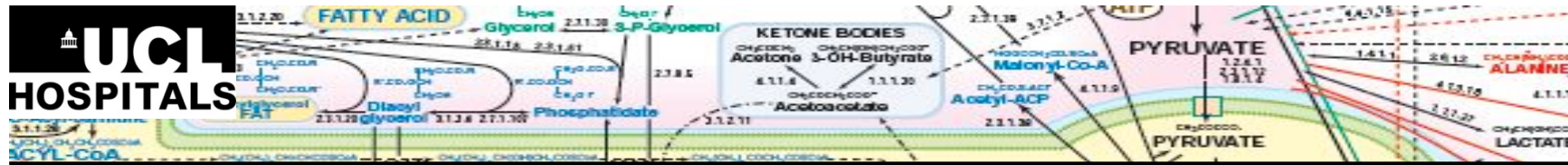


**Elaine Murphy**  
**Charles Dent Metabolic Unit**  
**National Hospital for Neurology & Neurosurgery, Queen Square**



## 26 year old female patient

**Diagnosis**  
**GSD1a**

### **Presentation**

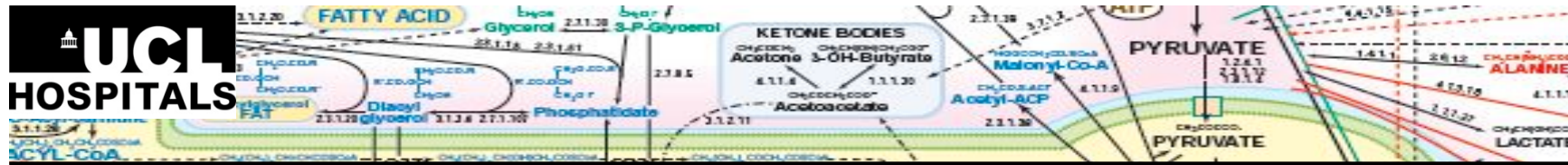
**< 1 year: diarrhoea, vomiting, hepatomegaly**

### **Treatment**

**Frequent feeds, regular uncooked cornstarch (UCCS)**  
**Never required overnight pump feeding**

### **Outcome**

**Rarely hypoglycaemia**  
**Low BMD, z-score -2.5 (2006)**



Re-referred in March 2010  
hypertension  
high random glucose levels

Had stopped daytime UCES (70g) for a year (bloated & 'unwell')  
Taking approximately 80g UCES at 11pm

Weight 94.55 kg, BMI 29.1 kg/m<sup>2</sup>  
Blood pressure 160/95 mmHg

Central obesity, some abdominal striae  
Hepatomegaly (6 cm)

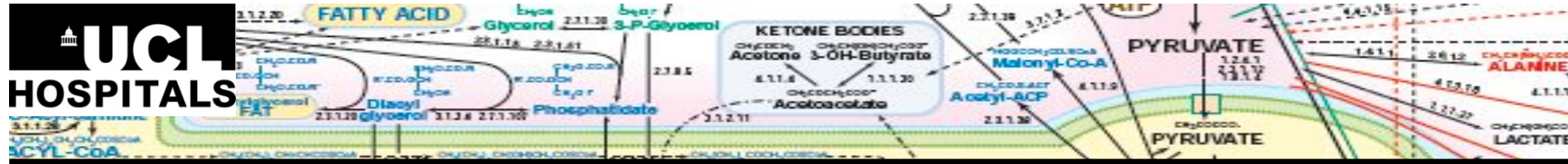
## Results

Random glucose **14.7** mmol/L  
Total Cholesterol **4.4** mmol/L  
Triglycerides **6.0** mmol/L

Urate **180** umol/L (266-474)  
Lactate **2.16** mmol/L (0.5-1.65)

