THE 8th NATIONAL CLINICOPATHOLOGICAL CONFERENCE ON PITUITARY DISEASE

Royal College of Physicians, Monday 6th March 2006 2006

Programme

9.30 **Welcome**
Mr Michael Powell (London)

Panel:	Professor Ashley Grossman	Endocrinology, London
	Dr Paul Carroll	Endocrinology, London
	Professor Brew Atkinson	Endocrinology, Belfast
	Professor Julian Davies	Endocrinology, Manchester
	Professor John Wass	Endocrinology, Oxford
	Professor Stafford Lightman	Endocrinology, Bristol
	Dr Richard Stanhope	Endocrinology, London
	Dr Nick Plowman	Radiotherapy, London
	Professor Michael Brada	Radiotherapy, London
	Dr Elena Wilson	Radiotherapy, London
	Dr Andy Platts	Neuroradiology, London
	Dr Fredrico Roncisoli	Neuropathology, London
	Professor Nicolas de Tribolet	Neurosurgery, Lausanne
	Professor John Pickard	Neurosurgery, Cambridge
	Mr Nick Thomas	Neurosurgery, London
	Mr Ian Sabin	Neurosurgery, London
	Mr Jeremy Rowe	Neurosurgery, Sheffield
	Professor Enrico de Divitiis	Neurosurgery, Naples

(Cases will be presented at approximately ten to fifteen-minute intervals)

9.35 **Pituitary Workshop 1**
Chair: Dr Mark Vanderpump (London) and Mr Michael Powell (London)

9.35 **Pituitary Headache**

1. Persistent Headache In Patient With Acromegaly In Remission
Barrington-Ward E, Mendoza N, Meeran K, Todd JF (London)

2. Addition of Pegvisomant to Octreotide in Acromegalic With Resistant Headache
J Kisalu, M Vanderpump and P Goadsby (London)

3. Acromegalic Headaches
K Meeran (London)

A surgical option for a pituitary headache?
Severe acromegaly headache requiring subcutaneous Octreotide up to ten times a day
What treatment is best for headache in an acromegalic patient who achieves "safe" GH levels after transsphenoidal surgery?
Headache cured by bromocriptine therapy.
Surgery as a primary treatment for severe acromegaly headache

10.10 **Update and Commentary on Pituitary Headache**
Professor Peter Goadsby (National Hospital for Neurology and Neurosurgery, Queen Square, London)

10.30 **Focus: Dynamic MRI Imaging**
Ms Sue Pickman and Dr Andy Platts (Royal Free Hampstead NHS Trust)

10.45 **Coffee**

11.00 **Pituitary Workshop 2**
Chair: Dr Mark Vanderpump (London) and Mr Michael Powell (London)

11.00 **Open Case Presentations**

1. Lymphocytic Hypophysitis: A Diagnostic Approach
   SE Tomlinson, GT Plant and M Powell (London)

2. Challenges In The Management Of An Aggressive Corticotroph Tumour
   M Bell, JP Monson, PN Plowman, R Carpenter, G Alusi, I Sabin, WM Drake (London)

3. Bilateral Adrenalectomy As Primary Treatment For Pituitary Cushings To Maintain Fertility
   K Meeran and D Russell-Jones (London, Guildford).

4. Fertility versus Treatment in a patient with Nelson's syndrome
   E Barrington-Ward, N Mendoza, K Meeran and JF Todd (London)

5. Should Informed Consent For Transsphenoidal Surgery Include The Fact That The NHS May Not Support Gonadotrophin Deficiency Postoperatively And That Surgery Might Render Patients Irreversibly Infertile?
   K Meeran, N Neary and E Hatfield (London)

6. Management options of static non-functioning chiasmal lesions
   C Ward and J Norris (Haywards Heath)

7. A Difficult TSHoma: Potentially Life Threatening?
   T Peng Yeow, J Ahlquist and M Powell (Southend, London).

8. The Endocrine Management Of A Patient With Neurosarcoidosis
   ECI Hatfield and K Meeran (London)

12.30 **Lunch**

13.30 **Debate: Gamma knife treats the surgeon/doctor more than the patient**
Jeremy Rowe (Sheffield) and Michael Brada (London)
Chair: Dr Gerry Conway

14.00 **Focus: Update on Endoscopic Surgery**
Professor Professor Enrico de Divitiis (Naples)

1. Case Study in Acromegaly
   K Gnanalingham (Manchester)

14.30 **Pituitary Workshop 3**
Chair: Dr James Ahlquist (Southend) and Miss Joan Grieve (London)

