MANAGEMENT OF PATIENTS WITH PITUITARY DISORDERS ON THE NEUROSUGERY WARDS – RESPONSIBILITIES OF THE METABOLIC REGISTRAR

We have clear links with DCN and a responsibility for the management of patients with pituitary disease. Whoever is the registrar for the week should liaise closely with the consultant on call to ensure that on going management of patients is assessed at an endocrine consultant level. This should be done throughout the week but it would be appropriate for any cases to be discussed at the Thursday clinical meeting so as to allow for general learning and exchange of ideas.

It is important to remember that not all patients seen through DCN will have a set of 'Western' notes. The vagaries of the admin system in the Western mean that DCN patients have an individual set of notes. It should be part of the registrars' task to ensure that any relevant documentation appearing in the DCN notes should also be copied into the Western notes (eg. pathology reports, MRI/CT scan reports, pre-operative visual fields particularly if presents with visual field defects etc). If the patient has yet to have a set of Western notes then it is important that these are made up at the time the patient is discharged from DCN.

It is important that the registrars document all discussions in the DCN casenotes, but also dictate either a letter or a summary of their involvement at the end of the week. This will then carry over into the Western case sheet. It can be confusing when patients attend the follow up endocrine clinic if such a dictated note is not available. The notes should contain a clear management plan for the patient.

Pre-Operative Assessment

Endocrine texts give clear instructions on how to test the hypothalamic pituitary axis but in some patients the clinical presentation is such that little time is available before decisions are required to be made. A classic example of this would be the patient presenting with a visual field defect due to a pituitary tumour. It is important in such instances to know exactly how to test the endocrine system and the following represents guidelines in this area:-

PROLACTIN

It is crucial that a prolactin level is known prior to surgery as macroprolactinomas, even with field or visual acuity defects, may be managed with medical therapy alone. If there is no pre-op prolactin level available, registrar on-call is to ensure that a specimen to be couriered directly to the Clinical Biochemistry Department at the RIE where prolactin levels can be measured urgently and be available within a matter of hours. Thus, if the PRL >6000 mU/l start quinagolide 25mcg daily and discuss with the on-call consultant. Evaluation on an individual basis for PRL between 2000 – 6000 mU/l. Visual fields will require close monitoring in the initial stages of therapy.

GLUCOCORTICOID

A short synacthen test (SST) should be performed (the time of day is not critical for this test) unless the clinical history is suggestive of recent pituitary infarction when the SST is likely to be invalid (a normal response is a post-synacthen plasma cortisol ≥460nmol/l). Following pituitary infarction, if surgery is imminent, then treat with glucocorticoids without more complicated testing. If surgery is to be deferred, an elevated random cortisol (>460nmol/l) would be indicative of an intact HPA system.

MINERALOCORTICOID

This is not relevant for pituitary/hypothalamic disease. If hyponatremia is present, it is dilutional and is strongly suggestive of glucocorticoid deficiency.

THYROID

Plasma thyroxine is the important investigation. Pituitary tumours may produce glycoproteins which are not functional, but which may be detected by, for example, the TSH assay. Thus, TSH levels are uninterpretable in pituitary disease.

GONADAL STATUS

In males, testosterone should be measured. Regular menses in a premenopausal women may be taken as evidence of an intact HPG system (providing there is no use of hormonal contraception). Oestradiol is an unhelpful investigation in women. LH/FSH are of little practical value but may be of help in post-menopausal women where levels should normally be high, but are often low in pituitary disease.

GROWTH HORMONE

Growth hormone deficiency cannot be diagnosed without a stimulation test as many normal people have undetectable plasma levels.

If a clinical suspicion of acromegaly exists then the diagnostic test is an oral glucose tolerance test (OGTT) but if time does not allow for this (pituitary infarction and/or acute visual impairment) then two random growth hormone levels may be helpful in retrospect. Blood should also be taken for IGF-$_1$.

