

Hypoglycaemia

DOMTRU GP Injectable Masterclass Nov 10 2019

Is it a big deal?

Dr. Hamish Russell
Staff Specialist Endocrinologist
Liverpool Hospital

YES

(Even if an individual has not had problems
yet !)



Barriers to achieving target HbA1c		
Patient factors	Health care professional factors	Health-care system factors
Diet/exercise/work/environment	Clinical inertia	Access to healthcare professional
Lack of understanding or education or appreciation Language barrier, cultural differences	Lack of understanding or education or appreciation	PBS medication restrictions
Medication omission	Too busy	Access to subsidized technology
Fear of injections	Lack of support	
Physiology/Beta cell failure/insulin resistance	Medications not sufficiently efficacious or physiological	
Lack of financial/personal/family support	Consideration of patient preferences	
Comorbidities e.g renal/liver/cardiac disease, cognitive impairment	Fear of causing hypoglycaemia	
<u>Hypoglycaemia</u>	Medication interactions, side-effects or contraindications	
Psychological factors /depression/anxiety		
Lack of engagement		
Burnout		
Fear of hypoglycaemia, fear of weight gain, fear of side effects		
Medication burden, medication interactions, side-effects or contraindications		

Hypoglycaemia – a few definitions

- Plasma glucose less than 4.0 mmol/l.
- Severe hypoglycaemia – an event requiring assistance of another person (e.g administer carbohydrates, glucagon, call an ambulance etc). Note that BGL level is not part of definition and that neurological recovery following the return of glucose to normal is considered sufficient evidence that the event was induced by a low plasma glucose.
- Impaired hypo awareness/hypoglycaemia unawareness- Reduced or absent symptoms of hypoglycaemia due to defective counterregulatory responses to hypoglycaemia.

Hypoglycaemia- how common?

- Severe hypoglycaemia
 - 30 to 40% of people with Type 1 DM have an average of 1 to 3 severe hypo episodes each year
 - Insulin treated Type 2 DM – approximately 1/3rd as frequent
- Mild to moderate hypoglycaemia- approximately 50 x more frequent than severe hypoglycaemia in both Type 1 and 2 DM

Significance- Morbidity

- Acute:
 - Decreased motor skills, visual acuity, auditory processing, mood, impaired cognition, altered behavior, decreased consciousness/unconsciousness/seizure.
 - Falls/accidents/motor vehicle accidents/hospitalisations (average 4 days in hospital after severe hypo).
 - Possible precipitation of cardiovascular and cerebrovascular events.
- Ongoing:
 - Potential negative effect on activities of daily living, quality of life e.g sleep, mood, depression, anxiety, impact on relationships, work, ability to drive, increased fear of subsequent hypoglycaemia.
 - Possibly cognitive dysfunction/dementia in Type 2 DM (less clear assoc in T1DM).
 - Inability to achieve target glycaemic control

Significance- Mortality

- Between 4-10% of deaths in patients with Type 1 DM caused by hypoglycaemia.
- Probably caused by cardiac arrhythmias.
- Hypoglycaemia postulated to be the mechanism for the excess mortality seen in the intensive glycaemic control arm of the ACCORD study.
- Severe hypoglycaemia associated with increased mortality in ACCORD, VADT and ADVANCE studies.

Hypoglycaemia- who is at risk?

- More frequent in profound insulin deficiency- Type 1 diabetes or advanced Type 2 DM
- More frequent with duration of diabetes.
- More common with insulin and sulfonylurea treatment (and glinides)
- Low risk with metformin, DPP-IV inhibitors, TZD's, SGLT-2 inhibitors, GLP-1 receptor antagonists.
- Intensive glycaemic control- 3 x risk of severe hypo in DCCT (risk with a given HbA1c decreasing with time with advances in diabetes management)

