Diabetes and Pancreatic Cancer

Pancreatic Cancer UK Society
Louise Hopewell
Diabetes Specialist Nurse
Wednesday 09/10/19

The Christie NHS
NHS Foundation Trust

Learning Objectives

- ✓ To understand that managing patients with diabetes or at risk of developing diabetes is both essential and achievable

- ✓ To increase awareness of the challenges patients and their families face when managing the complexities of both diabetes and pancreatic cancer

Topics to be discussed

- ✓ Diabetes
- ✓ Diabetes and Cancer
- ✓ Challenges Managing Pancreatic Cancer : glycaemic and nutritional perspective
- ✓ Is it important to manage glycaemia ?
- ✓ Case Studies
- ✓ Key messages

Types of Diabetes

- T1DM-an immune mediated condition associated with beta cell destruction leading to absolute insulin deficiency
- T2DM-peripheral insulin resistance and beta cell dysfunction
- T3cDM -pancreatogenic diabetes(impairment in endocrine function leading to pancreatic exocrine damage)
- Steroid induced diabetes
- Gestational diabetes
- Monogenic diabetes
- (T3 DM Alzheimers)

Glucose lowering agents

- Biguanides
- Sulphonylureas
- Prandial Glucose regulators
- Alpha-Glucosidase inhibitors
- GLP 1 - Incretin mimetics
- SGLT-2 Inhibitors
- DPP-4 Inhibitors

Insulin

- Rapid acting insulin analogue

Novorapid,Humalog, Apidra, Fiasp

- Short acting insulin

Actrapid,Humulin S, Hypurin porcine neutral, Hypurin bovine neutral, Insuman rapid

- Intermediate acting insulin

Insulatard, Humulin I, Insuman Basal, Hypurin porcine isophane, Hypurin bovine isophane

Insulin

- Long-acting analogue

  Lantus, Levemir, Degludec,Toujeo,Abasaglar

- Premixed (biphasic)

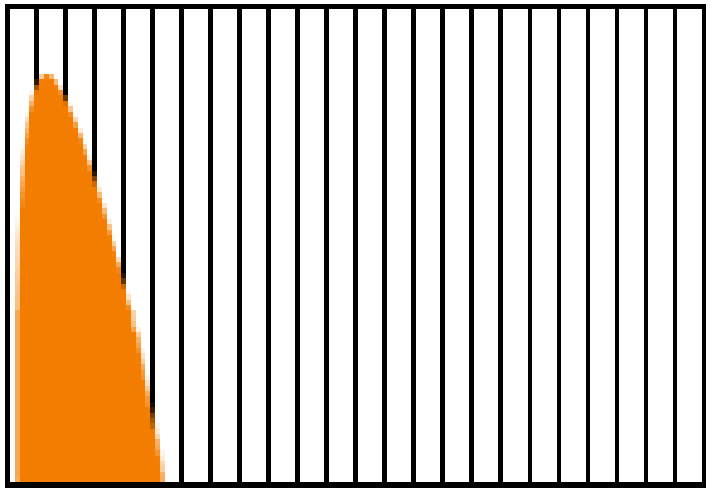
  Humulin M3, Insuman Comb15,25,50, Hypurin porcine 30/70 mix