ANTIDIURETIC HORMONE (VASOPRESSIN)

Diabetes insipidus is rare in association with pituitary tumours but may be present in patients with hypothalamic disease. Unless the clinical history is suggestive of diabetes insipidus no formal testing is necessary pre-operatively. If there is clinical suspicion, a random plasma sodium/osmolality and an early morning urine osmolality can be performed.

Remember that cortisol deficiency can mask diabetes insipidus and polyuria and polydipsia may develop quite suddenly following hydrocortisone replacement therapy.

Peri-Operative Endocrine Therapy

Any deficiencies demonstrated pre-operatively are likely to persist post-operatively and nothing is gained by attempting to withdraw therapy in the immediate post-operative period. Thus, if thyroxine or hydrocortisone are needed pre-operatively the patient should be discharged from hospital taking this treatment. Subsequent re-testing may be considered at a later date (see below).

THYROID

- It is not thought necessary to render patients euthyroid prior to emergency pituitary surgery. Clearly if deficiency has been demonstrated thyroxine can be started but its effects will not be apparent for some weeks. There is no place for prescribing triiodothyronine in this situation.

- Do not give thyroxine pre-operatively unless ACTH/cortisol status is normal, or hydrocortisone is being given (it may unmask latent adrenocortical insufficiency).

- Thyroxine has a half-life of 7-8 days, therefore a normal pre-operative level is unlikely to become abnormal for a week. There is no need therefore for an emergency assessment of thyroxine status immediately post-operatively.

GLUCOCORTICOIDS

All patients should receive hydrocortisone peri-operatively, even if glucocorticoid reserve is normal.

- l00mg hydrocortisone to be given intravenously immediately pre-operatively then 8 hourly for the first 24 hours.

- On the second post-operative day 50mg intravenous or orally at 8 am and 6 pm should be given.

- On the third post-operative day if the patient is well, 10mg in the morning and 5mg in the evening should be given.

If the operation has not been straightforward or the patient is unwell, parenteral hydrocortisone may be continued longer or oral hydrocortisone given in double replacement doses. Any deviation from a rapid recovery post-operatively should be considered on an individual basis. Always discuss problems with an endocrine consultant.

A 8.00am plasma cortisol (before giving oral hydrocortisone therapy) should be measured on the 3rd post-operative day assuming a straightforward course. If ≥460nmol/l then stop hydrocortisone treatment. If <460nmol/l then continue hydrocortisone therapy.

It is not clear how long after pituitary damage the SST will become abnormal in patients who are rendered ACTH deficient but for practical purposes it should <u>not</u> be used as an assessment of pituitary function until 6 weeks post-operatively. An ITT may need to be performed to provide definitive evidence of normality or deficiency.

DIABETES INSIPIDUS

<u>Diagnosis</u>

Polyuria is common after neurosurgery and usually results from delayed excretion of perioperatively administered fluids or an osmotic diuresis due to corticosteroid-induced glycosuria or the use of mannitol. The diagnosis of post-operative cranial DI must therefore depend on both:-

(i) demonstration of <u>hypotonic</u> (<250mosmol/kg) <u>polyuria</u> (>2ml1kg.h^{-1}) with

(ii) an increased plasma sodium (≥143mmol/l) or osmolality (≥300mosmol/kg), after exclusion of glycosuria, mannitol administration or renal failure.

Plasma sodium is a more reliable guide than osmolality in this acute phase.

In adults a urinary output of ≥200ml/hr of hypotonic urine associated with a plasma sodium ≥143mmol/l establishes the diagnosis.

Patterns of Post-operative DI

The onset is within 24h of surgery

(i) Transient DI; occurs after transphenoidal surgery:DI gradually resolves over *2-5* days.
(ii) Prolonged or permanent DI; after suprasella operations.
(iii) Triple response: suprasella surgery; initial cranial diabetes insipidus followed after 4-8 days by a transient remission (or even SIADH) lasting 2-8 days followed by a recurrence of permanent DI.

