:: Central Diabetes Insipidus

- *This document is a translation of the French recommendations drafted by Dr Morlet and Pr Brue, reviewed and published by Orphanet in 2009.*
- *Some of the procedures mentioned, particularly drug treatments, may not be validated in the country where you practice*.

Synonyms:

Neurogenic diabetes insipidus

Definition:

Diabetes insipidus is characterised by **deficiency in the secretion of antidiuretic hormone** (ADH or AVP), resulting in **hypotonic** (<250 mmol/kg H_2O) **polyuria** (>30 mL/kg body weight). **It may be hereditary or acquired**. This ADH deficiency may be secondary to a disorder affecting one of the sites involved in ADH secretion (supraoptic and paraventricular nuclei in the hypothalamus) or affecting the hypothalamic-pituitary axis. The aetiology of central diabetes insipidus **in adults and in children** varies: it may be idiopathic, tumoral (craniopharyngioma, metastasis, etc.), post-surgical, due to histiocytosis, post-traumatic, infectious, due to a metabolic storage disorder, autoimmune or granulomatous in origin. **The basic treatment is desmopressin acetate in oral (**DDAVP®, DDVAP® Melt, Desmotabs®, DesmoMelt®**), injectable (**DDVAP®, Octim®**) or intranasal solution/nasal spray** (DDVAP®, Desmospray®, Octim®).

Further information:

See the Orphanet abstract

Pre-hospital emergency care recommendations
Call for a patient suffering from central diabetes insipidus

Synonyms

- Diabetes insipidus of central origin, neurogenic diabetes.

Mechanisms

- Deficiency in the secretion of antidiuretic hormone (ADH), secondary to a disorder affecting the supraoptic and paraventricular nuclei of the hypothalamus or the hypothalamic-pituitary axis with varying aetiology, including tumoral (craniopharyngioma, metastasis, etc.), post-surgical, idiopathic, histiocytosis, post-traumatic, infectious, metabolic storage disorder, autoimmune and granulomatous.

Specific risks in emergency situations

Problems with hydration, signs of which are clinical and identifiable from laboratory results, rendering diagnostics in pre-hospital care virtually useless and difficult for mobile emergency and resuscitation units; clinical signs correlate to disturbances in levels of sodium, their severity and rapidity of onset:

- intracellular dehydration, with normal sodium levels where there is compensatory polydipsia or hypernatraemia in the absence of hydration
- hyperhydration with hyponatraemia in cases of desmopressin overdose: there is a direct correlation between clinical signs and the degree of hyponatraemia

Commonly used long-term treatments

- **Desmopressin acetate**: oral (DDVAP®, DDVAP® Melt, Desmotabs®, DesmoMelt®), injectable (DDVAP®, Octim®) or intranasal solution/nasal spray (DDVAP®, Desmospray®, Octim®)

Complications

- be alert to any causes of dehydration that may be masking or, conversely, that may be being masked by the diabetes insipidus
- be alert to any other anterior pituitary deficiencies, particularly corticotropic

Specific pre-hospitalisation medical care

- Symptomatic correction of the circulating volume once a specimen has been collected to test blood electrolytes, if possible.
- Transfer to the intensive care or resuscitation unit

For further information

- The Pituitary Foundation: www.pituitary.org.uk
- Please visit www.orpha.net and type the name of the disease -> in the summary page click on “Expert centres” on the right tab -> select “United Kingdom” in the “Country” field in the Expert centres page.

Recommendations for hospital emergency departments

Emergency situations

1. Intracellular dehydration

Sodium levels remain normal where polydipsia is compensating for polyuria. If hydration is impossible (coma, psychiatric disorders, sedation during resuscitation, elderly patients or young children), **hypernatraemia** will develop, **with intracellular dehydration and plasma hyperosmolarity**.

- be alert to any causes of dehydration that may be masking or, conversely, that may be being masked by the diabetes insipidus

- **Immediate diagnostics:**
  - Assess the severity:
    - Clinical signs **- drowsiness, asthenia, behavioural disorders, fever of central origin, fits, coma, cerebromeningeal haemorrhage -** correlate with the degree of hypernatraemia and rapidity of onset
    - **Thirst**: sometimes intense
    - **Mucosal dryness**
    - **Polyuria**
    - **Weight loss**
  - Emergency laboratory tests:
    - **Blood electrolytes, plasma osmolarity, diuresis, urinary osmolarity and urinary specific gravity**
      - HyperNa >145 mmol/L, plasma osmolarity >300 mOsmol/L associated with hypotonic polyuria pOsm >300 mOsmol/kg water) and low urinary specific gravity (<1005)
- **Emergency treatment:**
  - **SYMPTOMATIC and AETIOLOGICAL TREATMENT**: designed **to correct** any abnormality in **circulating volume**, also **plasma hypertonicity**
    - **ADMINISTRATION OF DDAVP (desmopressin acetate)**
      - **If the patient is unconscious:** injectable (subcutaneous, direct i.v. or i.m. (1 mL = 4 µg)):
        - **Adult**: 1 to 4 µg/d in 2 injections
        - **Infant**: 0.2 to 0.4 µg/d in 2 injections
        - **Child**: 0.4 to 1 µg/d in 2 injections
      - **If the patient is conscious:**
        - per os: tabs. desmopressin acetate 0.1 and 0.2 mg. 0.1 to 0.2 mg x3/d or (desmopressin acetate 60, 120 or 240 µg)
        - nasal route: spray: 10 µg by spray. 10 to 20 µg in adults, repeat if necessary

