiency (PEI)

Pancreatic head 60 -90%

Pancreatic body/tail 30 -50% (Sikkens et al,2014)

4 Metabolic

Hyper metabolism and catabolism

Complex metabolic disorder which is poorly understood and difficult to treat

(Fearon, et al, 2011, 2013)

Cancer cachexia

Weight loss

Different to simple starvation

- **Weight loss**
  - 36 - 80% of patients with pancreatic cancer develop cancer cachexia (Fearon, et al, 2006, Bachmann, et al, 2009)
  - 40% of patients at time of surgery have cancer cachexia (Bachmann, et al, 2008)
  - 40% overweight/obese patients have sarcopenic obesity (Tan et al, 2009)

  - **Weight loss is an independent predictor** for reduced response rates to chemo/radiotherapy (Bachmann, et al 2008, 2009)
  - Reduced post operative outcomes (Pausch, et al, 2012)
  - Reduced survival (Tan, et al, 2009)

Affects quality of life due to reduced functional status and body image

Less then 10% weight loss – responds to nutritional support

Symptoms of fat maldigestion and Steatorrhoea

- 90% reduction in function before evidence of maldigestion ???
- Lipids are the most sensitive to deactivation due to ph. 7-8 and proteases
- Digestion of carbohydrate and protein throughout the gut starting in the mouth
- Reduction in oral intake of fat to manage symptoms – check if patients have done this

Any combination of or all:

Pale
Floating
Difficult to flush
Greasy
Sticky
Large volume stool
Diarrhoea/constipation
Foul smelling
Wind and bloating
Pain
Urgency

Pancreatic Enzyme Replacement Therapy (PERT)

- Source: Porcine (allergy, vegetarian/vegan an
- Capsule containing enteric coated granules (le 2mm)
- Temperature and ph. sensitive
- No clear maximum treatment guidelines
    - 400 000 units of lipase per day
    - 10 000 units per kg/day
    - 5000 – 4000 IU lipase per g fat

PERT Preparations

Manufacturer	Product name	Lipase /U	Enteric coated
Abbott (Mylan)	Creon 10 000 Creon 25 000 Creon 40 000 Creon micro	10 000 25 000 5000/g	Yes Yes gastro resistant granules
Merck	Nutrizym 22	22 000	Yes - minitablets
Janssen - Cilag	Pancrease HL	25 000	Yes - minitablets
Essential	Pancrex granules Pancrex V capsules Pancrex V 125 capsules Pancrex V Forte tablets Pancrex V Powder Pancrex V tablet	5000 /g 8000 2950 5600 25 000/g 1900	No No No Yes No Yes

Right time, right place..... Right ph.

- **Goal..... enough active enzymes in the duodenum with food**

- 44 000 - 75 000 with a meal and 22 000-50 000 with a snack/nutritious fluids/supplements
- Adjust to fat content of meal/snack
- Take at the start of eating, during and at the end of a meal (Dominguez-Munoz, 2013)
- Small amount of cold liquid
- Take capsules whole (do not sprinkle on food, crush or chew)
- If need to open – mix microspheres with acid fruit puree or yogurt
- Omit enzyme with small portions of fat free foods/fluids
- Varies from patient to patient:
  - Functional pancreatic tissue
  - Differing amounts of fat in the diet
  - Anatomical

- **Side effects** – Flatulence, abdominal bloating, nausea, mouth ulcers, anal irritation
- Constipation ?due to improved digestion.
- Fibrosing colonopathy (50 000 U lipase/kg/body weight)

Improving nutritional status

- Manage symptoms (liaise with GP/hospital)
- Pancreatic enzyme replacement therapy (PERT) understanding, compliance, dose adjustments, timings
- Diagnose and treat endocrine insufficiency - nutritional messages for secondary diabetes
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- **Provide nutritional support**

- Exercise – lean body mass (Fearon, 2014)
- Psychological support

Unresolved symptoms

- Check compliance and understanding
- “sounds like a lot”
- ? Is dose sufficient (increase)
- Add PPI (lipase active ph 5.5)
- Antidiarrheal agent

- Consider other causes:

  Small bowel Bacterial Overgrowth (SBBO)

