Diabetes

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MB.ChB.DA.MRCA

History of diabetes

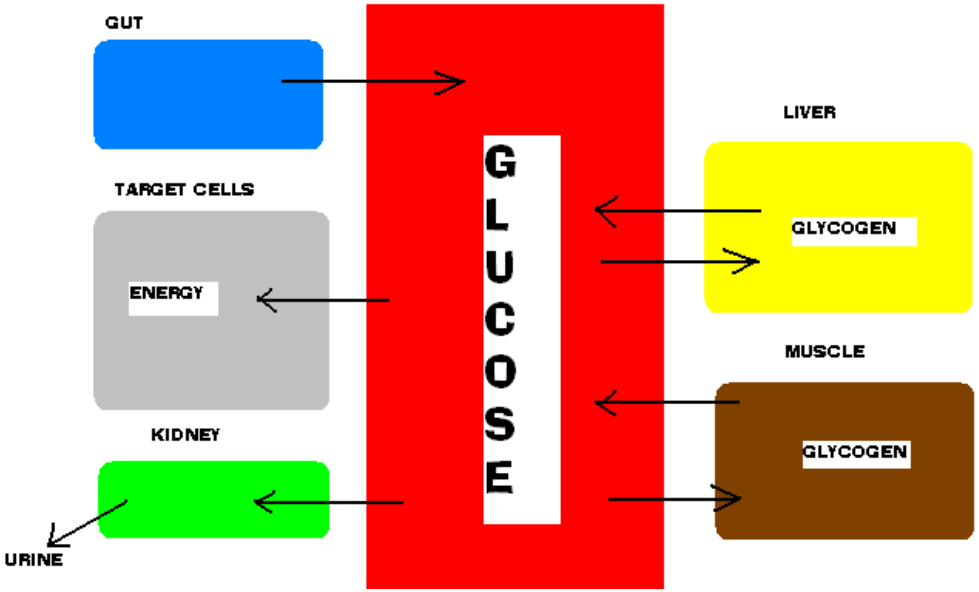
- Discovered as an illness involving the production of sweet urine in 250BC
- 1889 relationship between diabetes and the pancreas discovered
- 1922 first patient treated with insulin
- 1923 Nobel Prize for discovery of insulin

What is Diabetes Mellitus?

- Abnormally high blood sugar levels
- Lack of insulin production (Type I) 5%
- Resistance to the effects of naturally produced insulin (Type II) 95% and associated with obesity

Sugar metabolism

- All cells use glucose and oxygen to produce energy
- This glucose enters the body via the gut

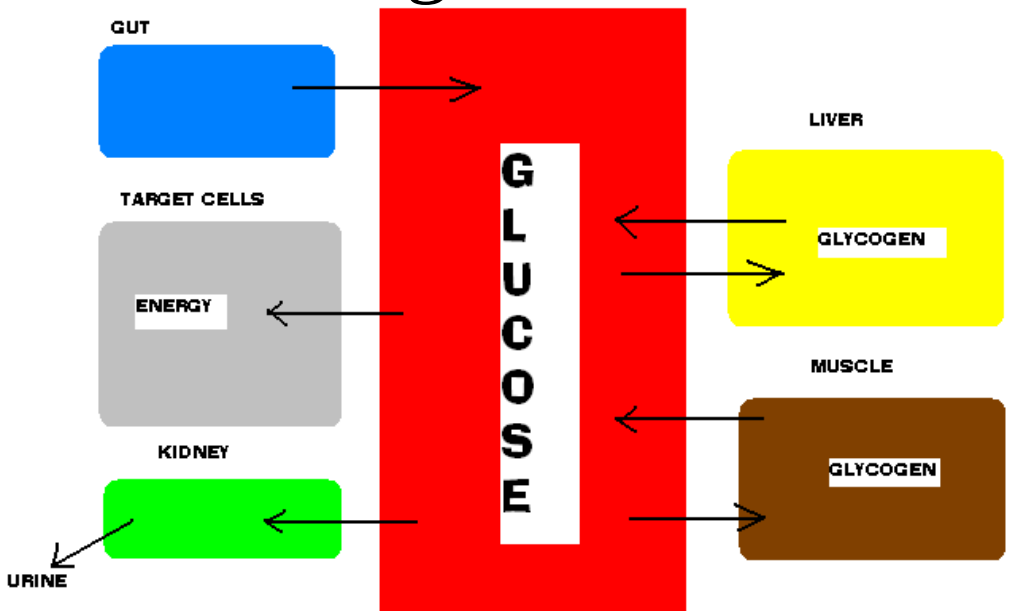


Sugar metabolism

- Most cells can store some glucose to use when supplies are inadequate
- Intracellular glucose stores will last only an hour
- Nerve cells cannot store glucose and are entirely dependant on blood glucose for their metabolism and survival

Sugar metabolism

- Sugar is stored in larger quantities in liver and muscle cells. It is stored as glycogen and can be released into the circulation when blood sugar levels fall



Sugar metabolism

- Glycogen stores will last 24-36hrs
- When glycogen stores are depleted, energy production depends on the breakdown of fat and protein
- Excess glucose in the bloodstream is excreted in the urine or converted to glycogen for storage

Classification of diabetes

Type I

- Onset at young age
- Generally not obese
- Insulin needed
- Auto-immune disease

Type II

- Onset after 40yrs
- Often obese
- Insulin generally not needed
- Multiple underlying factors

Epidemiology of diabetes

- Type I
  - 5-10% of all cases
  - 1 in 400 children/adolescents
- Type II
  - 90-95% of all cases
  - 1 in 3 adults will develop diabetes at some point in their lives
  - BMI>30 increased likelihood of diabetes