        NB: where diabetes insipidus is being controlled by intranasal desmopressin acetate, **the dose of injectable** desmopressin acetate solution with comparable efficacy **is equal** to roughly **one tenth of that administered intranasally.**
    - **COMPENSATION FOR FLUID LOSS**: if the neurological status permits, give the patient water to drink; alternatively, rehydrate via the intravenous route: 2.5% dextrose
    - **Oral or i.v. rehydration may be given at up to 1 L/h**
    - **Amount of water to be administered: water deficit = 60% x weight x ([Na/140]-1)**
    - **Do not correct sodium levels too quickly:** the aim is 10 nmol/L every 24 hours, particularly in longstanding cases of hypernatraemia

- **MONITORING:**
  - Weight
  - Blood pressure
  - Level of consciousness
  - 24h urine output
  - Blood electrolytes

2. Hyperhydration with hyponatraemia:

Hyperhydration with hyponatraemia may be observed in the event of DDAVP overdose or a concomitant change in the thirst centre (e.g. due to a traumatic lesion).

DDAVP OVERDOSE:

Clinical signs (nausea, vomiting, anorexia, headaches, clouding of consciousness, coma, seizures, absence of thirst, even distaste for water) **are correlated with the degree of hyponatraemia and rapidity of onset**. Laboratory results will show **hyponatraemia**.

- **Immediate therapeutic measures**
  - Stop desmopressin acetate treatment
  - **For asymptomatic hyponatraemia or where there are few symptoms:** restrict fluid intake: 500 to 700 mL/24h
  - **Symptomatic hyponatraemia: caution** must be exercised **when correcting** disorders since there is a **major risk of central pontine myelinolysis**
  - **Coma or fits**: Hypertonic NaCl infusion, taking care not to correct sodium levels by more than 1 mmol/h or by more than 12 mmol on the first day

Orientation:

- Where: the nearest hospital: intensive care or resuscitation, depending on clinical status, then refer to the Department of Endocrinology.
- When: depending on the severity of the electrolyte and consciousness disturbances

Drug interactions and precautions for use:

- **Carbamazepine** (Tegretol®, also in Tegretol® Retard and Carbagen® SR): can potentiate release and action of ADH. Stimulates AVP secretion and increases its action at renal level.
- **Clofibrate**: stimulates production of AVP.
- **Chlorpropamide, Indometacin/Indomethacin**: increase the release of ADH and enhance anti-diuretic activity.
- **Lamotrigine** (Lamictal®): risk of hyponatraemia.
- **Thiazides:** can reduce diuresis by triggering moderate sodium depletion.
- **Glibenclamide**: reduction in antidiuretic activity.
- **Valproic acid** (Depakote®, Convulex®): one case of transient diabetes insipidus developed under Depakote®.
- **Loperamide** (Imodium®, also in Imodium® Plus): as gastrointestinal motility is slowed down, there is a risk that the antidiuretic effect of desmopressin acetate may increase.

Anaesthesia

- Monitor fluid levels, diuresis and plasma osmolarity during
  - surgical procedures
  - situations in which patients are unable to satisfy their thirst or to take desmopressin acetate treatment
- The intravenous route is used for administration

Preventive action to be taken

- Ensure correct **compensation** in respect of **any other associated anterior pituitary deficiencies, particularly corticotropic** deficiency.

Additional therapeutic measures and hospitalisation

- In the event of problems regulating thirst:
  - **quantify and monitor fluid intake**
  - **adjust intake in line with diuresis**
  - **adjust the amount of dietary salt given**
- Consider air-conditioning during periods of particularly hot weather
- Provide patients with easy and frequent access to toilets
- Tell parents and the family about the disease and how it is managed
- Educate the patient

Organ donation

- There are no data in the literature that contraindicate **organ donation**; this will need to be **considered in the light of the pathology underlying the onset of diabetes insipidus.**
- Bear in mind that, since **brain death often accompanies central diabetes insipidus**, particularly close attention needs to be paid to water metabolism. Treatment for diabetes insipidus needs to be started early and includes DDAVP replacement therapy, which will subsequently be adjusted in line with diuresis.

Emergency telephone numbers

- Please visit www.orpha.net and type the name of the disease -> in the summary page click on “Expert centres” on the right tab -> select “United Kingdom” in the “Country” field in the Expert centres page.

Documentary resources

- Ann Fr Anesth Reanim. 2006 May;25(5):525-7. Epub 2006 Feb 28. [Transient central diabetes insipidus during a valproic acid poisoning]
- Lancet. 2000 Aug 19;356(9230):656. Hyponatraemia associated with lamotrigine in cranial diabetes insipidus. Mewasingh L, Aylett S, Kirkham F, Stanhope R.
- Eur J Clin Pharmacol. 1999 Jun;55(4):305-9. Changes in gastrointestinal motility influence the absorption of desmopressin. Callréus T, Lundahl J, Höglund P, Bengtsson P. Department of Clinical Pharmacology, Lund University Hospital, Sweden.
- Crit Care Med. 1994 Aug;22(8):1301-5. Brain death in pediatric intensive care unit patients: incidence, primary diagnosis, and the clinical occurrence of Turner’s triad. Staworn D, Lewison L, Marks J, Turner G, Levin D. Department of Pediatrics, University of Texas, Dallas.

These recommendations have been compiled in collaboration with Dr Nathalie Morlet and Prof. Thierry Brue at the Reference Centre for Rare Diseases of Pituitary Origin (DEFHY) and with Mme Nathalie Ducasse of the French Diabetes Insipidus Association (AFDI)

Completion date: 27 March 2009

Translation: Orphanet UK

Date of translation: May 2013

These recommendations have been translated thanks to the financial support of Shire