- Premixed (biphasic) analogue

  Humalog mix 25,humalog mix 50, Novomix 30

Rapid/Short Acting Insulins

Onset, Peak, Duration



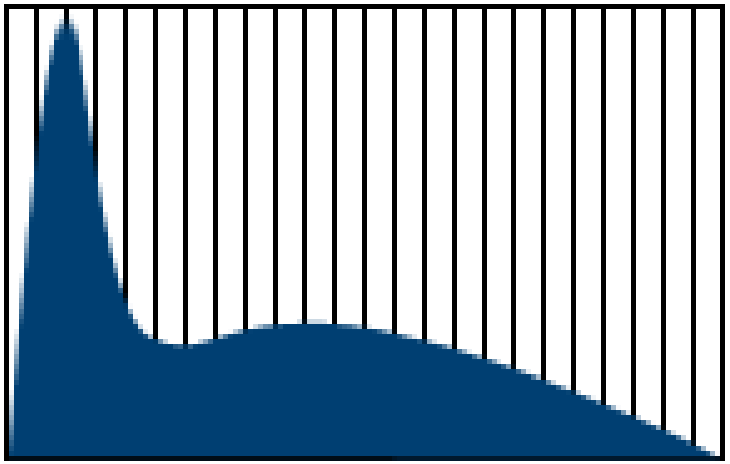
Novorapid Insulin

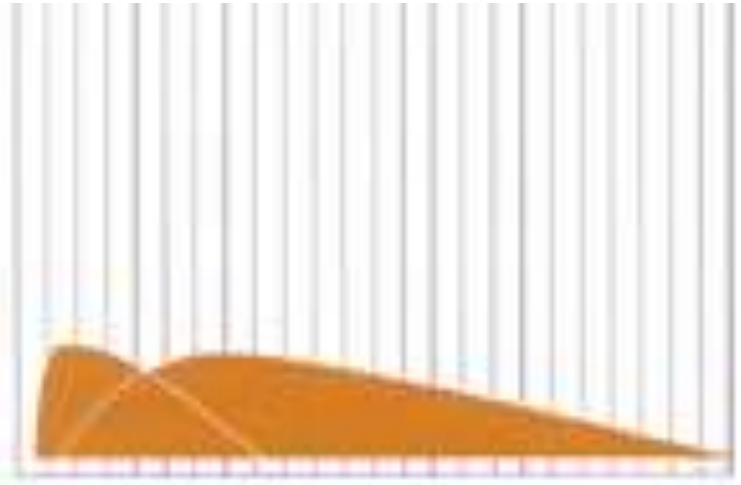
- **Onset:** within 10 -20 minutes
- **Maximum effect:** 30-240 mins
- **Duration:** 2-5 hours

Actrapid Insulin

- **Onset:** within 30 minutes
- **Maximum effect:** 1-3 hours
- **Duration:** 8 hours

Pre Mixed Insulins
Onset, Peak, Duration

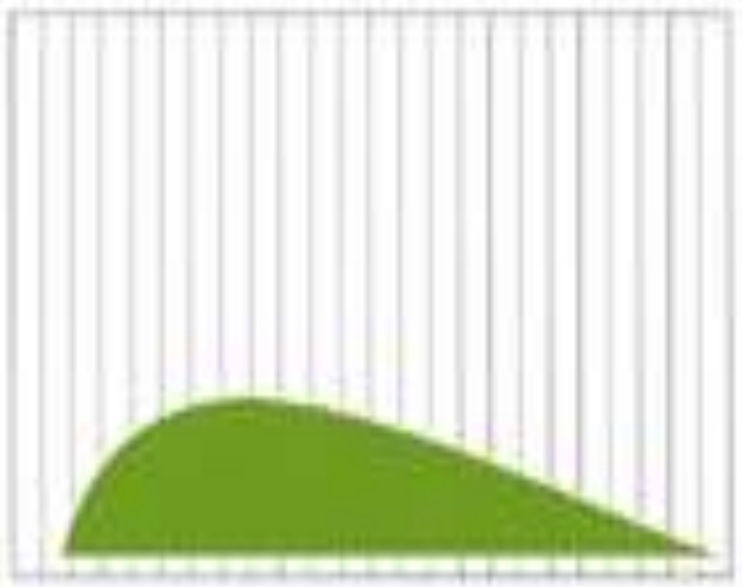




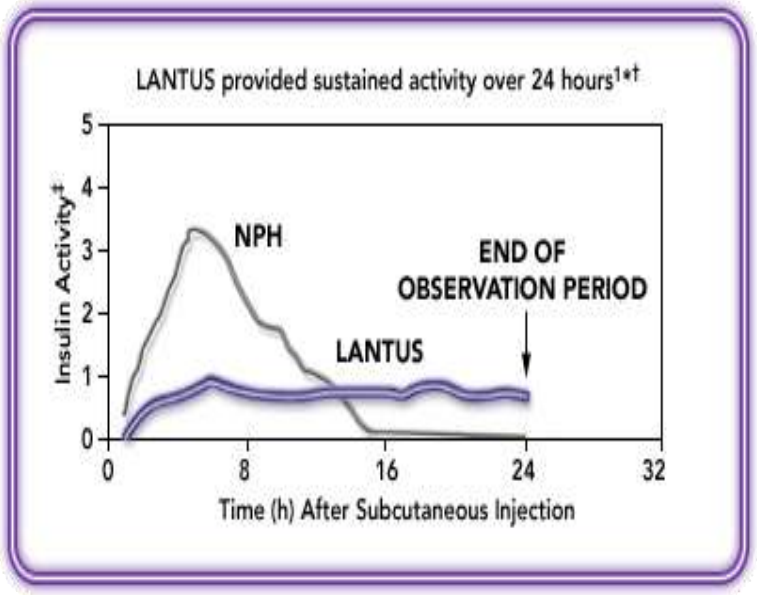
Novomix 30 Insulin
Onset: 10-20 minutes
Maximum effect: 30-240 minutes
Duration: 11-24 hours