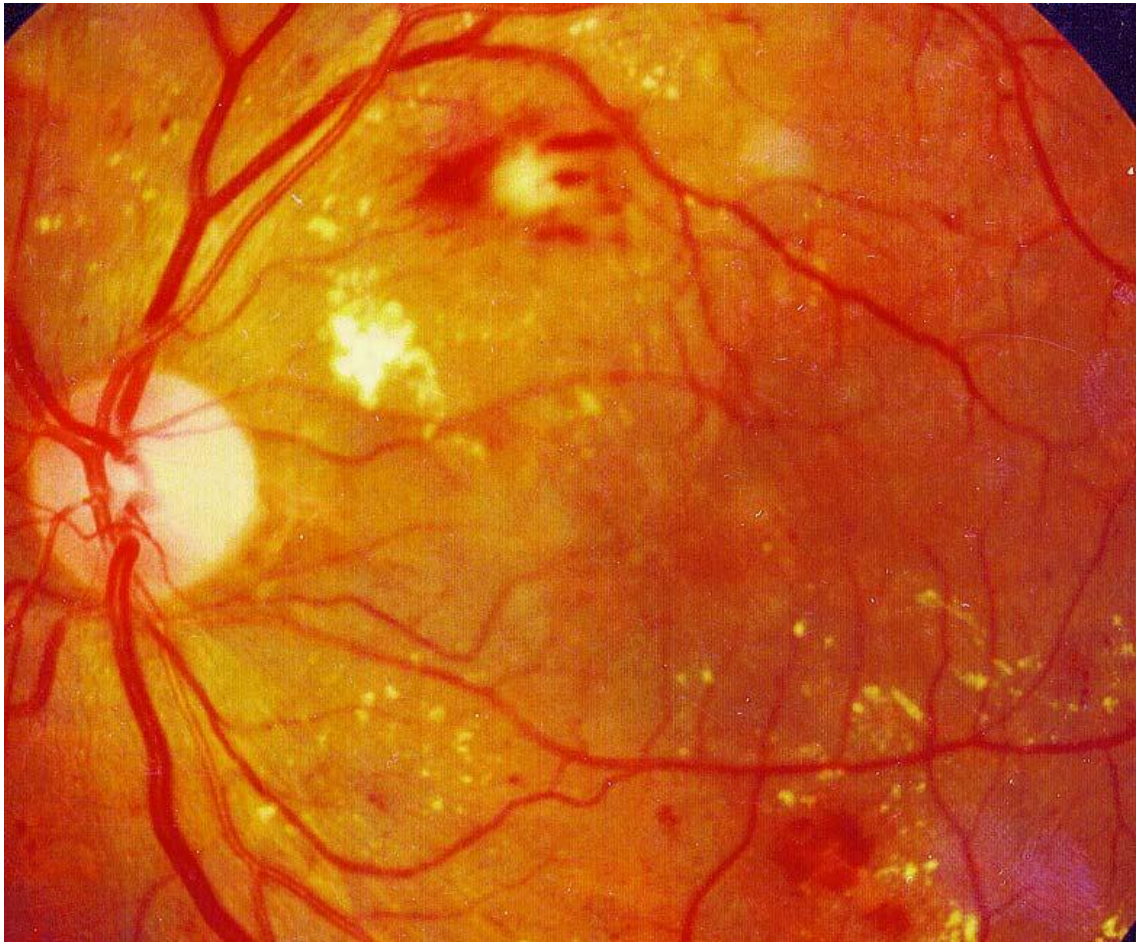
Symptoms of diabetes

- Polyuria - glucose acts as an osmotic diuretic when it is excreted in the urine
- Polydypsia - the polyuria results in severe dehydration and thirst
- Fatigue
- Recurrent infections
- In severe cases, diabetic coma

Long term complications of diabetes

- Chronic hyperglycaemia leads to a number of serious problems that can be life threatening
- The tighter the control of blood sugar, the fewer complications will occur
- Immune system malfunction leading to recurrent, potentially severe infections

Diabetic retinopathy potentially leading to blindness

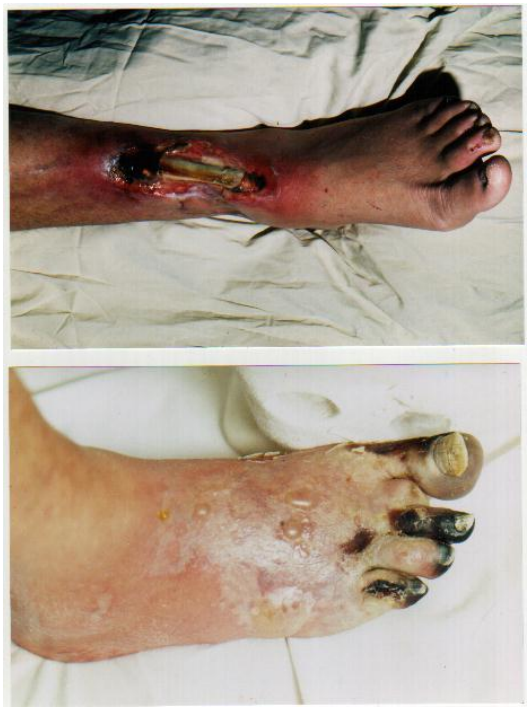


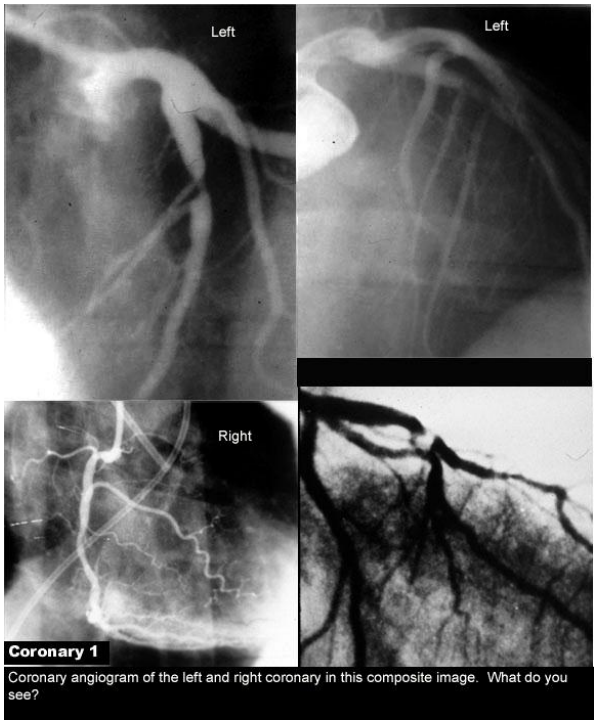
Diabetic neuropathy

Leading to foot ulcers etc

Macro-vascular disease

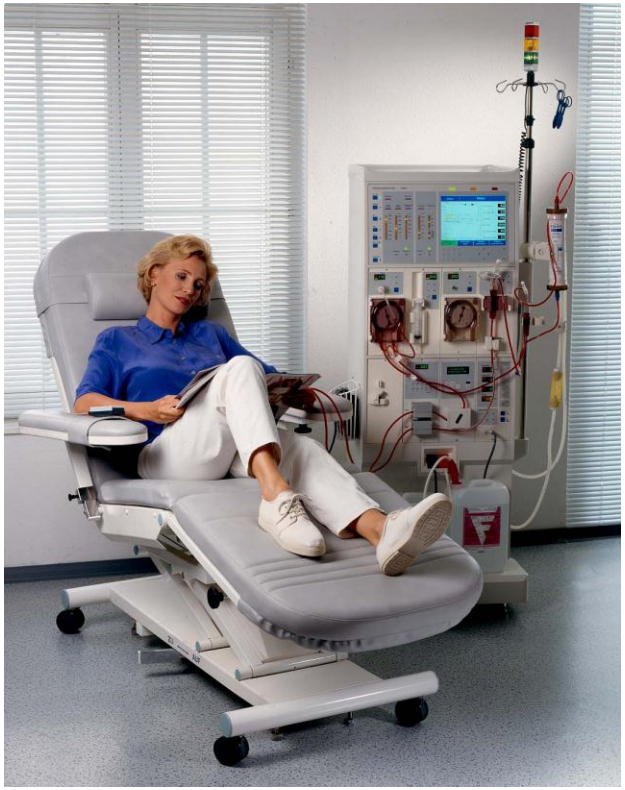
Leading to hypertension, coronary artery disease, poor peripheral circulation etc.





Micro-vascular disease

Leading to renal failure, cardiac failure etc.



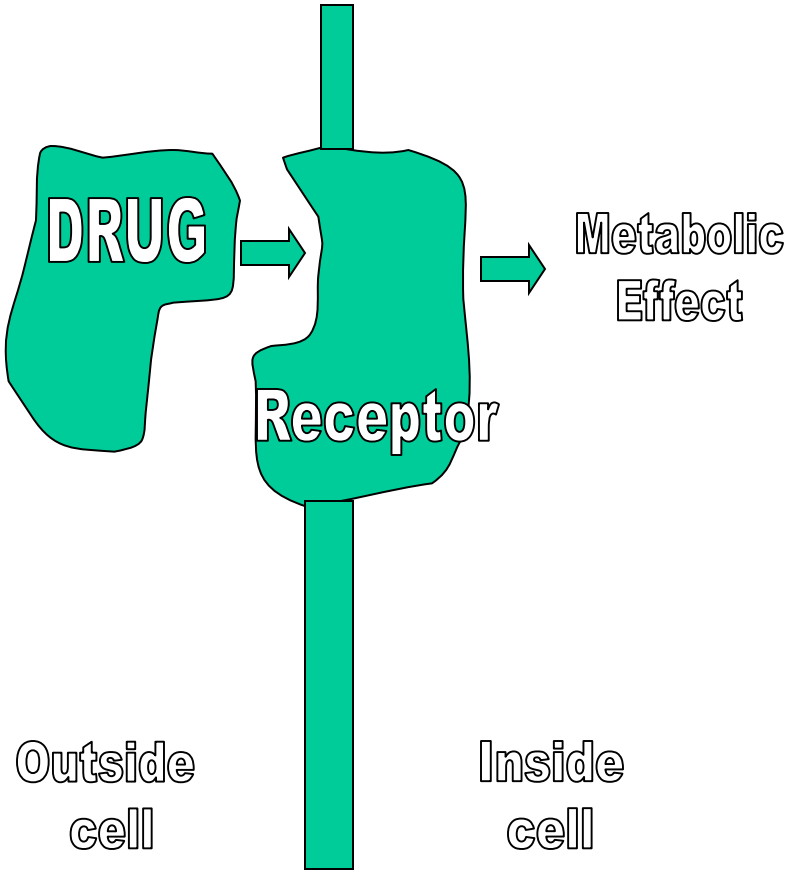
Normal blood sugar control

- Insulin synthesised and stored in the Beta Islet Cells of the pancreas
- It is released into the bloodstream in response to a rise in the blood sugar content of the arterial blood supplying the pancreas
- Insulin binds to receptors on the target cell in order to exert its effect

Receptors

When a compound combines with its receptor, a conformational change occurs.