Other causes/contributors of hypoglycaemia

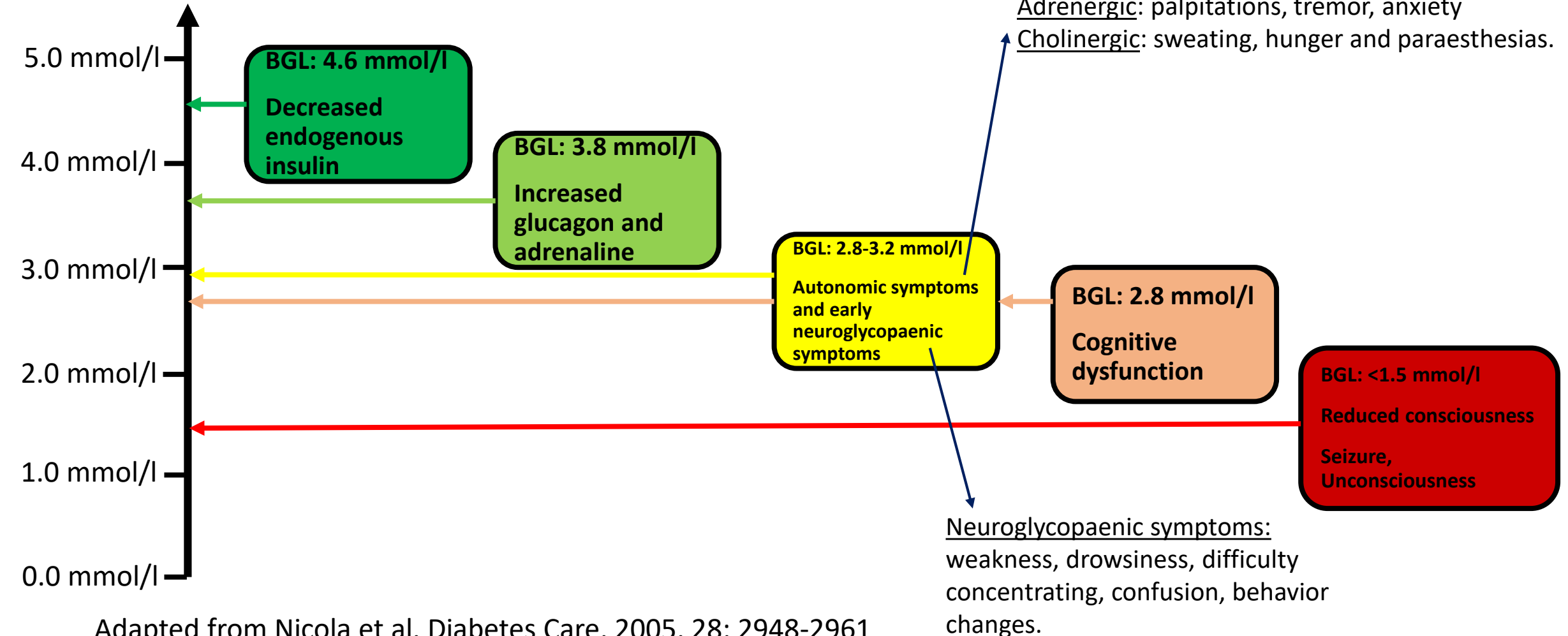
- Dietary –inadequate carbohydrate intake, missed or delayed meals
- Exercise/physical activity
- Excessive dose/inappropriate timing of sulfonylurea or insulin
- ETOH
- Acute renal impairment
- Liver disease
- Elderly- age related decline in renal and hepatic function, decreased counterregulatory response to hypoglycaemia, comorbidities, decreased ability to detect to respond to hypoglycaemia (e.g due to cognitive impairment)
- Adrenal insufficiency
- Malabsorption e.g. coeliac disease
- Gastroparesis
- Impaired hypoglycaemia awareness- Hypoglycaemia unawareness
- Previous hypoglycaemia