Humulin M3 Insulin
Onset: within 30 minutes
Maximum effect: 2-8 hours
Duration: 24 hours

Intermediate/Long Acting Insulins
Onset, Peak, Duration

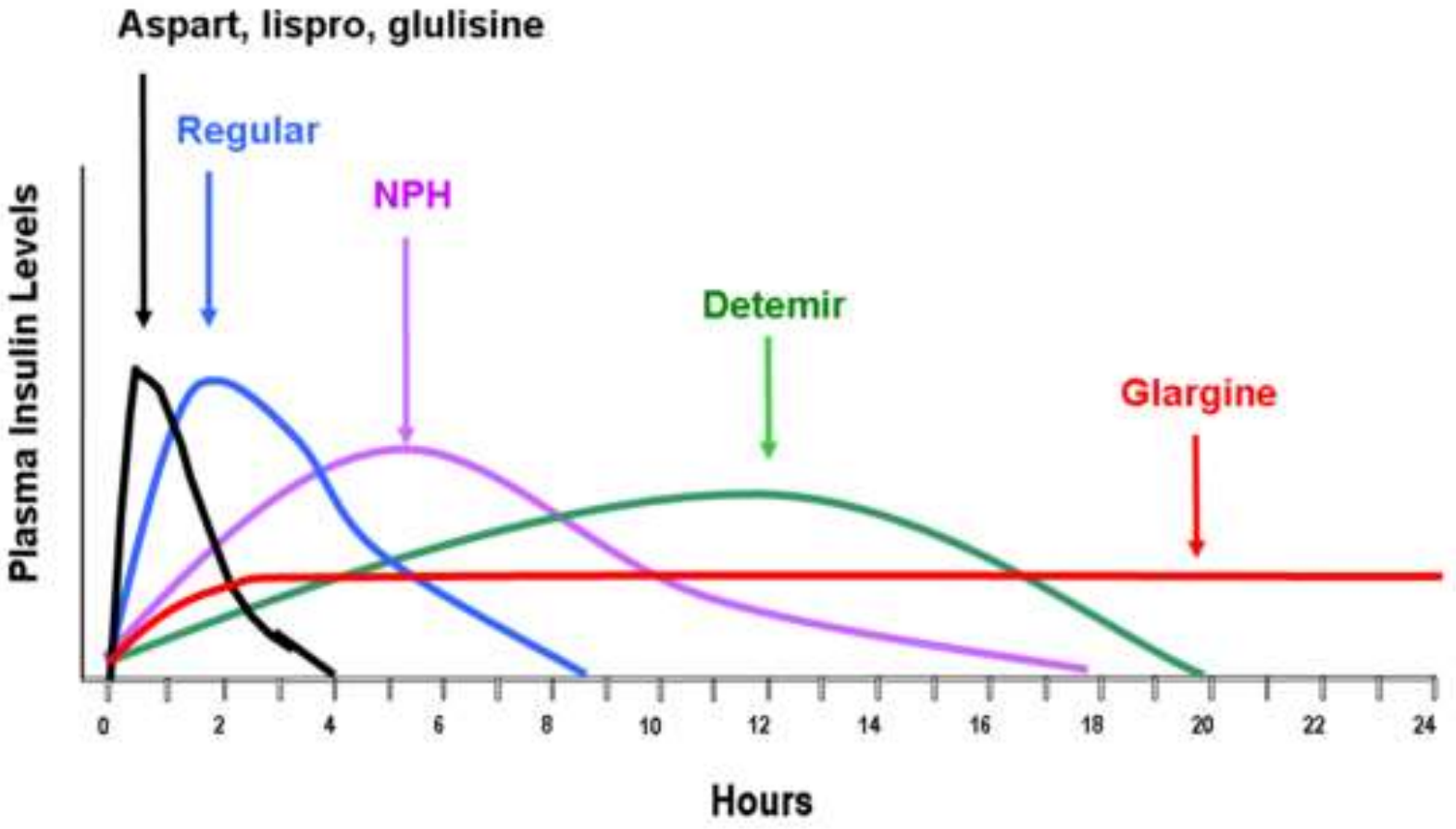