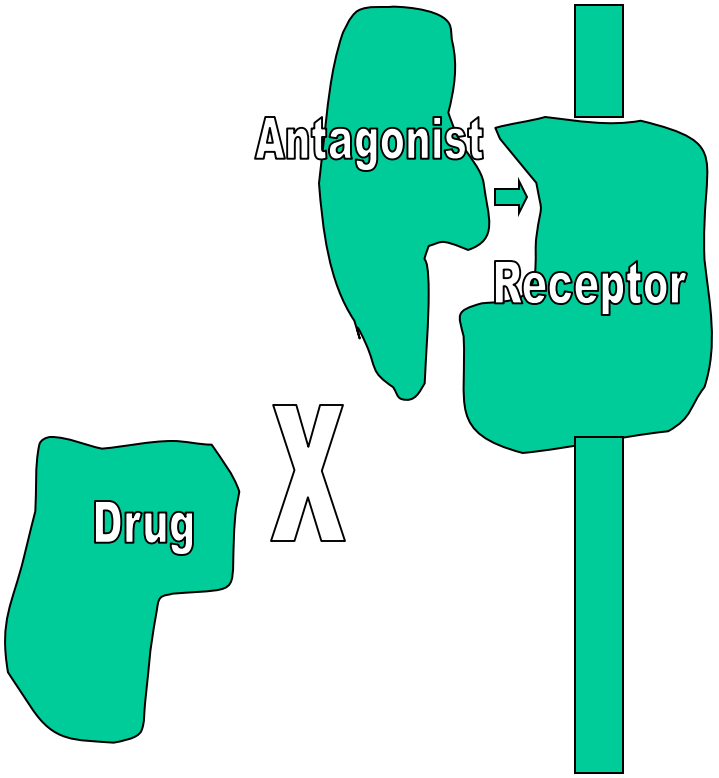
This results in an activation or inhibition of intracellular mechanisms producing a metabolic effect.



Receptor antagonists

These compounds bind to the receptor and prevent activation of the receptor by another compound.

They do not produce a conformational change in the receptor and hence the metabolic effects are not initiated.



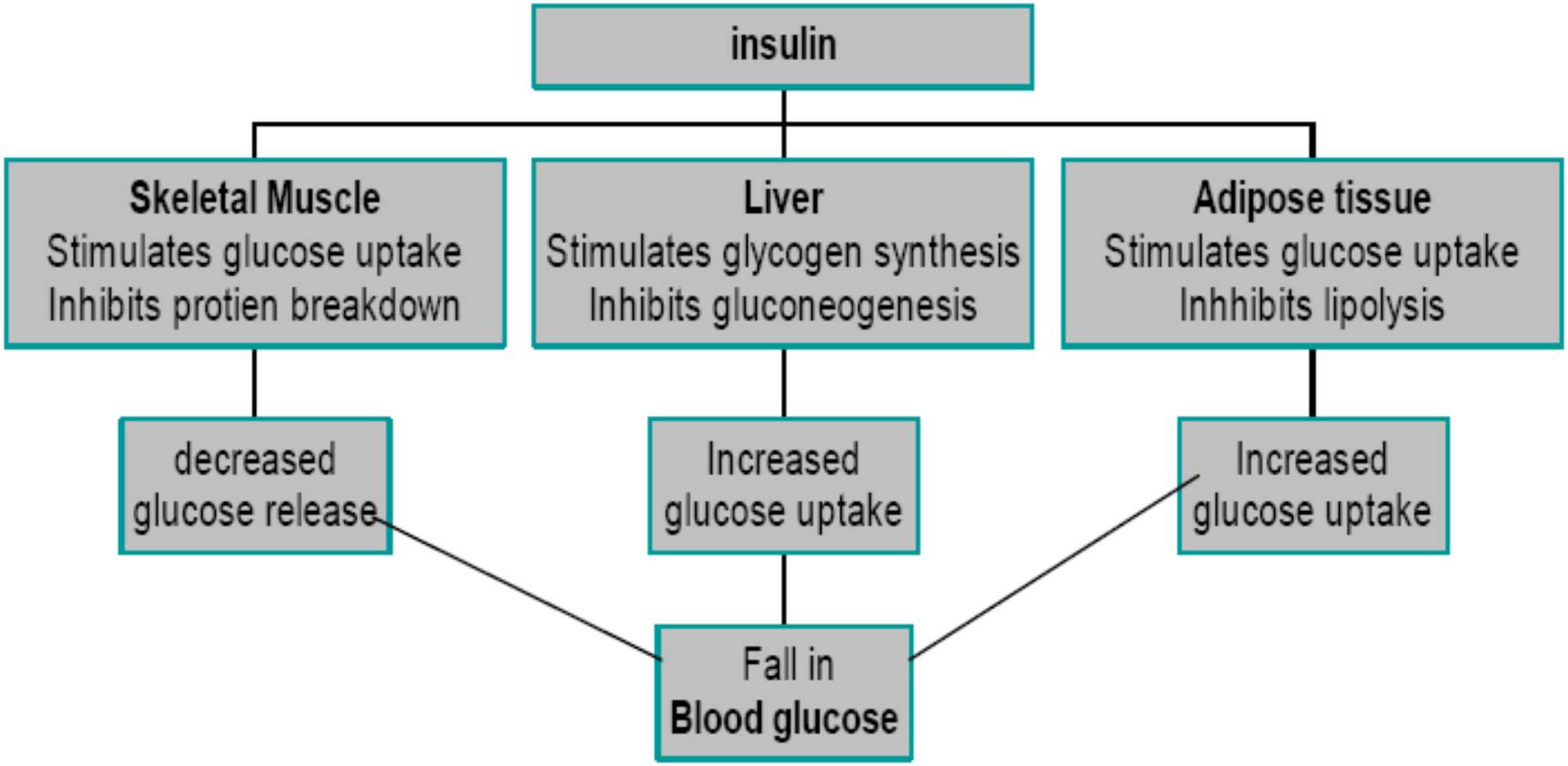
Insulin receptors

- The number of insulin receptors on the target cells varies inversely with the concentration of insulin to which they are exposed
- A continuous high concentration of insulin leads to a reduction in receptor numbers
- This leads to insulin resistance as occurs in obesity

Mode of action of insulin

- Increases the utilisation of glucose by the target cell to produce energy
- Increases glucose uptake by the target cell to facilitate the increased cellular metabolism