Normal renal, liver and bone profiles

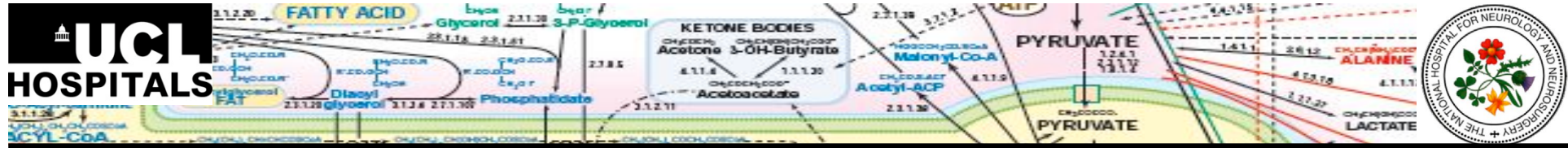
Admit for  
24 h monitor glucose profiling  
Bone DEXA scan  
Liver MRI scan  
Review of diet and therapy



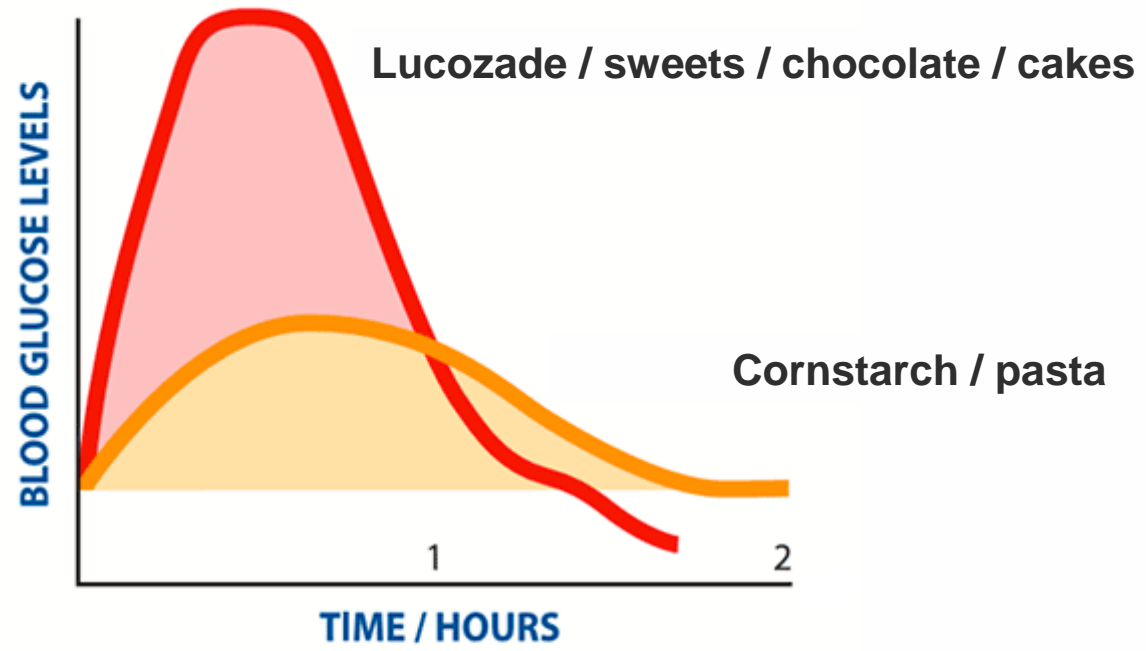
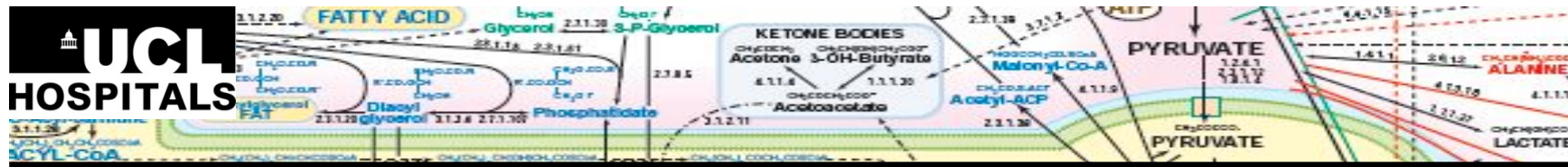
## 26 year old patient with GSD 1a