Onset: within 30 -90 minutes
Maximum effect: 6-8 hours
Duration: 11-24 hours

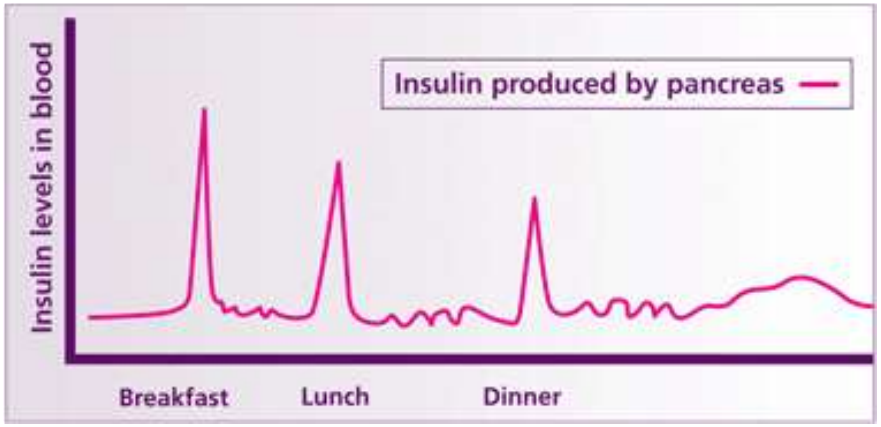


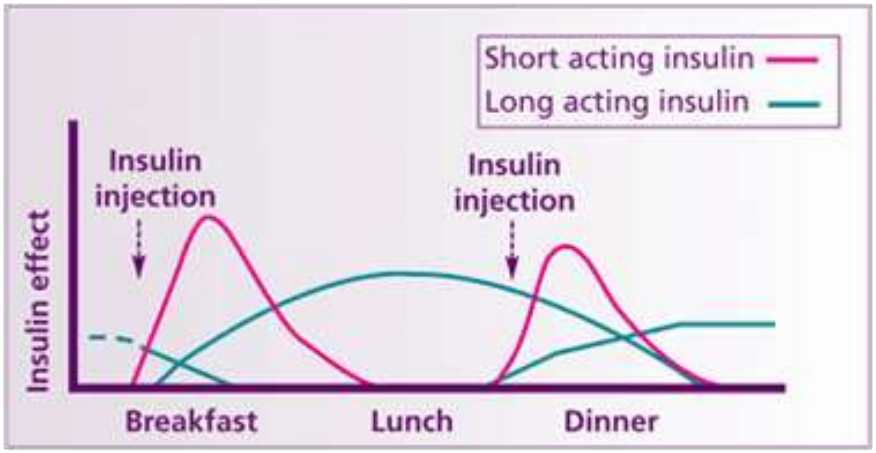
Maximum effect: little no peak
Duration: up to>24 hours