14.30 **Acromegaly**

1. Acromegaly- A Dilemma in Treatment
   C Johnston (Hemel Hempstead)

2. A Difficult Case Of Acromegaly.
   RS Moisey and SM Orme (Leeds)

3. Acromegaly; Might Primary Medical Management Be Preferable To Surgery?
   ECI Hatfield, N.Mendoza and K Meeran (London)

15.15 **Tea**

15.30 **Pituitary Workshop 4 –**
Chair: Dr James Ahlquist (Southend) and Miss Joan Grieve (London)

Craniophayngiomas

1. Management Of Cystic Craniopharyngioma
   TM Galliford, E Barrington-Ward, W Dhillo, N Mendoza, K Meeran, and JF Todd (London)

2. Recurrent Cystic Craniopharyngioma
   A Banerjee, J Turner, W Dhillo, N Mendoza, A Falconer and K Meeran (London)

3. GH Deficiency In Craniopharyngioma
   S Baldeweg and M Powell (London)

4. A Boy With Craniopharyngioma.
   V.Nermithan and S Chakrabarty (Southend)

16.10 **Update on Craniophayngiomas**
Richard Stanhope (Great Ormond Street Hospital, London)

16.30 **Pituitary Workshop 5**
Chair: Dr Stephanie Baldeweg (London)

Radiotherapy

1. Multi-Focal Neurological Signs After Pituitary Radiotherapy.
   S Shaw, J Ahlquist and J Benjamin (Southend, Romford)

2. Meningioma Treated With Stereotactic Fractionated Radiotherapy
   NM Neary, ECI Hatfield, JJ Turner, ND Mendoza and K Meeran (London)

3. Management Of GH Replacement In A Patient With Growth Of Residual Tumour
   ECI Hatfield, N Mendoza and K Meeran (London)

17.00 **Close**
Dr Gerry Conway (London)

Pituitary Workshop 1 - Pituitary Headache

1. Persistent Headache In Patient With Acromegaly In Remission
Barrington-Ward E, Mendoza N, Meeran K, Todd JF
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine, London

SK is a 52-year old woman who was diagnosed with acromegaly and underwent a transsphenoidal hypophysectomy in 1996. Post operatively, GH levels were adequately suppressed on OGTT (mean GH level 2.1mU/L) and dynamic pituitary function test revealed no abnormality and therefore she required no further treatment, although a post operative scan revealed residual tumour in the left cavernous sinus. Since her original operation, she has complained of an intermittent left sided headache but over the past year this has become much more severe and persistent so that now she has it most of the time. A recent pituitary and brain MRI shows persistent left cavernous sinus invasion, which has not changed since 2001. A recent OGGT shows that she remains in remission with mean GH levels of 3.5mU/L. She is due to have a trial of Octreotide therapy to establish whether this is an 'acromegalic headache'. We would appreciate the panel's expert opinion as to the treatment options in this patient, given that she has a large residual tumour in the left cavernous sinus, which may be contributing to her symptomatology?

2. Addition of Pegvisomant to Octreotide in Acromegalic with Resistant Headache
J Kisalu, M Vanderpump and P Goadsby
Royal Free Hampstead NHS Trust and National Hospital for Neurology and Neurosurgery, Queen Square, London

A 48-year old lady presented in 1999 with history of headaches and was found to have acromegaly with a large intrasellar tumour and GH>100mU/l. Post transsphenoidal surgery in December 1999, the headaches initially improved. Significant tumour residue was present and she received radiotherapy in September 2001. On DA therapy and Octreotide LAR GH levels have been maintained at 5-10mU/l and the IGF1 just above the reference range. Headaches have persisted and significantly affected her quality of life. Pegvisomant therapy was added which has reduced the IGF1 to low normal and signigicantly reduced the frequency of headaches.

3. Problem Headaches In Acromegaly
Karim Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

A surgical option for a pituitary headache?
A Banerjee, W Dhillo, N Mendoza, J Todd and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

A 40 year-old Moroccan man presented with a 5-year history of very severe headaches, not relieved by simple analgesia. Acromegaly was confirmed by a raised GH 10.1 mU/l, not suppressed by an OGTT. A MRI scan showed a right pituitary macroadenoma with expansion into the pituitary fossa displacing the pituitary stalk to the left, without invasion of the optic chiasm or cavernous sinus. Following transsphenoidal surgery, his GH was undetectable. Three months post operatively there was a recurrence of his headaches, persistent and severe, but GH remained undetectable. Octreotide initially relieved the headaches but he could not afford to take this long term. Further surgery was carried out a year later, with immediate post-operative resolution of the headaches. Histology of the pituitary tissue confirmed sparsely granulated somatotrophic cells. Nearly a year on he remains symptom free and biochemically cured of acromegaly. Can we advocate surgery for headache alone as this man's acromegaly was in remission when he had his second operation?

