The Association for Clinical Biochemistry & Laboratory Medicine

Better Science, Better Testing, Better Care

Summary of Endocrinology Society Guidelines

Title	Evaluation and management of adult hypoglycaemic disorders
Journal Reference	Cryer PE, Axelrod L, Grossman AB, Heller SR, Montori VM, Seaquist ER, et al. Evaluation and management of adult hypoglycemic disorders: an Endocrine Society Clinical Practice Guideline. J Clin Endocrinol Metab. 2009 Mar;94(3):709–28.
Date of Review:	*February 2019*
Summary of Condition (Max 250 words)	Investigation for hypoglycemia should be considered if the Whipple's triad; plasma glucose <3.0mmol/L, symptoms of hypoglycemia (neuroglycopenic) with symptomatic relief after correcting plasma glucose, are present. This guideline has different approaches for evaluating a patient with or without diabetes mellitus and it states that hypoglycaemic events are rare in patients without diabetes mellitus. When a spontaneous hypoglycemic episode cannot be observed, circumstances to recreate symptomatic hypoglycemia should be intimated under medical supervision i.e. during a fast of up to 72 h or after a mixed meal. Suggested protocols for diagnostic prolonged fast (table 4) and mixed-meal tests (table 5) can be found in this guideline. Clinical evaluation of patients **during** a hypoglycaemic episode should include the following biochemistry tests in the first instance: • Plasma glucose • Insulin & C-peptide • β-hydroxybutyrate (β-OHB) • Drug history to exclude hypoglycemia agents The cause of hypoglycaemia, based on biochemistry parameters can be determined using the table below in symptomatic patients:

Cause	Underlying pathology	Biochemistry
Drugs e.g. insulin or secretalogue, alcohol Accidental, malicious or surreptitious	**Insulin overdose, low glycogen stores secondary to poor dietary intake associated with alcohol excess**	**Insulin: >3 C-peptide: <0.2 β-OHB: ≤2.7 Antibody: Neg**
Critical illness	**Hepatic, renal or cardiac failure, sepsis**	**Insulin: <3 C-peptide: <0.2 β-OHB: ≥2.7 Antibody: Neg**
Hormone deficiency	**Cortisol, glucagon or epinephrine**	**Insulin: <3 C-peptide: <0.2 β-OHB: ≥2.7 Antibody: Neg**
Endogenous hyperinsulinism	**Insulinoma, Nesidioblastosis or autoimmune hypoglycaemia**	**Insulin: ≥3 C-peptide: ≥0.2 β-OHB: ≤2.7 Antibody: Neg/Pos**

Units: Insulin - µU/mL, C-peptide – ng/mL, β- OHB – mmol/L

	For patients with diabetes the risk factors for hypoglycemia include • Excessive or ill-timed doses of insulin or insulin secretalogue, • Reduced exogenous glucose intake • Increased glucose utilisation • Increased sensitivity to insulin • Lowered endogenous glucose production (e.g. with alcohol) • Reduced insulin clearance in renal failure. It is recommended that urgent treatment of hypoglycemia should be accomplished by ingestion of carbohydrates or by parenteral glucagon or glucose. Patients with diabetes should be concerned about hypoglycaemia if blood glucose if falling rapidly or is ≤3.9mmol/L. With a history of hypoglycaemic unawareness it is recommended that a 2 to 3 week period of hypoglycaemic avoidance can lead to a return of awareness.
Overview of assays (150 words max)	As the tests described in this guideline are routine, with maybe the exception of β-OHB, there are no special considerations for sampling. Nevertheless these samples should be collected together during a hypoglycaemic event to accurately interpret the cause (see table above). 1. Glucose - AMALC* for Glucose 2. C-peptide - AMALC for C-peptide 3. Insulin - AMALC for Insulin. Antibodies to native insulin may cause a falsely low insulin result but these antibodies are very rare. It should also be noted that with renal failure, insulin clearance may be reduced causing higher than normal concentrations. 4. β-hydroxybutyrate – β -OHB is determined by a enzymatic kinetic assay measuring reduction of NADH spectrophotometrically at 340nm, via the action of dehydrogenase. Antibodies used to determine autoimmune causes of hypoglycaemia e.g. Glutamic acid decarboxylase (GAD) antibodies are present in ~70% patients with Type I at the time of diagnosis. This is a service provided by immunology. *AMALC = Analyte Monographs alongside the National Laboratory Medicine Catalogue (aka ACB monographs).
Lab professionals to be made aware	✓ Chemical Pathologist ✓ Clinical Scientist
Impact on Lab	☐ Moderate
Please detail the impact of this guideline (Max 150 words)	The investigations of hypoglycaemia will depend on whether the patient has diabetes or not but in the general population the incidence of hypoglycemia is relatively low. Clinical scientists should endeavor to educate service users regarding the timing of samples to allow for accurate interpretation of abnormal results. This guideline advocates frequent measurements of glucose after administration of 1.0mg glucagon to determine whether the cause is endogenous or exogenous insulin. Overall there is a moderate impact to the laboratory services, both biochemistry and immunology, regarding investigation of hypoglycemia. It should be noted this guideline does not cover more serious causes of hypoglycaemia in children, and that unexpected hypoglycaemia ±fever

	should be fully investigated according to local protocols for ?metabolic disease.

Impact on Lab

- **None**: This guideline has no impact on the provision of laboratory services
- **Moderate**: This guideline has information that is of relevance to our pathology service and may require review of our current service provision.
- **Important:** This guideline is of direct relevance to our pathology service and will have a direct impact on one or more of the services that we currently offer.

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