  Bile salt malabsorption

  Coeliac disease (Bustillo, et al. 2009)

Literature search of diabetes secondary to pancreatitis and pancreatic cancer (2002 – 2017)

- Type 2 diabetes and obesity risk factor for pancreatic cancer.
- Diabetes develops up to 24 - 36 months prior to diagnosis of pancreatic cancer ?tumour affecting insulin resistance?
- Limited research in the UK

- Various terms used within the literature: pancreatogenic, secondary, pancreatic cancer diabetes mellitus (PC-DM), Type 3c, Type3cDM

- Since 2008 Type 3c has increasingly been used in the literature

- Prevalence ????? **5 – 10% of all diabetics**

- 50% of type 3c misclassified in specialist centres (Ewald, 2013)

- Lack of resources and understanding –
  - under and misdiagnosis
  - Inappropriate health messages and nutritional advice

- ? Newly diagnosed diabetic with weight loss – screen for pancreatic cancer

Classification

World Health Organisation (1999)

and

American Diabetes Association (2014)

3c Diseases of the exocrine pancreas

- Fibrocalculous pancreatopathy
- Pancreatitis
- Trauma/pancreatectomy
- Neoplasia
- Cystic fibrosis
- Haemochromatosis
- Other

Etiologic classification of diabetes mellitus.

I. Type 1 diabetes (β-cell destruction, usually leading to absolute insulin deficiency)
   A. Immune mediated
   B. Idiopathic
II. Type 2 diabetes (may range from predominantly insulin resistance with relative insulin deficiency to a predominantly secretory defect with insulin resistance)
III. Other specific types
   A. Genetic defects of β-cell function
      1. MODY 1 (Chromosome 12, HNF-1α)
      2. MODY 3 (Chromosome 20, HNF-4α)
      3. MODY 2 (Chromosome 7, glucokinase)
      4. Other very rare forms of MODY (e.g., MODY 8: Chromosome 13, insulin promoter factor-1; MODY 6: Chromosome 2, NeuroD1; MODY 7: Chromosome 9, carboxyl ester lipase)
      5. Transient neonatal diabetes (most commonly ZAC/HYAMI imprinting defect on 6q24)
      6. Permanent neonatal diabetes (most commonly KCNJ11 gene encoding Kir6.2 subunit of β-cell K_{ATP} channel)
      7. Mitochondrial DNA
      8. Others
   B. Genetic defects in insulin action
      1. Type A insulin resistance
      2. Leprechaunism
      3. Rabson-Mendenhall syndrome
      4. Lipoatrophic diabetes
      5. Others
   C. Diseases of the exocrine pancreas
      1. Pancreatitis
      2. Trauma/pancreatectomy
      3. Neoplasia
      4. Cystic fibrosis
      5. Hemochromatosis
      6. Fibrocalculous pancreatopathy
      7. Others
   D. Endocrinopathies
      1. Acromegaly
      2. Cushing's syndrome
      3. Glucagonoma
      4. Pheochromocytoma
      5. Hyperthyroidism
      6. Somatostatinoma
      7. Aldosteronoma
      8. Others
   E. Drug or chemical induced
      1. Vacor
      2. Pentamidine
      3. Nicotinic acid
      4. Glucocorticoids
      5. Thyroid hormone
      6. Diazoxide
      7. β-Adrenergic agonists
      8. Thiazides
      9. Dilantin
      10. γ-Interferon
      11. Others
   F. Infections
      1. Congenital rubella
      2. Cytomegalovirus
      3. Others
   G. Uncommon forms of immune-mediated diabetes
      1. Stiff-man syndrome
      2. Anti-insulin receptor antibodies
      3. Others
   H. Other genetic syndromes sometimes associated with diabetes
      1. Down syndrome
      2. Klinefelter syndrome
      3. Turner syndrome
      4. Wolfram syndrome
      5. Friedreich ataxia
      6. Huntington chorea
      7. Laurence-Moon-Biedl syndrome
      8. Myotonic dystrophy
      9. Porphyria
      10. Prader-Willi syndrome
      11. Others
IV. Gestational diabetes mellitus

Patients with any form of diabetes may require insulin treatment at some stage of their disease. Such use of insulin does not, of itself, classify the patient.

