



British Society for Paediatric Endocrinology and Diabetes

DIABETES INSIPIDUS (DI)

The quantity of water retained in the body is closely controlled by several mechanisms, one of the most important of which is a hormone (a chemical secreted into the blood by an endocrine gland) secreted by the posterior pituitary gland, a structure which lies deep within the brain. This is called vasopressin or anti-diuretic hormone (ADH) because its function is to control the loss of water as urine from the kidneys. In order to do this, normal concentrations of cortisol are required to facilitate water retention. The amount of ADH secreted by the posterior pituitary is determined by sensors in the brain which monitor the concentration of the blood. If the blood becomes too concentrated more ADH is secreted and the kidneys retain water, if it is too dilute less ADH is secreted and the kidneys release more urine. Adults on average drink and pass about a litre and a half of fluid each day and children proportionately less. If their fluid intake increases the blood concentration falls, the secretion of ADH is reduced and more urine is passed, if their fluid intake reduces the opposite happens.

Cause:

If for any reason the function of the posterior pituitary gland fails, the secretion of ADH is inadequate and the kidneys lose too much water. DI can occur spontaneously without any apparent cause and is then referred to as idiopathic DI. It may also be genetically determined or can result from destruction of the posterior pituitary by disease such as Langerhans cell histiocytosis and sarcoidosis, meningitis, a head injury or a tumour. The gland can be shown well on CT or MR scanning of the brain and a scan is always needed in investigation. The increased loss of urine (polyuria) is reflected by a greatly increased thirst and fluid intake (polydipsia) but eventually it may become impossible to take in enough water and the person with this condition will become dehydrated. Additionally, DI can result from an inability of vasopressin to act on the kidney, which results in polyuria and polydipsia that does not respond to vasopressin administration, and this is referred to as nephrogenic DI. The cause for this may be genetic, often occurring more frequently in boys as the gene for the vasopressin receptor is on the X chromosome. However, the condition can also occur in girls. Other causes include the administration of lithium, and metabolic abnormalities such as chronic low concentrations of potassium (hypokalaemia) and high concentrations of calcium (hypercalcaemia).

Symptoms:

The presenting symptoms of DI are thus excessive urine output and excessive thirst. Depending on the degree to which ADH secretion is lost the symptoms can be quite mild or so great that some affected children virtually give up eating and lose a lot of weight. If fluid is not immediately available they will drink from flower vases, lavatory cisterns, puddles or anywhere else. In general affected children remain well but if they become dehydrated they may seem obviously ill. When these symptoms are first noticed many parents and professionals naturally assume this is a behavioural problem and try to restrict the child's drinking. This is obviously very upsetting for a child with severe thirst but is fortunately seldom harmful.



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Investigations:

In order to screen for DI, it may be necessary to perform early morning paired blood and urine tests, with measurement of plasma and urine osmolality. This can often exclude diabetes insipidus if the urine is concentrated relative to the plasma osmolality, particularly if there has been no fluid intake overnight. If the results are equivocal, in order to formally assess the concentrating power of the kidneys, it is usually necessary to deprive the child of fluid for some hours, measuring the concentration of the blood and the urine. This is a potentially dangerous test, and must be performed in a tertiary centre where such tests are performed regularly and under close supervision. DI is one of the most important reasons for failure to concentrate the urine normally. There are other causes, some of them much more common, including diabetes mellitus, in which the excessive urine production is due to glucose in the urine, and excessive drinking for psychological reasons, which is seldom seen in children. If the diagnosis of DI is proven then DDAVP needs to be administered in a controlled environment. This is a synthetic form of vasopressin and in central diabetes insipidus, the blood concentration then decreases with an increase in urine concentration, and a fall in urine losses and hence a reduced thirst then ensues. In nephrogenic DI, there is no response to DDAVP.

Treatment:

ADH is available but is destroyed in the stomach so can only be given by injection. Fortunately similar and even more effective chemical compounds have been developed which are well absorbed through the lining of the nose and adequately absorbed by mouth. The most effective of these is DDAVP or Desmopressin. This is available as a fluid which can be measured into a small tube and blown up the nose (easier than it sounds) which allows exact adjustment of the dose. Most children require a dose from 5-20micrograms each 12 hours to control water balance fully. There is also available a spray, Desmospray, which delivers a standard dose of 10mcg and tablets, Desmotabs, which contain 100-200mcg. Oral DDAVP is now widely used, and has largely superceded the intranasal DDAVP as a safe and efficacious alternative. It is given in doses of 5-200 µg given 2-3 times a day. Treatment of nephrogenic DI can be difficult and involves the use of thiazide diuretics, indomethacin and amiloride.

Outlook:

This clearly depends on the cause of the problem but in general DI is a permanent condition. However, in central DI, it is virtually always possible to restore normal fluid intake and output with DDAVP and so relieve the symptoms completely.