Impaired hypoglycaemia awareness - Hypoglycaemia unawareness

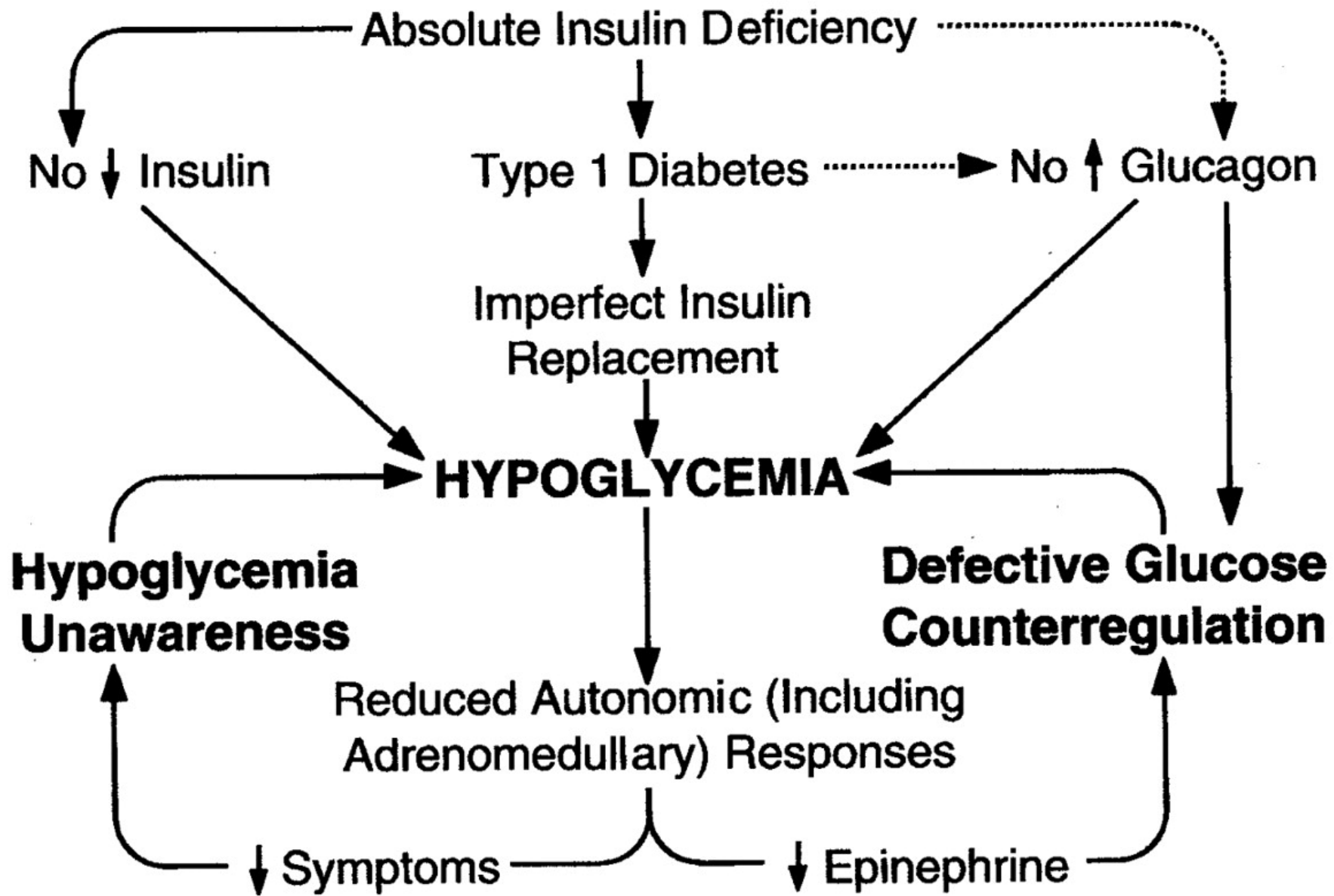
- Reduced or absent symptoms of hypoglycaemia due to defective counterregulatory responses to hypoglycaemia.
- At least 6 x risk of severe hypoglycaemia.
- Induced by preceding hypoglycaemia.
- 2 moderately severe hypo episodes enough to reduce subsequent counterregulatory hormone responses.
- Can be reverse after 2-3 weeks of scrupulous avoidance of hypoglycaemia.

Counterregulatory responses and hypoglycaemia symptoms in an individual without diabetes

Blood glucose level



Adapted from Nicola et al. Diabetes Care, 2005, 28; 2948-2961



Clarke hypoglycaemia awareness survey

For use in Continuous Glucose Monitoring Eligibility Assessment: Type 1 Diabetes; Age 21 Years and Over; Eligible Concessional Status; supplied under the National Diabetes Services Scheme.

Questions	Score
<p>1 The category that best describes you (choose only one)</p> <p><input type="checkbox"/> I always have symptoms when my blood sugar is low (A)</p> <p><input type="checkbox"/> I sometimes have symptoms when my blood sugar is low (R)</p> <p><input type="checkbox"/> I no longer have symptoms when my blood sugar is low (R)</p>	
<p>2 Have you lost some of the symptoms that used to occur when your blood sugar was low?</p> <p><input type="checkbox"/> Yes (R) <input type="checkbox"/> No (A)</p>	
<p>3 In the past six months how often have you had moderate hypoglycaemia episodes where you might have been confused, disoriented or lethargic and were unable to treat yourself?</p> <p><input type="checkbox"/> Never (A) <input type="checkbox"/> Once a month (R)</p> <p><input type="checkbox"/> Once or twice (R) <input type="checkbox"/> More than once a month (R)</p> <p><input type="checkbox"/> Every other month (R)</p>	
<p>4 In the past year how often have you had severe hypoglycaemia where you were unconscious or had a seizure or needed glucagon or intravenous glucose?</p> <p><input type="checkbox"/> Never (A) <input type="checkbox"/> 8 - 11 times (R)</p> <p><input type="checkbox"/> 1 - 3 times (R) <input type="checkbox"/> > 12 times (U)</p> <p><input type="checkbox"/> 4 - 7 times (R)</p>	
<p>5 How often in the last month have you had readings < 3.9 mmol/L with symptoms?</p> <p><input type="checkbox"/> Never <input type="checkbox"/> 2 to 3 times/week</p> <p><input type="checkbox"/> 1 to 3 times <input type="checkbox"/> 4 to 5 times/week</p> <p><input type="checkbox"/> 1 times/week <input type="checkbox"/> Almost daily</p>	
<p>6 How often in the last month have you had readings < 3.9 mmol/L without symptoms?</p> <p><input type="checkbox"/> Never <input type="checkbox"/> 2 to 3 times/week</p> <p><input type="checkbox"/> 1 to 3 times <input type="checkbox"/> 4 to 5 times/week</p> <p><input type="checkbox"/> 1 times/week <input type="checkbox"/> Almost daily</p>	
<p>Scoring Q5 & Q6: R = answer to Q5 is less than answer to Q6; A = answer to Q5 is greater than or equal to answer to Q6</p>	
<p>7 How low does your blood sugar go before you feel symptoms?</p> <p><input type="checkbox"/> 3.3 - 3.8 mmol/L (A) <input type="checkbox"/> 2.2 - 2.7 mmol/L (R)</p> <p><input type="checkbox"/> 2.8 - 3.3 mmol/L (A) <input type="checkbox"/> < 2.2 mmol/L (R)</p>	
<p>8 To what extent can you tell low blood sugars by your symptoms?</p> <p><input type="checkbox"/> Never (R) <input type="checkbox"/> Often (A)</p> <p><input type="checkbox"/> Rarely (R) <input type="checkbox"/> Always (A)</p> <p><input type="checkbox"/> Sometimes (R)</p>	
<p>Total: (count the number of 'U's, 'R's and 'A's) U= A= R=</p>	