Insulin –comparisons of action

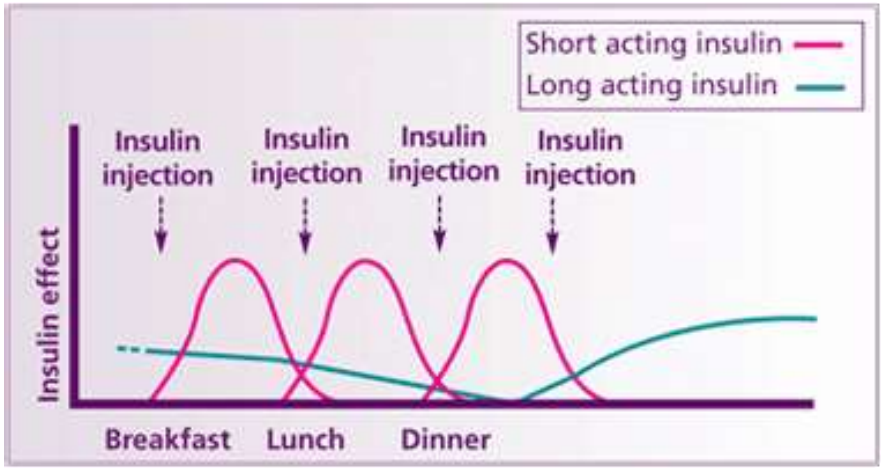


Insulin – regimens



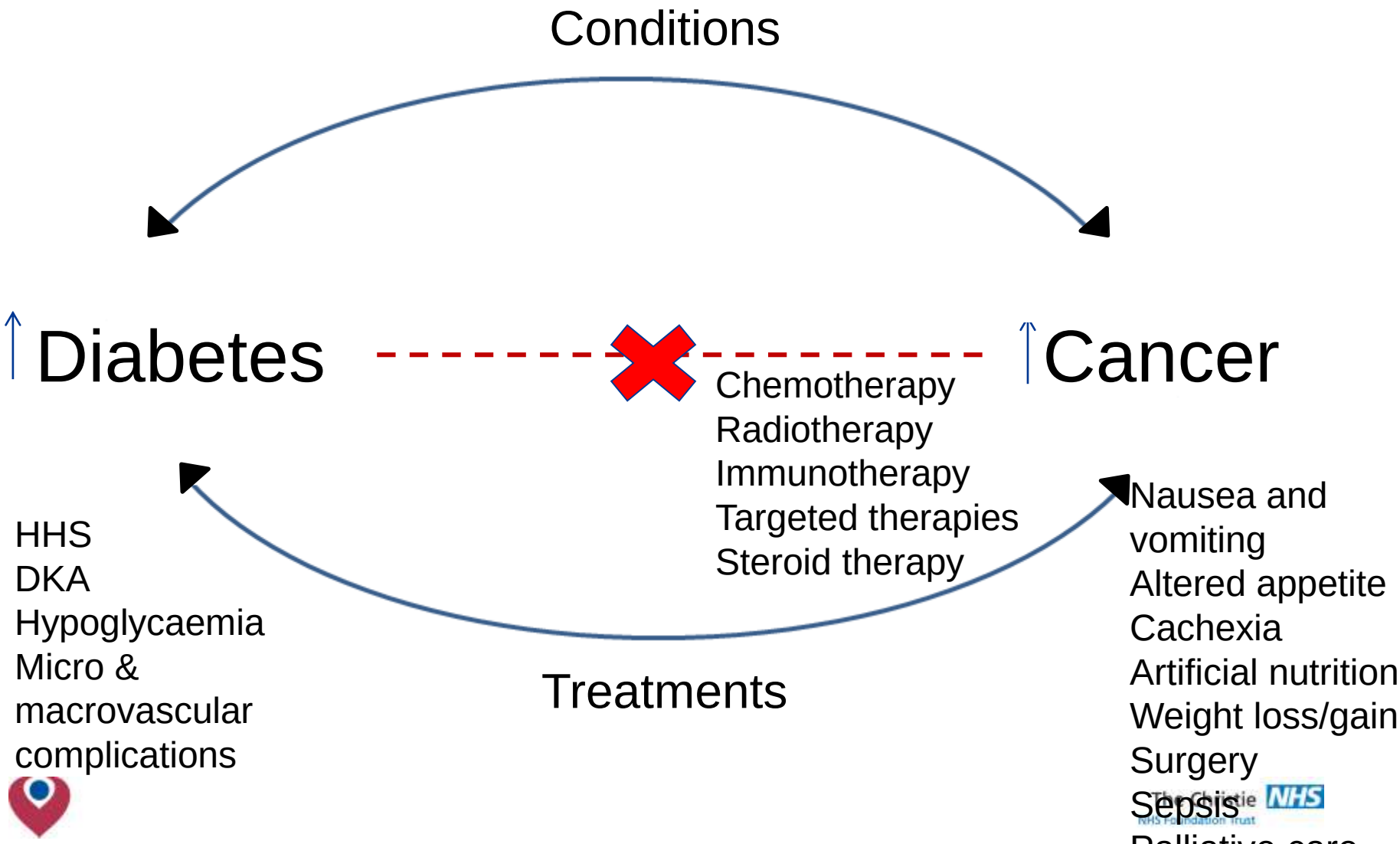


mixed insulin regimen



basal bolus regimen

Diabetes and Cancer



Diabetes and Pancreatic Cancer (PC)