Management

Record urine output and, if the patient is polyuric, osmolality at least every 6 hours for the first 24 hours. Measure plasma Na^+ every 8-12 hours for 24 hours if polyuria occurs. Only once the diagnosis of cranial DI has been confirmed (see above) should DDAVP be given parenterally, 1-2µg intramuscularly. This usually provides antidiuresis for 12-24 hours and should be accompanied by fluid intake to maintain balance. Hypotonic fluids (oral water/iv dextrose) are recommended unless there is concomitant circulatory collapse when isotonic NaCl is safer. Occasionally larger doses of desmopressin are needed especially during the first day of DI. Both over-hydration and dehydration are risks in patients with coma or defective thirst due to hypothalamic dysfunction. Therefore, repeat doses of desmopressin should only be administered if polyuria recurs.

Initially the plasma sodium should be measured at least daily and then, if the cranial DI remits (particularly after suprasella surgery), should be monitored regularly over 14 days to detect SIADH or recurrent cranial DI. Inappropriate antidiuresis is managed by water restriction (500-1000ml/dy) until the likely relapse of cranial DI occurs.

SECRETORY PITUITARY TUMOURS

Post-operative assessment of patients with Cushing's disease is dealt with in a subsequent protocol (Investigation of Cushing's Syndrome). Patients with acromegaly should generally undergo an OGTT at 6 weeks, but should be discussed with a consultant endocrinologist.

Pre-Discharge Management

Fill in a blue endocrine referral sheet and give to the metabolic nurses. Most patients will undergo routine testing of pituitary function at 6 weeks post-op. The nurses will arrange this and will ensure that a clinic appointment is made for 8 weeks post-op for patients attending the Western General Hospital Endocrine clinic and all patients referred from Fife Hospital (VHK and QMH).

Endocrine follow-up

The following Endocrinologists would appreciate a telephone call, email or a discharge summary from the on-call Endocrine registrar. 6 weeks follow-up will be arranged in the referring hospital:

- Dr Fiona Green, Dumfries and Galloway Royal Infirmary
- Dr Peter Leslie, Dr Olive Herlihy, Borders General Hospital
- Dr Norman Peden, Dr Christopher Kelly, Dr Alison McKenzie, Stirling Royal Infirmary
- Dr James Walker, Dr Karen Adamson, St John's Hospital

For RIE patients, Endocrine registrar is responsible for informing the referring Endocrine consultant on discharge so that 6-week follow-up testing and out-patient clinic appointments can be organised in OPD2 at RIE.

The precise nature of the 6 week tests should be determined on an individual basis. In general, for patients with a non-functioning tumour and no pre-operative hormone deficiencies the following should be requested:

- Urea and electrolytes
- Free T4
- Short synacthen test (patient to omit evening and morning doses of hydrocortisone)
- Testosterone (men)/SHBG/Calculated free testosterone

While we have a robust mechanism for assessing glucocorticoid reserve following pituitary surgery in patients who had normal reserve pre-operatively, we are less clear in how we manage patient who are glucocorticoid deficient pre-operatively. In theory, glucocorticoid function (and indeed any other pre-op hormone deficiency could recover post-op. It is suggested, therefore that post-operatively when clinical status is stable (say at around three months) consideration should be made as to whether it would be appropriate to reduce glucocorticoid replacement in order to perform a short synacthen test and/or reduce thyroxine and sex steroid replacement for the same reasons. It may be that in certain circumstances it is so clear that endocrine function will not return that such efforts may not be worthwhile and this needs to be discussed with the relevant consultant.

Following pituitary surgery it has been agreed that the responsibility for organising the post-operative MRI scan (usually done at 3 months) lies with the neurosurgeons. The registrar on call must ensure that the scan would be discussed at an appropriate pituitary radiology meeting held monthly so that decisions regarding the appropriateness or otherwise of radiotherapy can be made.

Protocol updated on June 2010 by Wei Leng Teoh
In the next protocol update

- Re-audit the relationship of Day 3 cortisol and 6 weeks' SST with a view to consider assessing the Day 3 cortisol threshold.
- To discuss further changes to PRL threshold to commence dopamine agonist.