Scoring: 'U' response indicates hypoglycaemia unawareness. Four or more 'R' responses implies reduced hypoglycaemia awareness. 'A' response implies hypoglycaemia awareness

Based on: Clarke W, Cox DJ, Gonder-Frederick LA, Julian D, Schlundt D, Polonsky W. *Reduced awareness of hypoglycaemia in adults with IDDM.* Diabetes Care. 1995; 18(4): 517-522.

Units of measure converted from mg/dl to mmol/L as per onlineconversion.com/blood_sugar.htm

Impaired Hypoglycaemia awareness- Hypoglycaemia unawareness?

- My questions:
 - Do you sometimes check your blood glucose level without any symptoms and find that is low? If so, how low and how often?
 - How low does your blood glucose level go before you get symptoms?
 - +/- collaborative history from family/friends- evidence of hypoglycaemia without then being aware?

Nocturnal hypoglycaemia

- Increased risk overnight due to decreased intensity and recognition of counterregulatory responses.
- Patient may not wake up at the time- often asymptomatic or wakes later with headache or sweats overnight or partner notices is restless etc. Can be hypoglycaemic for a few hours.
- Risk for “dead in bed syndrome”.
- Consider if unexpected or problematic fasting hyperglycaemia (due to rebound from hypo).
- Advise patient to wake to check BGL overnight (e.g 2 am).
- Regular supper and reduce nocte insulin to see if fasting hyperglycaemia resolves. CGMS or flash BGL monitoring if available.

Prevention of hypoglycaemia (1)

- Restore hypo awareness if impaired or absent (avoid hypoglycaemia).
- Dietary advice
- Exercise- carbohydrate intake, reducing appropriate insulin dose in anticipation
- ETOH- adequate CHO intake, reduce long acting nocte insulin
- Recommend and review appropriate BGL monitoring
- Sulfonylurea dose or type adjustment or cessation
- Insulin regimen or dose adjustment
- Rapid acting instead of regular acting insulin
- Basal insulin –e.g. detemir, glargine (instead of protaphane, Humulin NPH)
- Consider change Lantus to Toujeo insulin
- Investigate with EUC, LFT's +/- am cortisol, coeliac serology, gastric emptying study.
- Negotiate an appropriate HbA1c for the individual.

Prevention of hypoglycaemia (2)

- Education on appropriate hypoglycaemia detection and management
- Consider glucagon kit and education for family/friend(s)
- Attend to unhelpful perceptions or behaviours around hypoglycaemia/diabetes management
- Structured education programs
 - Insulin Treatment and Training Program
 - DAFNE course
- Flash BGL monitoring
- Insulin pump
- CGMS (with or without insulin pump)
- Automated pump systems : Hybrid or closed loop pump systems
- Islet transplantation
- Combined pancreas/renal transplant



References:

Hypoglycaemia and Diabetes: A report of a workgroup of the American Diabetes Association and the Endocrine Society. Seaquist E et al, Journal of Clinical Endocrinology and Metabolism, May, 2013, 98(5): 1845-1859.

Minimizing Hypoglycaemia in Diabetes. Cryer P, Diabetes Care, Vol 38, Aug 2015, 1583-1591.