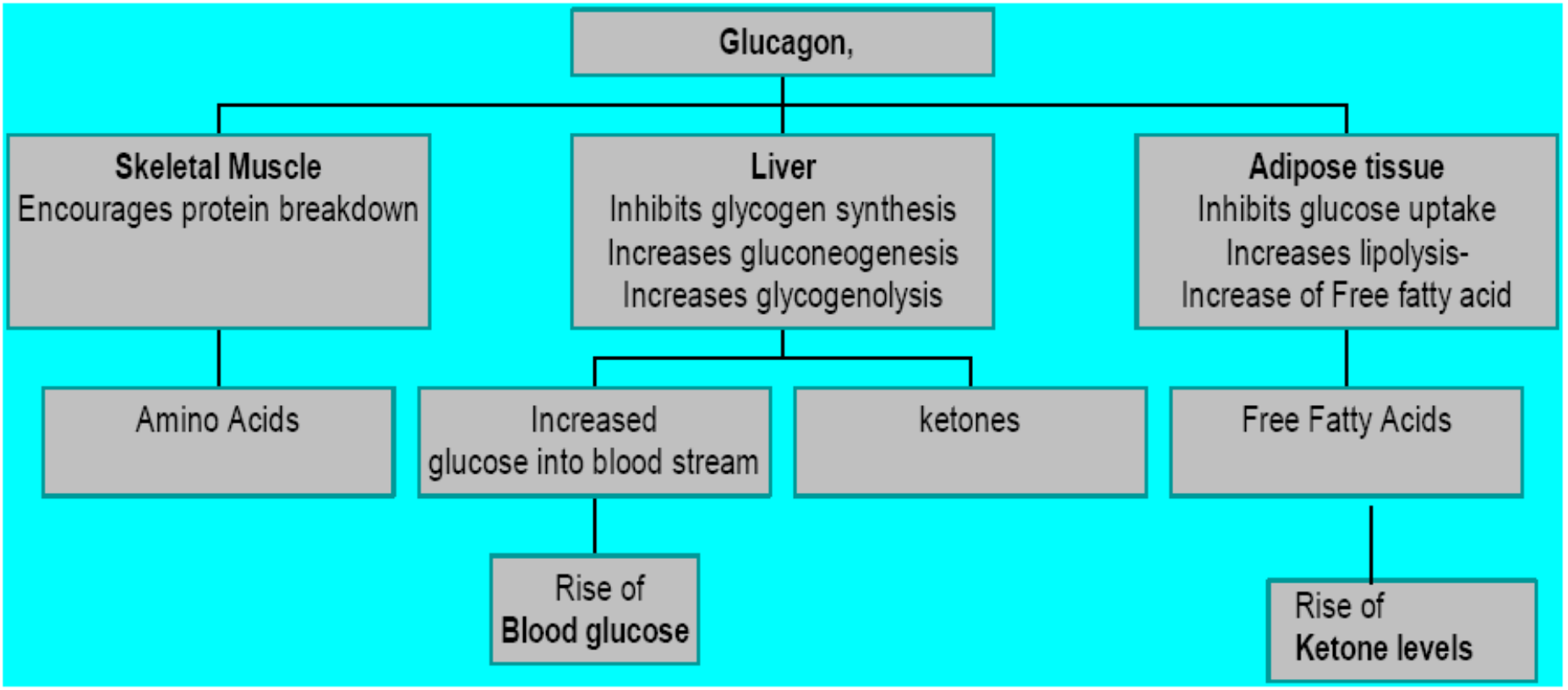
Principal actions of insulin



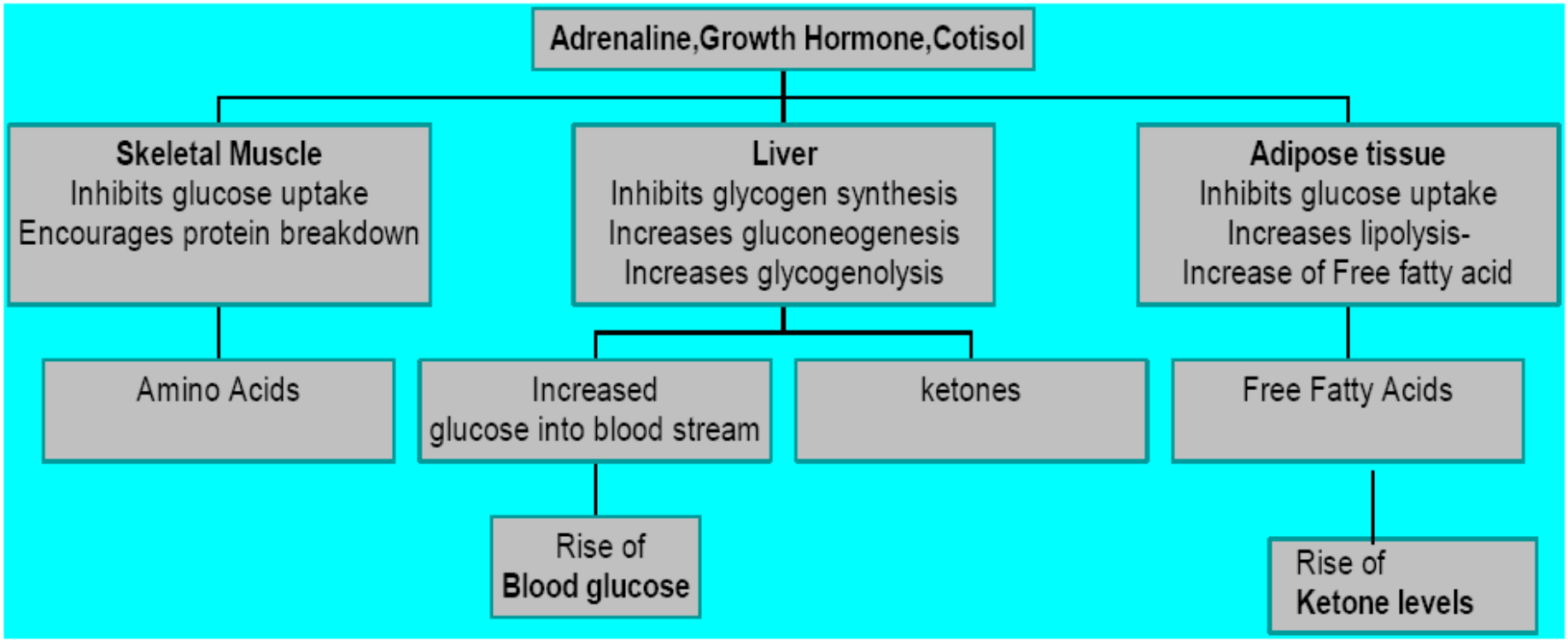
Hormones that tend to raise blood sugar

- Glucagon
- Adrenaline
- Adrenal steroids
- Growth hormone
- Thyroxine

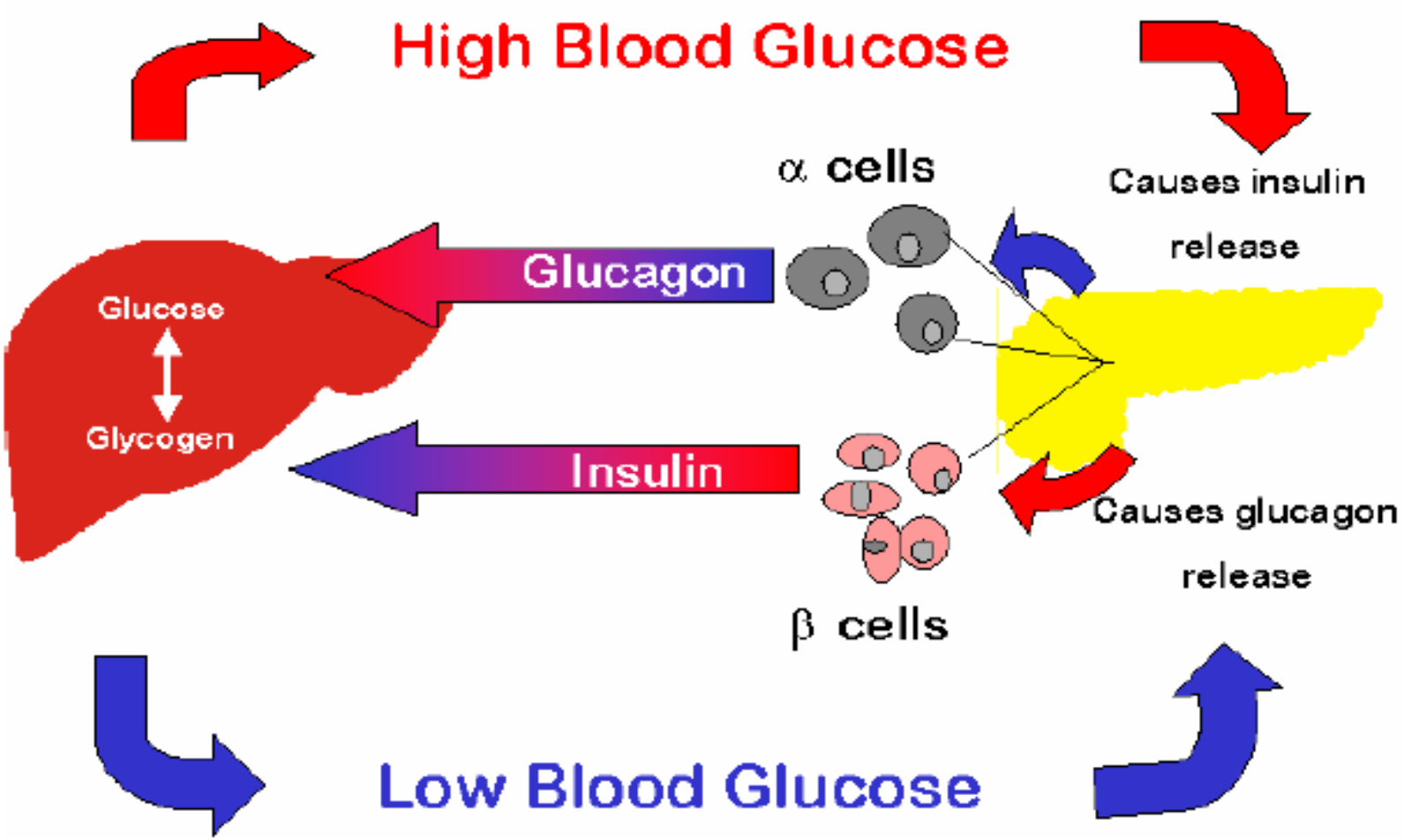
Principal actions of Glucagon .



Principal action of counter-regulatory hormones



Summary of blood glucose control



Treatment of diabetics

- Diet
- Insulin therapy (Type I, Type II)
- Oral hypoglycaemic drugs (Type II)
- Diabetics under 30yrs of age usually need insulin
- Over 30yrs 1/3 can be controlled by diet alone, 1/3 with oral hypoglycaemics, and 1/3 will need insulin

Insulin therapy

- Must be injected either s.c or i.v.
- Most in use today are genetically engineered forms of human insulin
- Previously obtained from beef or pork

Insulin preparations

- Rapid acting - begin to work 5mins after injection, peak action 2-3hrs and duration of action up to 4hrs
- Short acting - begin to work 30mins after injection, peak action at 2-4hrs with duration of action up to 6hrs

Insulin preparations

- Intermediate acting - begin to work 2-4hrs after injection, peak action at 2-3hrs with duration of action up to 18hrs
- Long acting - onset 6-10hrs after injection, and duration of action 20-24hrs

Additives to insulin preparations

- Suspended in lipid
- Anti-microbials to inhibit bacterial growth
- Ingredients to prolong activity
- May produce allergy

Insulin routines

- Best control is with 3 or 4 injections of short acting insulin managed by blood glucose measurement