- PC and diabetes have a bidirectional and complex relationship
- Approx 50% of patients with pancreatic cancer have diabetes and 85% have glucose intolerance
- This frequently manifests as early as 2-3 years pre pancreatic cancer diagnosis
- Conversely patients with new onset diabetes have a 5-8 fold increased risk of being diagnosed with pancreatic cancer within 1-3 years of developing diabetes

Diabetes and Pancreatic Cancer (PC)

- As with diabetes, obesity related insulin resistance and hyperinsulinaemia are thought to play a major role in the development of PC

- Proposed mechanism of this diabetes and PC link include hyperinsulinaemia and abnormalities in insulin/IGF receptor pathways – promotes survival and progression of early malignant cells by increasing tumour growth and decreasing cellular apoptosis

- Presentation and progression can be different to type 2 diabetes (type 3c)

- Sudden deterioration in glycaemic control in usually well controlled patient

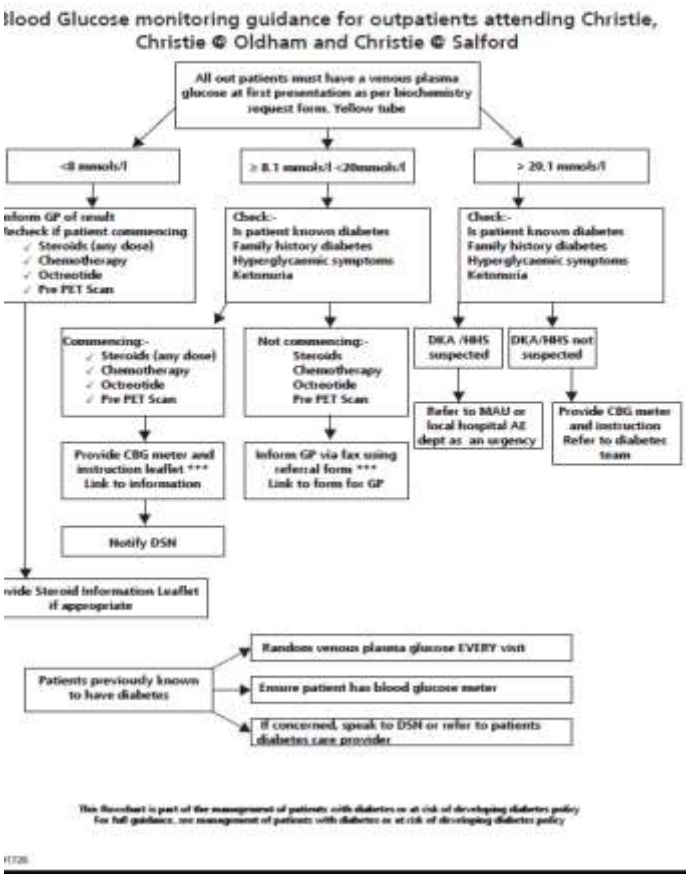
- Worse glucose control, profound weight loss

Diabetes and Pancreatic Cancer (PC)

- Total pancreatectomy results in total insulin deficiency and near absent glucagon production, all patients develop diabetes and will require insulin
- Near total pancreactectomy (95% pancreas resected) most patients will require insulin
- Proximal pancreatectomy (Whipples) 50% develop new onset diabetes
- Distal pancreactectomy (tail of pancreas malignancies) develop diabetes much less frequently as flow of pancreatic secretions is not normally interrupted
- Middle pancreactectomy as much of the pancreatic parenchyma is preserved the risk of endocrine insufficiency is reduced

- Management is therefore individual, challenging and complex

Management: Known Diabetes/at risk of developing diabetes



- ✓ All patients must have plasma glucose check at each visit
- ✓ All patients with known diabetes MUST be monitoring CBG

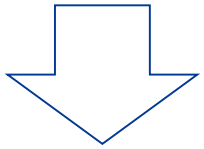
The Christie NHS
NHS Foundation Trust

Management – at risk of developing diabetes

- All patients check plasma glucose at each visit
- Plasma glucose >8.1 mmols/l –CBG monitoring as per Christie policy
- CBG > 12 mmols/l regularly start glucose lowering treatment
- Gliclazide used with caution renal/hepatic impairment
- Insulin therapy
- Post Pancreatectomy –individualised treatment but CBG can be very labile-decreased glucagon production