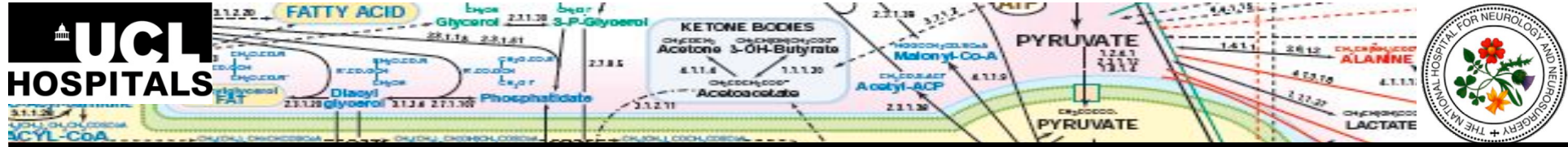
Day	Time	Context	Glucose mmol/L	Lactate mmol/L	Insulin mIU/L	c-peptide pmol/L
Monday	17:48	pre-dinner	18.7			
	19:50	2 h post-prandial	18.0			
	21:25	pre-UCCS	10.7			

**HbA1c 9.7%**



<b>Breakfast</b>	<p><b>2 slices bread</b>  <b>cheese spread</b>  <b>4 cream crackers</b>  <b>banana</b></p>
<b>Lunch</b>	<p><b>2 slices bread</b>  <b>cheese spread</b>  <b>4 cream crackers</b>  <b>yogurt</b></p>
<b>Dinner</b>	<p><b>Spaghetti or potatoes</b>  <b>chicken or sausages</b></p>





## Daily requirements

18 years

Energy

Protein

Glucose



Age



40

kcal/kg/day



0.83

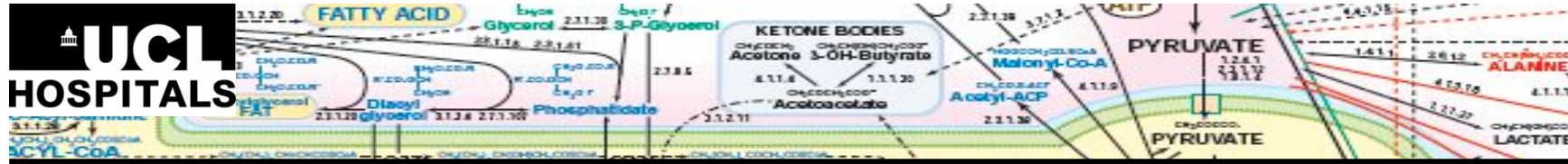
g/kg/day



2-4

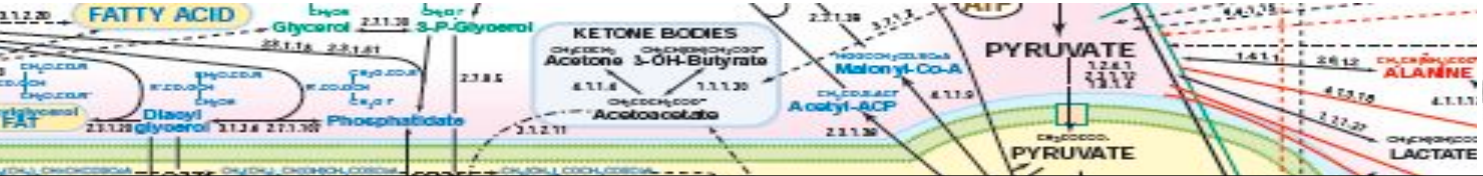
mg/kg/min





## 26 year old patient with GSD 1a

Day	Time	Context	Glucose mmol/L	Lactate mmol/L	Insulin mIU/L	c-peptide pmol/L
Monday	17:48	pre-dinner	18.7			
	19:50	2 h post-prandial	18.0			
	21:25	pre-UCCS	10.7			
Tuesday	08:20	fasting	8.2	5.48	5.1	346
	10:40	2 h post-prandial	10.4	4.25	48.6	1948
	11:56	pre-lunch	18.2			
	22:00 Midnight		11.9 11.1			
Wednesday	04:00		7.3			
	06:00		7.4			
	08:00		7.8			



## Cornstarch

Is important for.....