American Diabetes Association Dia Care 2014;37:S81-S90

Incidence of diabetes vs. methods used to diagnose hyperglycaemia in pancreatic cancer patients

	Patient history or medical records	Fasting blood glucose	HbA1c	OGTT 75g
% diagnosed as diabetic	12 – 29%	47%	41.7%	77% (diabetic and glucose intolerance)

Pathophysiology

- **Absence of islets** – total pancreatectomy
- (absolute deficiency of insulin, glucagon and pancreatic polypeptide)
- **Partial absence of functional islets** – chronic
- pancreatitis, partial pancreatectomy, severe acute
- pancreatitis
- **Paraneoplastic** – pancreatic ductal adenocarcinoma

<u>Potential mechanisms of hyperglycaemia</u>

Insulin deficiency

Immunopathogenesis

Hepatic insulin resistance caused by reduction in pancreatic polypeptide

Peripheral insulin resistance

Reduced incretin effect due to malabsorption of carbohydrate

- **Treatment and medication choice?**
- **Effect of diabetes on overall outcome and survival in pancreatic cancer?**
- **Need for evidence based guidelines on diagnosis and treatment?**

Case study – 68 year old female

- 2 week cancer wait referral
- Pancreatic head mass – suspected adenocarcinoma pancreas
- Referred to dietitian whilst attending MDT pancreatic clinic
- Struggling with poor appetite, lethargy, weight loss (8kg over previous 8 weeks), steatorrhoea, taste changes, jaundiced, polyuria and thirst
- Weight 57kg Height 1.68m BMI 20kg/m2
- Previous weight 65kg (12% weight loss over 2 months)
- Random blood glucose 28mmol/l
- Inoperable
- Referred to oncology for assessment for chemotherapy

Nutritional requirements
Out with the old in with the new!

Henry (2005)

- 10.2 x 57 + 572 = 1153
- 10% SF
- 1.25 PAL

- **Kcal 1585**

- Protein 0.2g/kg hyper metabolic
- **71g day**

- Previous BMI 23kg/m2
- Repletion

PENG (2018)

- Pancreatic cancer 24kcal /kg REE
- Range 22 – 27kcal/kg
- PAL 1.25

- **Kcal - 1567 – 1923**

- Protein 1g/kg if possible up to 1.5g/kg
- **57g – 85g**

Causes of weight loss

1. Hyperglycaemia - Newly diagnosed diabetic – type 3c/secondary
2. Maldigestion due to blocked pancreatic and biliary duct
3. Reduced oral intake due to GI symptoms, taste changes, lethargy
4. Tumour mediated hyper metabolism and cachexia

Treatment

Management of diabetes

Diabetic medication – gliclazide 40mg bd started by oncologist (4pm Friday)

Management of maldigestion

Commenced Pancreatic Enzyme Replacement 75 000 with meals and 50 000 with snacks

Nutritional support

Dietary advice – nutritional support – little and often, avoid simple sugars, High protein/high kcal, oral nutritional supplements

NICE guidelines

Pancreatic cancer in adults: diagnosis and management

Feb 2018

Nutritional management:

- Offer enteric-coated pancreatin for people with unresectable pancreatic cancer
- Consider enteric coated pancreatin before and after pancreatic cancer resection
- Do not use fish oils as a nutritional intervention to manage weight loss in people with unresectable pancreatic cancer
- For people who have had a pancreatoduodenectomy and who have a functioning gut, offer early enteral nutrition) including oral and tube feeding) rather than parenteral nutrition

Mental Health and CBT

Case study

- 72 year old male
- Diagnosed adenocarcinoma pancreatic head
- Surgical management with curative intent
- (Pylorus Preserving Pancreaticoduodenectomy PPPD)
- Post operative day 5 – 12 Gastric out let obstruction
- Post operative day 12 – 22 struggling with severe loss of appetite
- NG fed from day 7 – 22

Cognitive Behavioural Therapy

- Explored and managed physical symptoms
- Socratic questioning and guided discovery
- Thoughts and recognition of thinking
- Own experiences and experiences of others

Sister in law – previous colonic surgery and BO

- Avoid reassurance and advice giving

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