Challenges : glycaemic control

- Weight loss
- Requirement for nutritional supplements
- Nausea can be controlled but anorexia and taste changes can reduce calorie intake
- GI issues that occur due to PI e.g. diarrhoea
- Steroids increase hepatic glucose production and increase insulin resistance
- Chemotherapy mixed in dextrose
- Change in cancer treatment regimens



- Hypoglycaemia
- Hyperglycaemia
- Diabetic Ketoacidosis(DKA)
- Hyperosmolar Hyperglycaemic State (HHS)
- Osmotic symptoms
- Sudden deterioration in glycaemic control -masked

Challenges : points to remember

- Adjustment to glucose lowering regimes are essential
- These changes must be supervised by diabetes experts
- Regimes advised may not be standard diabetes management guidance
- Patients must be followed up closely
- Collaborative work with oncology and nutritional team is essential
- Hypoglycaemia- glucagon response
- Liver metastases –glucose response

- Consideration of the impact of pre existing diabetes related complications e.g. gastroparesis
- Patients with diabetes have increased risk of infection, electrolyte abnormalities, vascular events, renal insufficiency and neuropathy

Challenges :patients perspective

- Unnecessary hospitalisations
- Conflicting information
- Information overload
- Problems accessing strips etcLack of understanding
- Poorer glycaemic control than patient used to
- Different dietary advice
- Psychological impact

57 M Δ Metastatic Pancreatic Adenocarcinoma Dec 2016

Sept 2016 Type 2 diabetes diagnosed metformin 1gm bd
Dec 2016 CBG acceptable on metformin appetite poor ,weight loss
Jan 2017 Stop metformin start Gliclazide 40mg bd adjusted dose when having treatment PG 15.7mmols/l
Feb 2017 Increase glicalzide 80mg bd
March 2017 Weight loss ,osmotic symptoms ,fatigue Levemir insulin 8 units daily commenced
April 2017 Levemir insulin dose titrated 14 units daily CBG usually in single figures. Weight gain ,osmotic symptoms improve
Sept 2017 Levemir insulin 24 units BD plus Novorapid 8:8:8

`When the blood sugar is under control Henry feels good both mentally and physically`

58M Metastatic Pancreatic Adenocarcinoma March 2017

Recent diabetes diagnosis metformin 500mg TDS commenced and diet restricted

DSN review- stop metformin

Commence gliclazide 80/40mg

Do not restrict diet (avoid high sugar drinks)

Monitor CBG

Review 3 days later CBG 14-29mmols/l

Steroids

Levemir insulin commenced 16 units

CBG 9-13 mmols/l

Osmotic symptoms improved

Not fit for chemotherapy

Admitted to hospice for symptom control

Standard diabetes care is not recommended in these patients

61M Δ Pancreatic Adenocarcinoma Sept 2018

Sept 2017 Type 2 DM metformin
Inoperable
Folfirinox x 6 cycles no response
Chemo radiation with capecitabine
PG 13.9,13.0
Seeing GP – weight loss 20kg,nocturia,fatigue,polydipsia
No appetite ,poor taste
Plan review after treatment
DSN review
Monitor CBG
Restricting diet
Insulin commenced

GP advise to complete Chemo radiation and then they would discuss insulin therapy