Maintaining blood glucose levels & improving metabolic control (children and adults)

Promoting growth and well being (children)

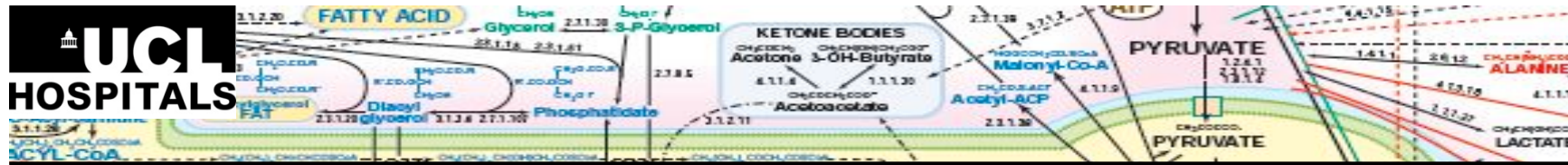
But.....

Is not a substitute for a varied diet / regular meals

Does not provide vitamins and minerals

Is not a quick treatment for hypoglycaemia

Is filling / causes bloating – can make it hard to encourage children to have other foods



## From a young age.....

Encourage variety of foods

Add vegetables (colour!) to the plate

Use water as well as sugar containing drinks

Allow / encourage children to cook

## As children / teenagers get older.....

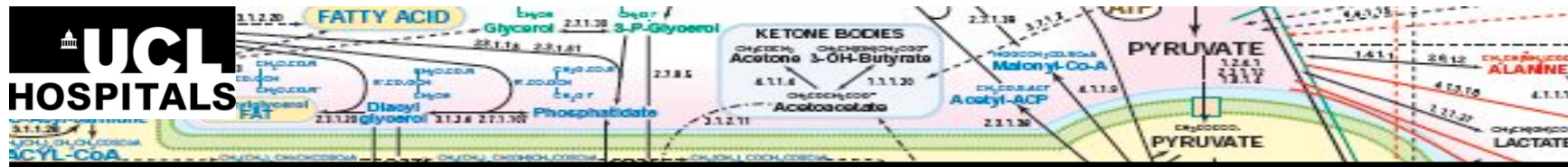
Think about food choices

Low GI options – pasta, rice, cereals, bread

Vegetables

Limit processed foods – cakes / sweets / chocolate / crisps

Limit use of sugary drinks



### Glycogen Storage Disorders

Rare 1:100,000

Low glucose production

Hypoglycaemia

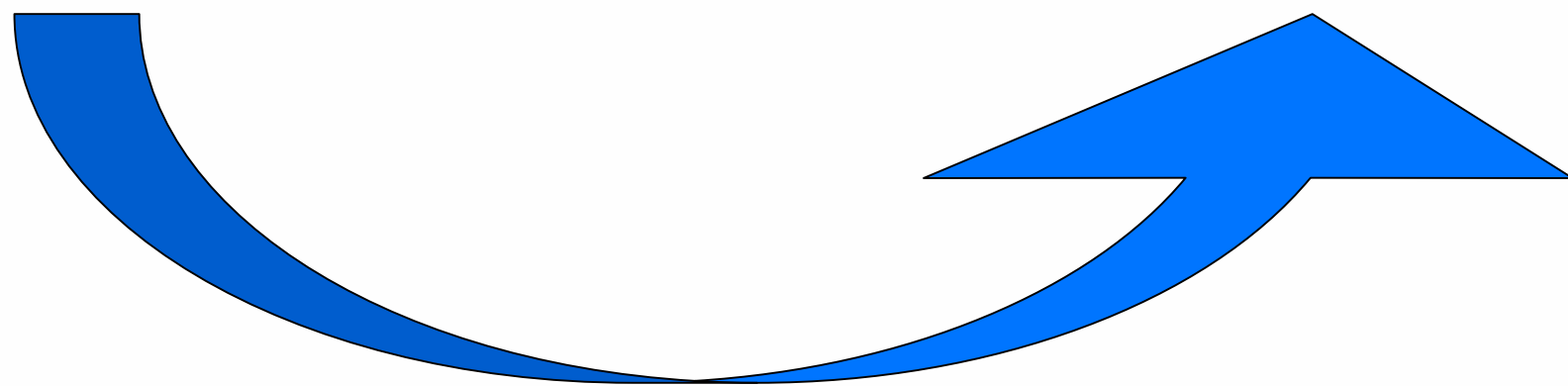


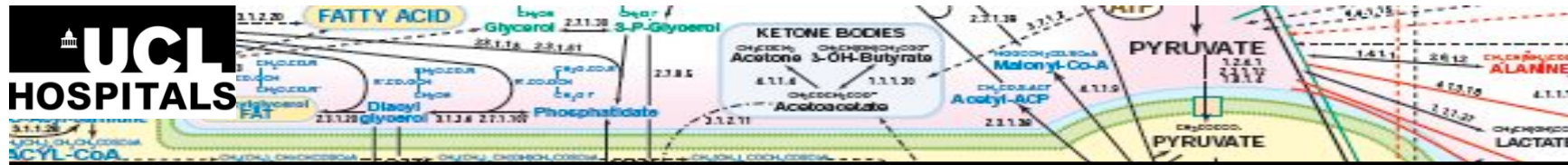
### Diabetes

Epidemic

High glucose production /  
reduced glucose utilisation

Hyperglycaemia





**1972 Moe PJ et al**

**Diabetes a rare complication of GSD III, (secondary to liver dysfunction)**

**2000 Oki Y et al**

**Adult patient with GSD III. Liver dysfunction and postprandial hyperglycaemia. Treated with voglibose (low risk of hypoglycaemia).