

***Please read this bit first***

The HPCSA and the Med Tech Society have confirmed that this clinical case study, plus your routine review of your EQA reports from Thistle QA, should be documented as a "Journal Club" activity. This means that you must record those attending for CEU purposes. Thistle will **not** issue a certificate to cover these activities, nor send out "correct" answers to the CEU questions at the end of this case study.

The Thistle QA CEU No is: **MT00025**.

Each attendee should claim **THREE** CEU points for completing this Quality Control Journal Club exercise, and retain a copy of the relevant Thistle QA Participation Certificate as proof of registration on a Thistle QA EQA.

## JANUARY 2009 - CHEMISTRY

### MINERALOCORTICOID DEFICIENCY SYNDROMES (MCD)

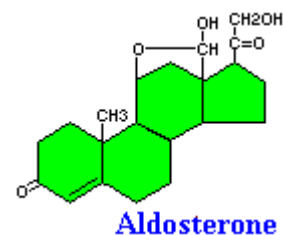
#### Definition

Corticosteroids are a group of natural and synthetic analogues of the hormones secreted by the hypothalamic-anterior pituitary-adrenocortical (HPA) axis. These include glucocorticoids, which are anti-inflammatory agents with a large number of other functions; mineralocorticoids, which control salt and water balance primarily through action on the kidneys; and corticotrophins, which control secretion of hormones by the pituitary gland.

Mineralocorticoids control the retention of sodium in the kidneys. In mineralocorticoid deficiency, there is excessive loss of sodium through the kidneys, with resulting water loss. Flurocortisone (Florinef) is the only drug available for treatment of mineralocorticoid deficiency, and is available only in an oral dosage form.

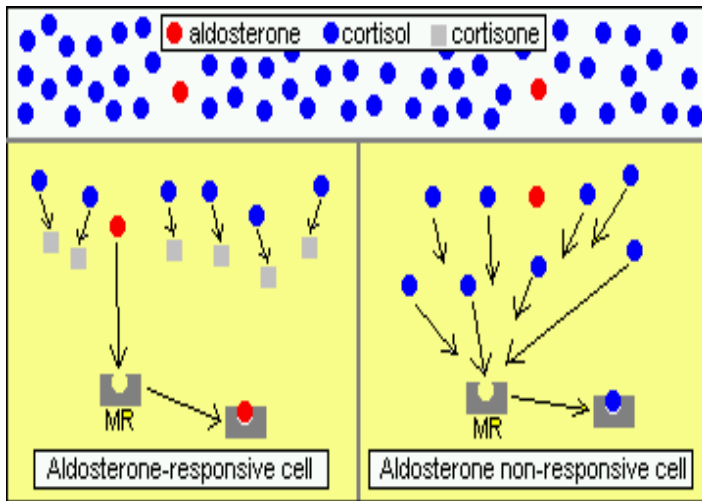
#### Aldosterone and Mineralocorticoid Receptors

The principal steroid with mineralocorticoid activity is **aldosterone**. A small fraction of the mineralocorticoid response in the body is due to cortisol rather than aldosterone. The mineralocorticoid receptor binds both aldosterone and cortisol with equal affinity. Moreover, the same DNA sequence serves as a hormone response element for the activated (steroid-bound) forms of both mineralocorticoid and glucocorticoid receptors. An obvious question is:



***How can aldosterone stimulate specific biological effects in this kind of system, particularly when blood concentrations of cortisol are something like 2000-fold higher than aldosterone?***

A large part of the answer is that, in aldosterone-responsive cells, cortisol is effectively destroyed, allowing aldosterone to bind its receptor without competition. Target cells for aldosterone express the enzyme 11-beta-hydroxysteroid dehydrogenase, which has no effect on aldosterone, but converts cortisol to cortisone, which has only a very weak affinity for the mineralocorticoid receptor. In essence, this enzyme "protects" the cell from cortisol and allows aldosterone to act appropriately. Aldosterone is not present in sufficient quantities to compete with cortisol.



### Causes of hyperkalaemic hyperchloraemic metabolic acidosis:

- Early uremic acidosis
- MCD
- Obstructive nephropathy
- Ingestion / Therapy
- Sulphur toxicity

### Causes of MCD

- Drugs - amiloride, brufen etc...
- Deficient cortisol and aldosterone - Addison's disease
- Deficient aldosterone and normal cortisol - Syndrome of hyporeninaemic hypoaldosteronism (Diabetes mellitus)
- Tubular unresponsiveness (increased aldo and rennin) - renal disease, renal transplants, sickle cell anaemia...

## Case History

MCD should be considered in patients' with an unexplained increased plasma potassium concentration even if there are other possible causes for abnormality. The danger in under investigation lies in missing a diagnosis of Addison's disease which can have disastrous consequences. Thus persistent hyperkalaemia should always be rigorously investigated, but prior to undertaking expensive and time consuming procedures, a detailed clinical history should be obtained particularly the drug history. These points are exemplified in the following case.

A 67 year old male with insulin dependent diabetes, on Frusemide and Amiloride therapy for mild heart failure was admitted after 24 hours of vomiting and his diabetes out of control. The routine plasma biochemistry revealed hyperglycaemia, hyponatraemia and hyperkalaemia. After 2 days of treatment with insulin and IV saline his diabetes stabilised, but after 7 days he still had hyperkalaemia. His clinician considered the possibility of Addison's disease and Syndrome of Hyporeninaemic Hypoaldosteronism and evaluated his cortisol, rennin and aldosterone status.

Day 1		Day 7		
Na	114	132	mmol/L	(132 - 144)
K	6	5.8	mmol/L	(3.2 - 4.8)
Cl	74	96	mmol/L	(98 - 108)
HCO <sub>3</sub>	24	25	mmol/L	(23 - 33)
Urea	16.5	7.6	mmol/L	(3 - 8)
Creat	0.12	0.09	mmol/L	(0.06 - 0.12)
Agap	22	17	mEq/L	(10 -17)
Gluc	41.6	12.0	mmol/L	(3.0 - 6.7)
Renin		9.7	ng/mL/h	(0.1 - 0.4)
Aldo		290	ng/L	(10 - 150)

The high renin and aldosterone levels indicated tubular unresponsiveness to aldosterone. The most likely cause was Amiloride therapy and this drug was subsequently discontinued. 4 days later the potassium normalised.

### Investigation of a suspected MCD

The investigation of a patient suspected of having one of the MCD syndromes should include a careful clinical examination; evaluation of plasma electrolyte values; measure of urine pH and evaluation of cortisol, rennin and aldosterone.

#### Suspect a MCD if:

1. Hyperkalaemia (artefactual\* and drug causes excluded)
2. No evidence of severe renal insufficiency (serum creatinine < 0.20 mmol/L)

May also have hyponatraemia and normal anion gap (hyperchloraemic) metabolic acidosis.

(\*Note - The most common cause of hyperkalaemia is artefactual - haemolysis, seepage from cell etc).

### References

Cases in Chemical Pathology: A Diagnostic Approach Edition 4 - Walmsley, Watkinson & Cain

### Questions

1. What are the functions of mineralocorticoids?
2. When would a MCD be suspected?
3. Discuss the causes of MCD.