- This can be inconvenient and many diabetics are stabilised on BD injections of mixtures of short and intermediate acting insulin preparations

Dose of insulin in diabetics

- Normal insulin production is 30-40 units/day
- 2/3 of total daily dose 30min before breakfast s.c.
- 1/3 of total daily dose 30min before evening meal s.c.
- Dose is modified according to blood sugar monitoring

Adverse effects of insulin

- Overdose leads to hypoglycaemia, coma, convulsions and may result in brain damage or death
- Treatment is by administration of i.v. glucose or i.m. glucagon if i.v. access is impossible
- Lipoatrophy at injection sites
- Allergy to additives

Oral hypoglycaemic drugs

- Sulphonylureas - Stimulate Beta Islet Cells of the pancreas to produce insulin. Will cause hypoglycaemia in normal subjects.
- Biguanides - Reduce absorption of carbohydrates from the gut, increase glucose uptake in the tissues in the presence of insulin. Do not cause hypoglycaemia in normal subjects.

Factors affecting control of diabetes

- Intercurrent illness
- Surgery
- Pregnancy

Anaesthesia in diabetics

- Tight control of blood sugar reduces the incidence of complications (surgical site infections), and may influence mortality.
- Long term effects of diabetes may affect the conduct of anaesthesia, and must be looked for and assessed in the pre-operative work up.

Complications of diabetes affecting anaesthesia

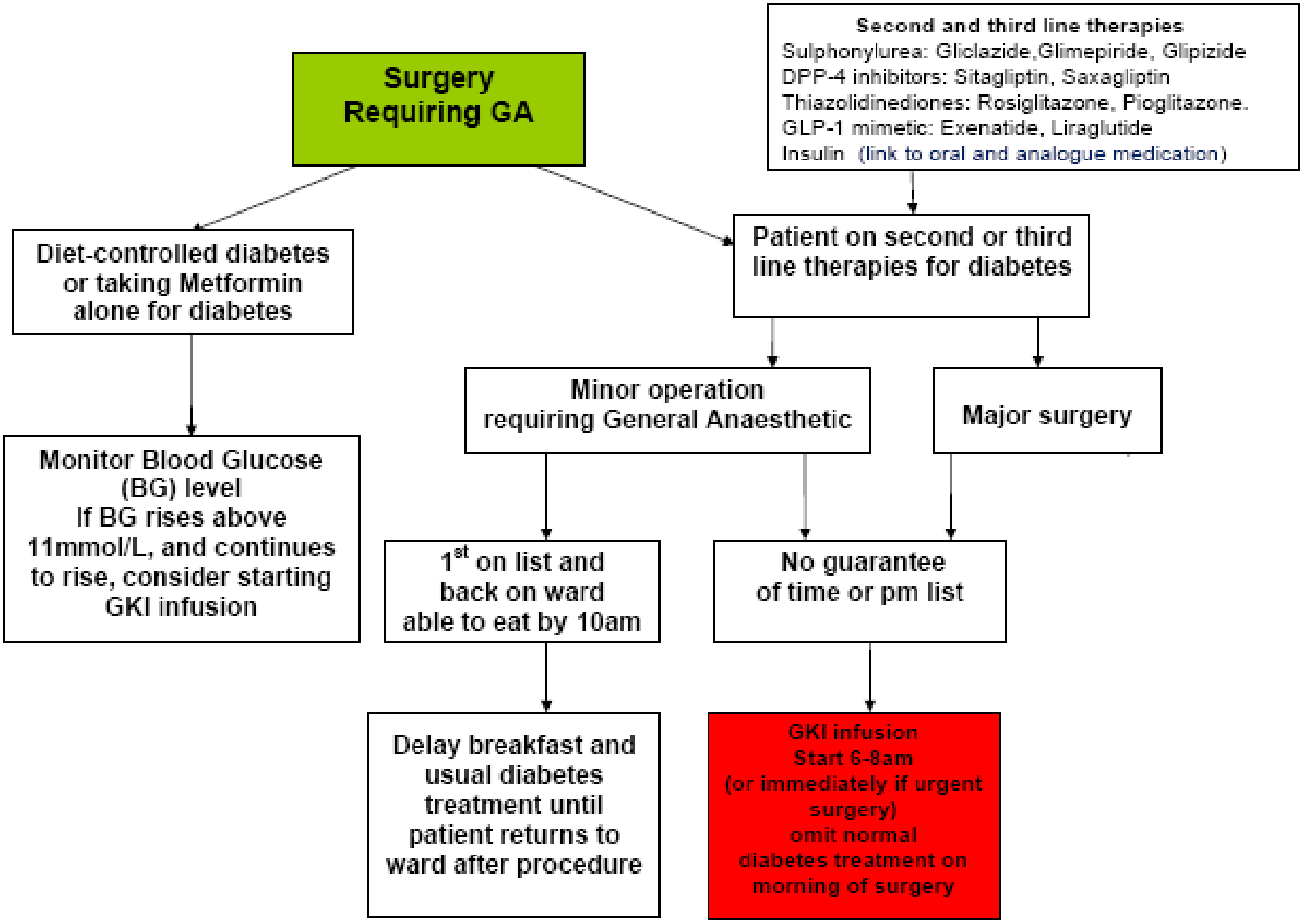
- Ischaemic heart disease (cardiac ischaemia, heart failure)
- Peripheral vascular disease (arterial lines etc, local blocks may be beneficial)
- Neuropathy (beware local/regional blocks, tendency to hypotension)
- Renal failure