**

**2005 Spiegel R et al**

**22 year-old male with GSD Ib developed diabetes secondary to pancreatic islet beta-cell insufficiency. Diabetes a 'late complications of GSD I'.**

**2009 Heba I**

**Patient with GSD III and fasting hyperglycaemia. Spontaneous resolution of hypoglycaemic attacks for several year prior to diabetes. Treated with insulin (avoid hepatotoxicity).**



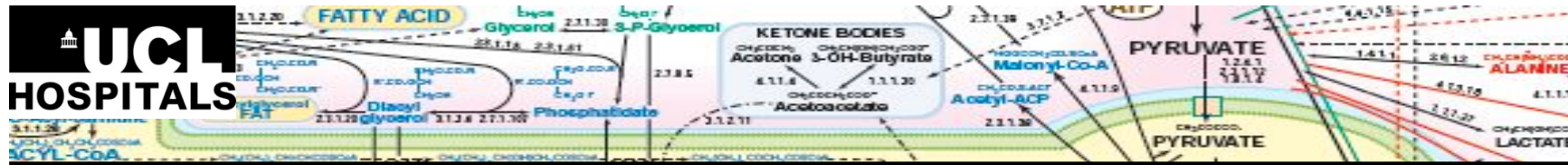
## From hypoglycaemia to hyperglycaemia.....

Initially patients with GSD I have hypoinsulinaemia as a consequence of secondary adaptation to the hypoglycaemic tendency

Early aggressive nutrition therapy, with frequent meals rich in carbohydrate, **metabolic syndrome like phenotype** (central obesity, insulin resistance with normoglycaemia and hyperinsulinaemia)

Insulin resistance in adult patients with GSD (euglycaemic clamp)

Hyperinsulinism in adult patients after UCCS load



Am J Vet Res. 1999 Apr;60(4):458-62.

**Glucose uptake in horses with polysaccharide storage myopathy.**

[De La Corte FD](#), [Valberg SJ](#), [MacLeay JM](#), [Williamson SE](#), [Mickelson JR](#).

Equine Vet J Suppl. 1999 Jul;30:324-8.

**Blood glucose clearance after feeding and exercise in polysaccharide storage myopathy.**

[De La Corte FD](#), [Valberg SJ](#), [Mickelson JR](#), [Hower-Moritz M](#).