Severe Acromegaly Headache Requiring Subcutaneous Octreotide Up To Ten Times A Day
NE Banerjee, NH Patel, N Mendoza, A Falconer and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine

A 31-year old lady presented with severe left retro-orbital pain. MRI scan showed a 2.6cm pituitary macroadenoma which was invading the left cavernous sinus. Acromegaly was confirmed by elevated GH (82mU/l), which did not suppress with OGTT. A hypophysectomy was performed during which the tumour

was seen to be eroding the pituitary fossa and emanating from it. Histology showed somatotrophic adenoma, which was densely granulated. Post-operative GH was 33.7mU/L. The patient continued to have severe debilitating headaches. She was started on Octreotide LAR, which did not help her headache for more than a few hours. The patient was then changed to the short-acting Octreotide preparation (200 mcg tds) to see if this improved symptoms. The patient gradually increased the dose to five times daily. Repeat GH was 10 with no suppression during OGTT. Repeat MRI showed an expanded sella with pituitary tissue invading the left cavernous sinus and left parasellar region extending to the medial aspect of the floor of the left middle cranial fossa. The patient was treated with radiotherapy. The patient continued to have severe headaches but had noticed some relief shortly after she had the Octreotide injections and changed her dose to 100 micrograms ten times daily. Her overall dose per day remained unchanged. A double blind placebo controlled trial revealed that the Octreotide was more effective than placebo particularly in the first hour after injection. Six months following radiotherapy, the patient subjectively reports requiring Octreotide less frequently.

1. Would this patient benefit from further surgery?
2. Have the panel any experience of headache improving after radiotherapy?
3. Is there any evidence that Octreotide causes dependence/ tolerance or rebound headaches? Is short acting Octreotide better than long acting Octreotide or Lanreotide for headache?
4. Would an Octreotide s/c infusion pump help or be a hindrance?

What Treatment Is Best For Headache In An Acromegalic Patient Who Achieves "Safe" GH Levels After Transphenoidal Surgery?

S Roberts, E Hatfield, N Mendoza and K Meeran.
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

Mr. AB is a 30-year old gentleman who presented with acromegaly in 2001 with a six month history of headache and sweats (random GH 33mU/l; IGF1 113nmol/l; OGTT: mean GH 50mU/l; MRI pituitary demonstrated 1cm pituitary adenoma). Transsphenoidal surgery achieved biochemical remission (mean GH 1.9mU/l) but cortisol deficiency. Postoperative headache was similar in character but became chronic with a constant throbbing in left frontal / retroorbital area with episodic radiation to occiput. No relief from analgesia or Sodium Valproate. A trial of Lanreotide and Octreotide were unsuccessful and a greater occipital nerve block did not relieve the pain. Recent assessment random GH 8.2mU/l; IGF1 73nmol/l; mean GH 5.2mU/l and postoperative MRI scans demonstrate small amount of residual pituitary tissue. The patient's main complaint is the headache. Would the panel consider transsphenoidal surgery or radiotherapy to treat an intractable headache in an acromegalic patient who has almost achieved biochemical remission? With most recent GH values how should we proceed?

Headache Cured By Bromocriptine Therapy.

S Roberts, E Hatfield and K Meeran.
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

A 68-year old gentleman presented with headaches. An MRI pituitary demonstrated an expanded pituitary fossa and a homogeneous enhancing intrasellar mass with modest suprasellar extension and involvement of the right cavernous sinus with extension laterally to the internal carotid artery. At presentation, serum prolactin was 33,000mU/l, confirming prolactinoma. On commencement of bromocriptine headache disappeared immediately. A series of pituitary MRI scans over a 2-year period demonstrate the bulk of tumour remains a similar size with reduction in right lateral extension but involvement of right cavernous sinus persists. Bromocriptine had an immediate effect on this gentleman's headache. Does the panel think this is due to mass effect or effect on hormone secretion?

Surgery As A Primary Treatment For Severe Acromegaly Headache

E Nemati, A Banerjee, N Mendoza and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

A 35-year old lady presented with severe right retro-orbital headache. A subsequent magnetic resonance imaging (MRI) scan showed a pituitary macroadenoma. Acromegaly was confirmed by an elevated GH (33mU/l), which was not suppressed during OGTT. The patient underwent a hypophysectomy. Random GH levels were halved post-operatively but they were not normal. The headaches did not improve. The patient was started on Octreotide, which was not effective in treating the headaches. Lanreotide was also unhelpful. Repeat MRI showed residual tumour on the right side of the pituitary fossa. The patient had

radiotherapy to the pituitary. There was no improvement in the headaches the patient was experiencing. Almost two years after the first operation, the patient had surgical re-exploration and excision of the residual tumour. There was complete remission of the headaches following this operation. OGTT confirmed biochemical remission of the acromegaly. The patient required hydrocortisone, thyroxine, DDAVP and female sex hormone replacement following the second operation.
Is repeat surgery worth considering in a patient with severe debilitating headaches and residual tumour?