Peri-operative control in diabetics

- Insulin requirements increase with surgery (part of the stress response)
- High blood glucose for short periods is not dangerous
- Low blood sugar may go undetected in unconscious patients and can result in brain damage

Peri-operative control in diabetics

- For major surgery, diabetics should be admitted early so that blood sugar control can be adjusted according to serial blood sugar measurements
- To compensate for bed rest, reduce calorie intake by 250-500 calories/day


Surgery Requiring GA
Second and third line therapies
Sulphonylurea: Gliclazide,Glimepiride, Glipizide
DPP-4 inhibitors: Sitagliptin, Saxagliptin
Thiazolidinediones: Rosiglitazone, Pioglitazone.
GLP-1 mimetic: Exenatide, Liraglutide
Insulin (link to oral and analogue medication)
Diet-controlled diabetes or taking Metformin alone for diabetes
Patient on second or third line therapies for diabetes
Monitor Blood Glucose (BG) level
If BG rises above 11mmol/L, and continues to rise, consider starting GKI infusion
Minor operation requiring General Anaesthetic
Major surgery
1st on list and back on ward able to eat by 10am
No guarantee of time or pm list
Delay breakfast and usual diabetes treatment until patient returns to ward after procedure
GKI infusion
Start 6-8am
(or immediately if urgent surgery)
omit normal diabetes treatment on morning of surgery

Peri-operative intravenous insulin therapy

- Use of GKI infusions
- Separate i.v. insulin, glucose and potassium infusions

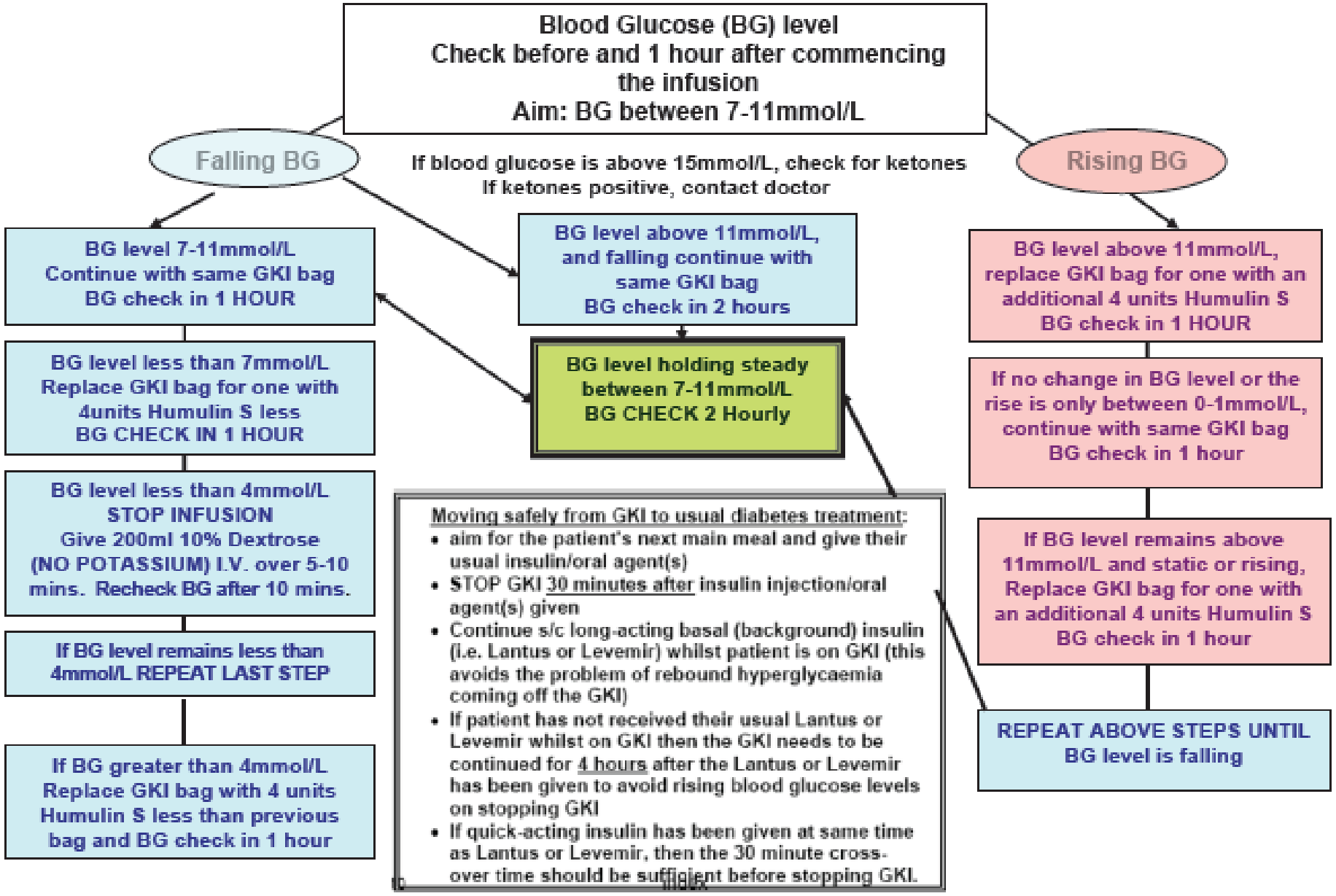
GKI infusions

- Administration of intravenous insulin will cause hypokalaemia, therefore additional potassium will be required
- Initiate infusion preoperatively if control is poor
- 500ml 10% Dextrose containing 16 units Humulin S and 10mmol of potassium chloride running at 100ml/hr

GKI infusions

- Monitor hourly blood glucose and serum potassium
- Adjust concentrations of insulin and potassium according to blood levels

Guidelines for adjustment of a GKI infusion



Separate Glucose/Potassium/Insulin infusions

- 10% dextrose containing 10mmol KCl run at 100ml/hr
- Insulin infusion (Humulin S) running at 2-4 units/hour
- Monitor hourly blood glucose and serum potassium
- Adjust concentration of potassium and rate of insulin infusion according to blood levels

Separate Glucose/Potassium/Insulin infusions

- Potentially dangerous
- If dextrose or potassium infusions stop and insulin infusion continues, there is a risk of hypoglycaemic coma and/or hypokalaemia
- Easier to alter infusion of 1 component than GKI infusion