Neuromuscul Disord. 2004 Oct;14(10):666-74.

**Insulin sensitivity and skeletal muscle glucose transport in horses with equine polysaccharide storage myopathy.**

[Annandale EJ](#), [Valberg SJ](#), [Mickelson JR](#), [Seaquist ER](#).

J Appl Physiol. 1996 Sep;81(3):1273-8.

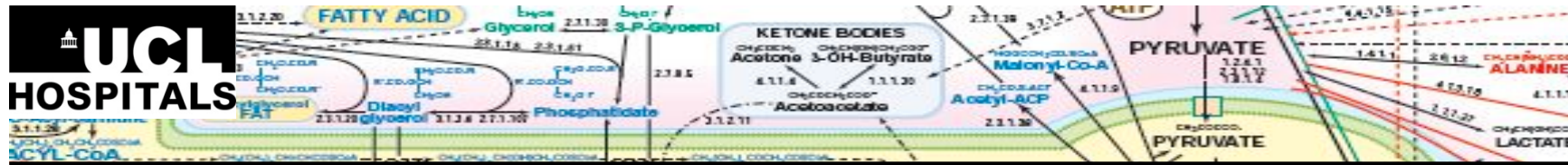
**Insulin resistance limits glucose utilization and exercise tolerance in myophosphorylase deficiency and NIDDM.**

[Dorin RI](#), [Field JC](#), [Boyle PJ](#), [Eaton RP](#), [Icenogle MV](#).

Am J Physiol Endocrinol Metab. 2002 Jun;282(6):E1267-75.

**Decreased insulin action in skeletal muscle from patients with McArdle's disease.**

[Nielsen JN](#), [Vissing J](#), [Wojtaszewski JF](#), [Haller RG](#), [Begum N](#), [Richter EA](#).



## Management of GSD & diabetes

### Individualised

### Prevention

Avoid obesity, promote physical activity, no more cornstarch than necessary (linear growth and well-being in childhood vs. obesity in adulthood)

### Detect hyperglycaemia as soon as possible

Pre- and post-prandial glucose levels

### If diabetes occurs

Check auto-antibodies especially in young non-obese patients (exclude type 1 diabetes)

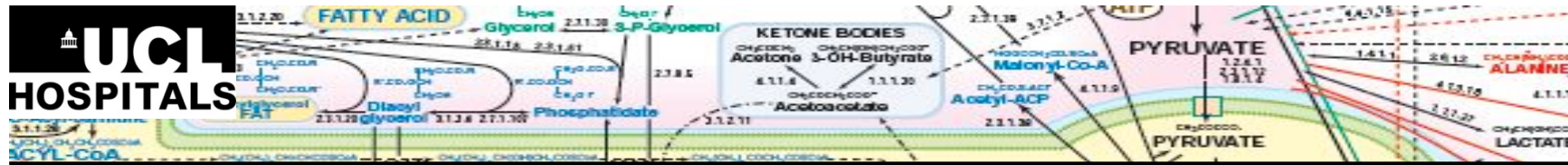
Measure plasma insulin and c-peptide (estimate pancreatic reserve)

Perform 24 h glucose monitoring to see the glycaemic pattern

Consider most appropriate treatments (which may need to be given alongside UCES)







### Glinides (Repaglinide)

Similar to sulfonylureas but with shorter hypoglycaemic effect

### $\alpha$ –glucosidase inhibitors (Acarbose)

Reduce the rate of digestion of polysaccharides primarily lowering postprandial glucose levels

Adverse effects: diarrhoea

### Pioglitazone

PPAR $\gamma$  modulator, increase the sensitivity of muscle, fat and liver to insulin.

Adverse effects: weight gain, fluid retention, risk for heart failure, bone loss

### GLP1 agonists (Exenatide, Liraglutide)

Augments glucose-mediated insulin secretion lowering postprandial glucose (advantages: weight loss, low risk hypoglycaemia)

Adverse effects: GI symptoms

### DDP4 inhibitors (e.g. Sitagliptin)

Enhance the effect of the endogenous GLP1 (advantage: weight neutral)