Importance of managing glycaemia

- Nephropathy
- Neuropathy
- Retinopathy

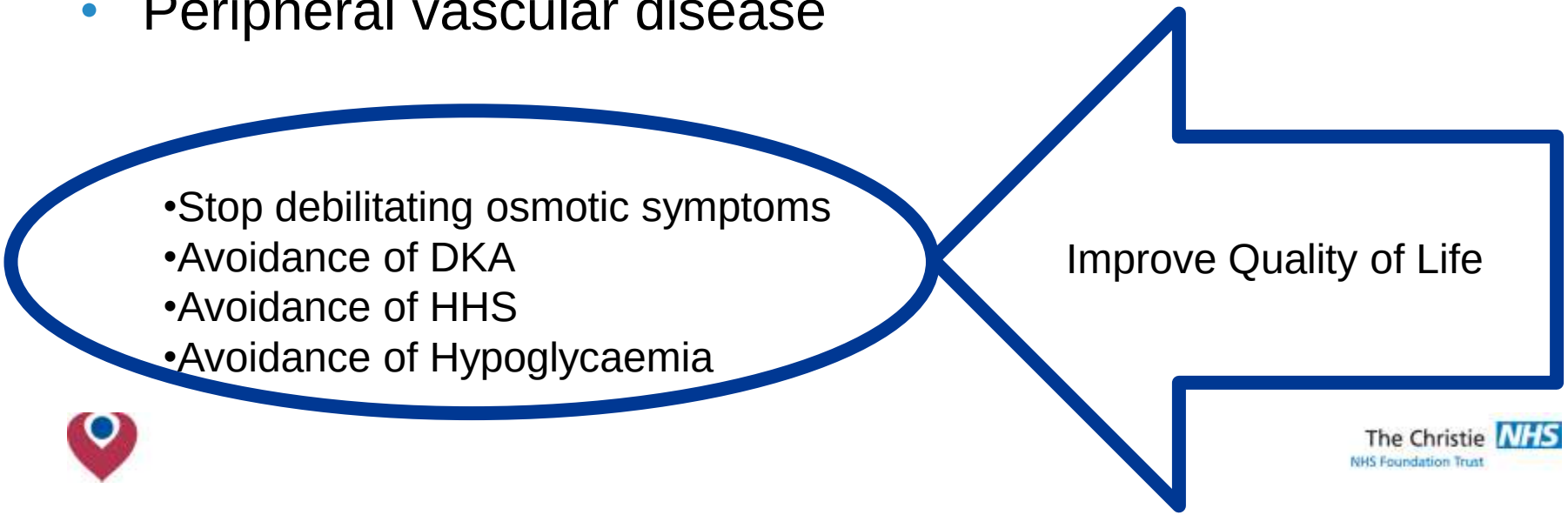
- Cardiovascular disease
- Peripheral vascular disease

- DKA
- HHS
- Hypoglycaemia

Importance of managing glycaemia

- Nephropathy
- Neuropathy
- Retinopathy

- Cardiovascular disease
- Peripheral vascular disease



Case: Not good news

2012
74 yr old man, recurrent ampullary adenocarcinoma
- partial pancreatectomy

- palliative chemotherapy, borderline PS
- Oral dexamethasone in OPD
- 24 hours later
  - Admitted to Salford Royal with DKA
  - Admitted to ICU
  - Died despite optimal management

Case reviewed

6 months prior: 6 clinic visits with random CBG 6.6 - 10.3 mmol/l

3 months prior: random CBG 16.1 mmol/l at clinic visit

1 month prior: random CBG 12.1 mmol/l : clinic proforma recommended GP check FPG

Clinic visit: no check of FPG
or review of prior BG's

- **62 M Δ** pancreatic ductal adenocarcinoma July 2017

Known type 2 diabetes 8 years
Metformin 1gm BD ,Alogliptin 25 mg OD
March 2017 rapid weight loss, abdominal pain, tired
Reviewed symptoms related to diabetes medications –changed
July 2017 DSN review HbA1c 76 mmols/l, CBG 14 – 19 mmols/l
Weight loss,(25% over last 6 months ,19kg)
Polyuria, polydipsia

- DSN/Dietitian review
- Metformin 1gm BD ,Alogliptin 25 mg OD stopped
- Levemir insulin commenced12 units daily
- Education
- Insulin dose adjusted so CBG 6-10mmols/l
- Novorapid insulin added in with meals and to troubleshoot high CBGs
- Hyperglycaemic symptoms improved
- Slight weight gain
- Risk of HHS reduced

Key messages

- Managing diabetes and pancreatic cancer is challenging and complex
- Deterioration of glycaemic control in patients with pre existing diabetes and the development of diabetes in others is common
- The co morbid conditions of Pancreatic Cancer and diabetes require 2 sets of interdependent goals, oncologic and glycaemic control
- Both sets of goals are determined primarily by life expectancy

Key messages

- Evidence demonstrates that better glycaemic control results in decreased morbidity, mortality and LOS
- Lack of attention to hyperglycaemia will increase risk of hospitalisation
- If we don’t look for hyperglycaemia by checking glucose we wont find it !!
- Focus on cancer care - do not always recognise wider co-morbidities

References

- Sah R et al 2013 New insights into pancreatic cancer paraneoplastic diabetes Nature Reviews Vol 10 423-433
- Flaherty AM 2012 Management of Diabets and Pancreatic Cancer Oncology Nursing Forum Vol 39,No 5 440 – 443
- Hillson R Pancreatitis, pancreatic cancer, and diabetes Practical Diabetes Vol 33 No 3 77-78