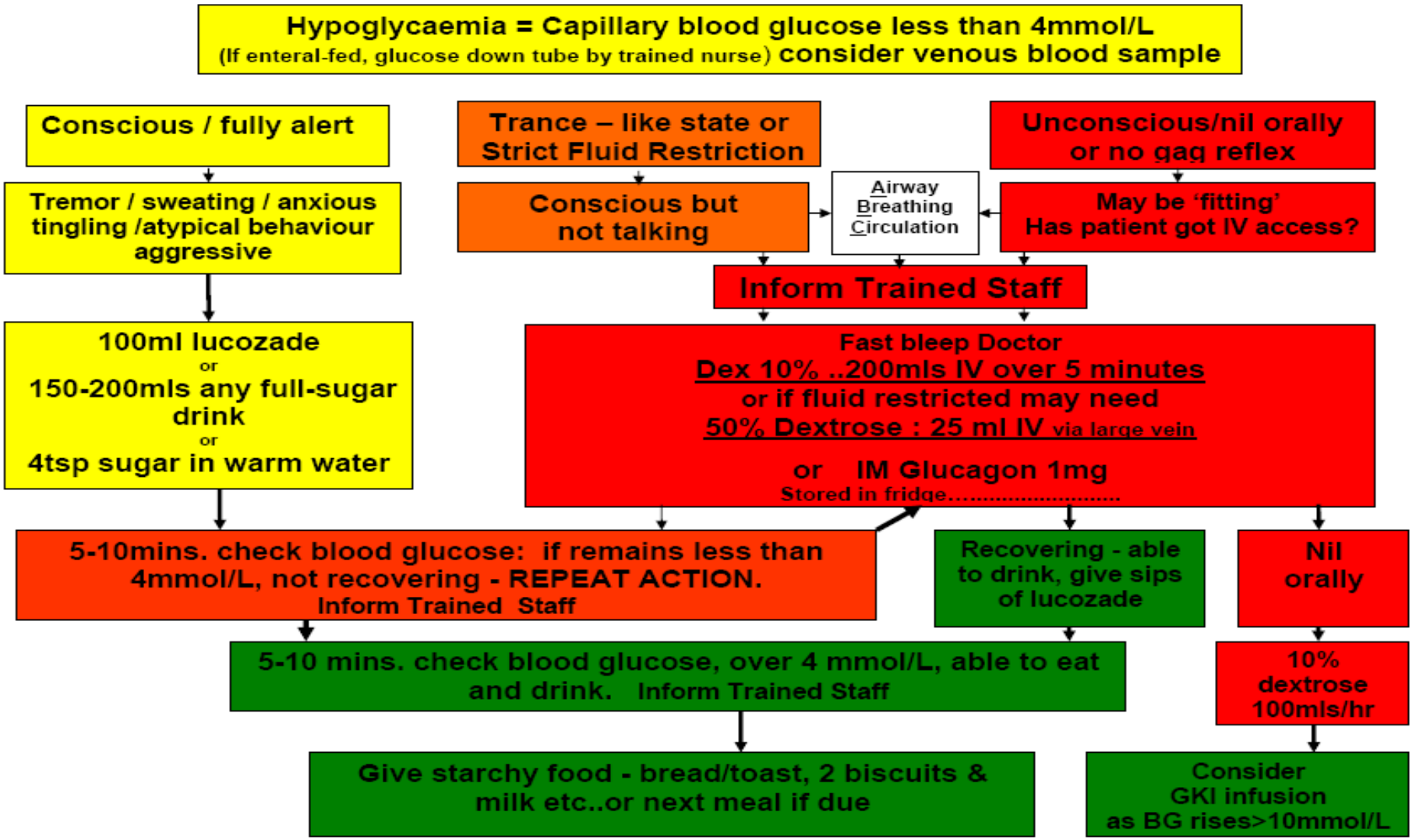
Diabetic coma

- Hypoglycaemia
- Hyperglycaemic coma

Hypoglycaemic coma

- Always due to relative insulin overdose
- Symptoms begin with confusion, progressing to convulsions, coma, brain damage and death

Hypoglycaemia



Hyperglycaemic coma

2 types characterised by the presence or absence of raised levels of ketones in the blood resulting in a metabolic acidosis.

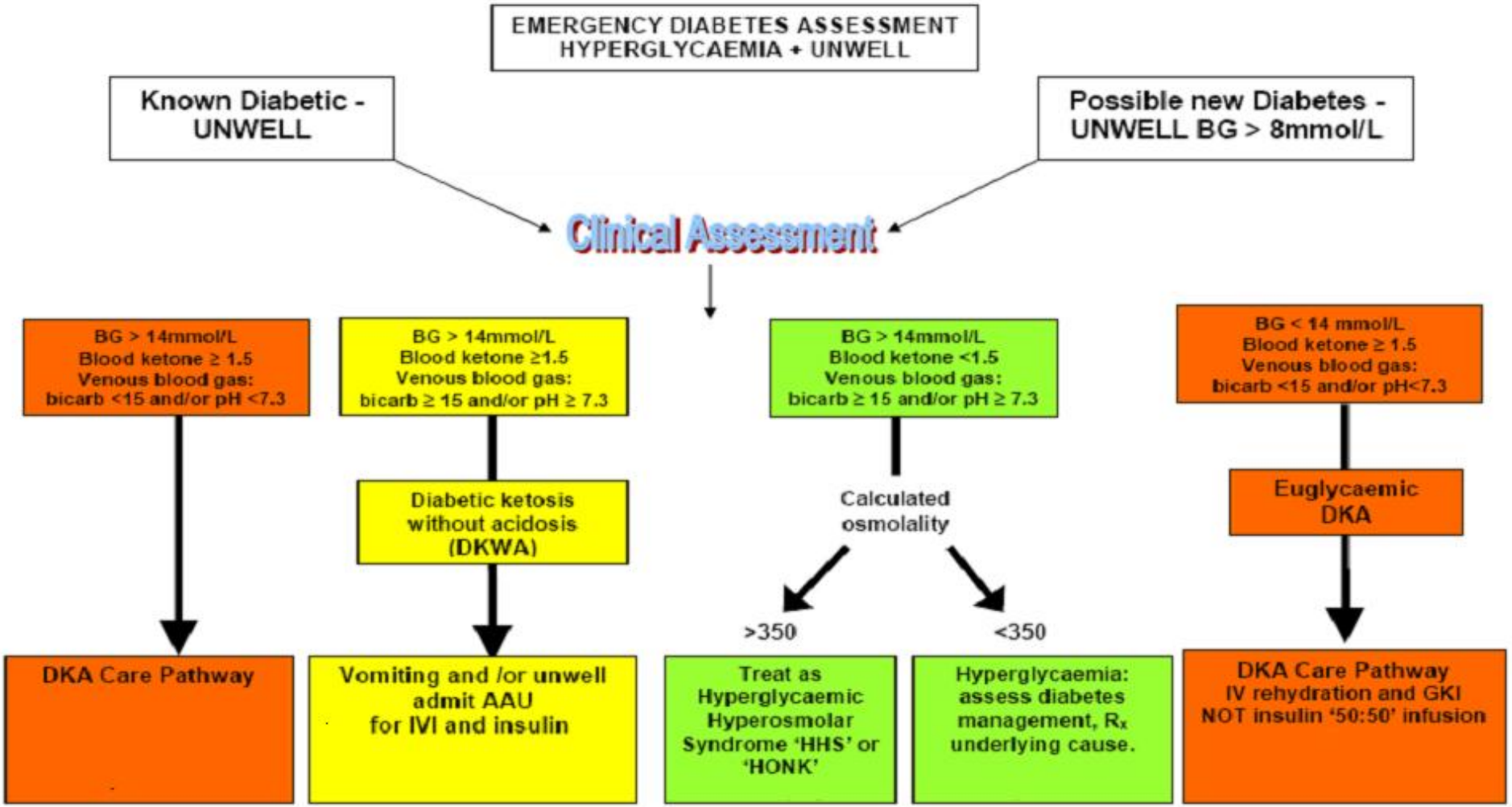
- Ketoacidosis (IDDM)
- Hyperosmolar syndrome (NIDDM)

Both result in severe dehydration and hypokalaemia.

Symptoms in hyperglycaemic coma

- Anorexia, nausea, and vomiting, polyuria and polydypsia.
- Abdominal pain may be present.
- Subsequent progression to altered consciousness or frank coma may occur.
- The initial examination usually shows Kussmaul respiration (gasping for breath - which also smells of acetone in ketoacidosis) together with signs of dehydration.
- Body temperature is normal, fever suggests the presence of infection.

Hyperglycaemia



Acute Management of Diabetic Ketoacidosis in Adults (patients ≥18 years)

If patient is between 16-17 yr old but physically immature/pubertal contact Paediatrics for advice first

Due to the significant mortality that DKA carries, the following clinical signs indicate the need for close monitoring within the Medical High Dependency Unit. Liase with RMO and Outreach Team.

- Unresponsive to treatment
- Hypotensive despite fluid replacement or requiring extensive fluid replacement, SBP <90mmHg, Pulse>100 beats/min
- GCS < 13 or inability to protect airway
- Sepsis (lactate ≥4mmol/L)
- HCO_3^- <5mmol/L
- pO2 < 10.0kPa or SaO2< 94%
- Pregnancy
- K^+ <3.5mmol/L on admission

ASSESSMENT

Step 1- Hour 0 to1

Doctor

- IV Cannula x 2 ❑
- BCP, Lab Blood glucose, FBC, CRP ❑
- Venous Blood Gas (if SaO_2<95% then perform ABG) ❑
- ECG ❑
- Consider Nasogastric tube if protracted vomiting /unprotected airway ❑
- consider LMWHeparin as VTE chart ❑
- Inform RMO1 (Bleep 404) ❑

Nurse

Monitor ½ hourly to hourly dependent on patients condition (severity of shock)

- TPR, BP, O_2 Sats, GCS,EWS ❑
- Hrly Capillary BG & Ketones ❑
- Fluid balance ❑
- Urinalysis ❑

Step 2 - Hour 2 to 4

- Repeat U & E's and lab blood glucose (the latter only if baseline BG >28mmol/L)

AND

- *VENOUS blood gas*

.....At end of hours 2 and 4

- Consider precipitants
  - CXR
  - MSSU
  - Blood cultures
  - Pregnancy test
  - Stool M,C & S
  - Foot examination

Consider inserting a urinary catheter if not passed urine after 2 hours

Step 3-Hour 5 and beyond

- U & E's for HCO_3^- twice daily until >19mmol/L
- Allow oral intake if bowel sounds present
- Vital signs stable & improving consider monitoring 4 hourly
- Prescribe patient's usual insulin - suspend whilst on GKI **UNLESS pt. takes Lantus or Levemir (=basal insulin 'BI') in which case give 'BI' as normal, concurrent with GKI.**

If patient fails to improve or deteriorates within first 4 hours contact the on-call consultant

TREATMENT

FLUIDS (see page 7-8 IVI prescription)

BAG

1st - 0.9% saline, 500ml STAT

2nd - 0.9% saline, 500ml over 30mins.

3rd - 0.9% saline, 500ml over 1 hour

BAG

4th - 0.9% saline, 500ml over 1 hour

5th - 0.9% saline, 500ml over 1 hour

6th - 0.9% saline, 500ml over 2 hour

Add potassium as per guidance

continue with

-0.9% saline 500ml over 2 hours until serum bicarbonate >15mmol/L ..then:-

-0.9%saline 500ml over 4 hours until serum bicarbonate ≥ 20mmol/L.

Watch for fluid overload particularly in the under 26's, elderly, heart/renal failure.

INSULIN (see p. 9 for insulin infusion prescription)

- 50 units Humulin S in 50ml 0.9% saline via syringe driver to be given IV
- Set rate:- generally at 6ml/hour however if patient has low BMI <20 set rate at 4ml/hr (may need to increase/decrease 1ml/hr to achieve aim)
- Aim:- for fall in blood glucose level between 3-5 mmol/L/hour
- Avoid:- drop in BG >5mmol/L/hr as risk of cerebral oedema (headache, reduced GCS → CALL CONSULTANT)
- Limit:- until or admission blood glucose is below 14mmol/L then

6) GKI Infusion

No recommended starting dose - consider the patient's response to the 50:50 insulin infusion

units in GKI	Equivalent to units/hr
16	3.2
20	4.0
24	4.8
28	5.6

POTASSIUM REPLACEMENT : cardiac monitoring if K^+ out of range

Venous K+	KCl per 500ml bag of 0.9% saline
> 5.5mmol/L	nil
3.5 – 5.5mmol/L	20 mmol
< 3.5mmol/L	40 mmol + senior review

Do not give more than 40mmol KCl per hour and use large vein

7) Convert back to usual subcutaneous insulin

When:-

- ❑ serum bicarbonate ≥20mmol/L,
- ❑ & blood ketones <0.3mmol/L
- ❑ & tolerating food
- ❑ administration of usual s/c insulin usually at meal times then…
- ❑ after 30 minutes stop GKI infusion

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Management of Hyperglycaemic Hyperosmolar Syndrome (HHS) Hyperosmolar Non-Ketotic Coma (HONK)

DIAGNOSIS:

1. Raised blood glucose (usually >40mmol/L)
2. Serum Osmolality >340mosm/L (2 x (Na+K)+ urea + glucose)
3. Absent or minimal ketonuria
4. Predominantly a state of dehydration rather than purely insulin deficiency – avoid too rapid a fall in blood glucose

INVESTIGATIONS:

1. Plasma Glucose, BCP, capillary blood ketones, ABG, FBC, blood cultures

2. ECG, CXR, MSU **NB**: Corrected Na=(Measured) Na+1.6x[(plasma glucose-5.5)/5.5]

IMMEDIATE MANAGEMENT: Start ASAP in A&E or AAU

1. 1 L 0.9% Saline infusion over 1 hour
2. 50units Humulin S in 50mls 0.9% saline via syringe driver
3. Set rate: for IV Humulin S insulin infusion at 6units/hour
4. Inform Outreach Team - bleep 075

GENERAL MANAGEMENT MEASURES:

1. Central line with CVP measurement may be necessary
2. Input/output chart (urinary catheter if oliguric/renal dysfunction present)
3. Insert NG tube if consciousness impaired (to prevent aspiration)
4. Unless contraindicated, full anticoagulation with s/c fragmin
5. Repeat U&E & glucose at 2hrs, 6hrs, 12hrs. and 24hours

BLOOD GLUCOSE (BG):

1. If BG falls >4mmol/hour, reduce insulin infusion rate by 2mls/hr i.e. reduce insulin infusion rate from 6ml/hr to 4ml/hr – aim is slow and steady resolution of hyperglycaemic state.
2. Switch to GKI as per standard protocol once BG<14mmol/L

FLUIDS: Care not to overload the elderly and patients with cardiac/renal problems

1. 1 L 0.9% Saline over 1 hour and then 1 L 0.9% Saline over 2 hours
2. 1 L 0.9% Saline over 2-4 hour (based on volume status/CVP reading)
3. 1 L 0.9% Saline over 6 hours maintenance until rehydrated

NB: If Na is > 160mmol/L, discuss with a senior about giving 0.45% Saline but only after pulse and blood pressure have been corrected.
There may be a paradoxical rise in serum sodium concentration during initial treatment due to a fall in BG and consequent fluid shifts that reduce dilutional volume.

POTASSIUM:

serum K^+	Addition
≤5.4mmol/L	40 mmol KCL /Litre bag 0.9% Saline
>5.4mmol/L	None

REFER EARLY:

- **To the on Call Medical Registrar/Consultant**
- **To the Diabetes Inpatient Team (DISN HRI: bleep 200, 4342; DISN CHH bleep 919, 3737) and Consultant Endocrinologist on-call (via switchboard)**