Pituitary Workshop 2 - Open Session

1. Lymphocytic Hypophysitis: A Diagnostic Approach
SE Tomlinson, GT Plant and M Powell
National Hospital for Neurology and Neurosurgery, Queen Square, London

Lymphocytic hypophysitis is a rare inflammatory disorder affecting the pituitary. Inflammation is thought to be immune mediated although the antigen is unknown. Incidence is increased in peri-partum women. Clinical presentation is characterised by headache, bitemporal hemianopia and pituitary hormonal failure. Imaging shows contrast enhancement of an enlarged pituitary during the acute phase. The differential diagnosis is of pituitary tumour (e.g. adenoma) therefore biopsy has been advocated as gold standard for diagnosis. We present a recent case series of pituitary hypophysitis occurring in both the peri-partum state and non peri-partum state. We aim to
1. Elucidate clinical and hormonal features
2. Compare and contrast the cases of post partum hypophysitis with those not related to pregnancy
3. Discuss features on imaging which may help discern inflammatory lesions from tumour
4. Discuss the role for conservative management over biopsy.

2. Challenges In The Management Of An Aggressive Corticotroph Tumour
M Bell, JP Monson, PN Plowman, R Carpenter, G Alusi, I Sabin and WM Drake
Barts, London

A 62-year-old lady with Cushing's disease underwent transsphenoidal surgery (TSS) and external-beam radiotherapy (45cGy) in January 2001. Histology confirmed an aggressive corticotroph tumour. Owing to persisting cortisol excess the patient underwent a bilateral adrenalectomy in June 2001. She remained well until February 2005 when she developed left temporo-occipital pain, dysphagia and hyperpigmentation. ACTH had risen from 136ng/L in December 2003 to 2568ng/L. MRI showed extensive recurrent tumour destroying the clivus and involving the occipito/C1 junction. Maxillary degloving surgery was performed to debulk the tumour. Immediately post-operatively ACTH dropped to 700ng/L but increased to preoperative levels shortly thereafter. ACTH levels were not reduced by either dexamethasone or Octreotide. Bromocriptine reduced ACTH by 37% and Cabergoline 0.5 mg daily was commenced. Gamma-knife radiotherapy, targeted at the totality of the recurrent tumour, including the occipito-C1 junctions, was given in April 2005. Follow-up imaging since then has shown stable residual tumour. This case illustrates the requirement for a multi-disciplinary approach to the management of aggressive corticotroph tumours. The opinion of the panel on future options in the event of future recurrence would be welcomed.

3. Bilateral Adrenalectomy As Primary Treatment For Pituitary Cushing's To Maintain Fertility
K Meeran, and D Russell-Jones.
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine and Royal Surrey County Hospital.

A 19-year old woman presented with typical features of Cushing's syndrome in 1998. Inferior Petrosal Sinus sampling confirmed a pituitary source, and the patient was offered transsphenoidal surgery. A pituitary MRI was normal, with no obvious adenoma. She was informed of the risk of infertility following transsphenoidal surgery, and she elected to have a bilateral adrenalectomy. Her symptoms resolved completely, and she remained well on Hydrocortisone and Fludrocortisone. Two years later (July 2000), her pituitary MRI remained normal. An ACTH level 2 hours after her morning hydrocortisone was 47 ng/l, unchanged over the two years. In 2003, she developed severe ulcerative colitis, requiring a total colectomy. In October 2004, and MRI in Guildford (to where she has now moved) showed a bulky pituitary, but no tumour was visualized, and the plan remained to watch and wait. Now, eight years post adrenalectomy (January 2006) she has delivered a healthy baby boy. Repeat pituitary MRI follows.

Should the patient now have pituitary surgery, radiotherapy, or wait until her family is complete?

4. Fertility Versus Treatment In A Patient With Nelson's Syndrome
E Barrington-Ward, N Mendoza, K Meeran and JF Todd
Hammersmith and Charing Cross Hospitals Endocrine Unit, Imperial College Faculty of Medicine, London

EN, a 30-year old female, was initially treated in Yugoslavia for Cushing's disease with transphenoidal hypophysectomy in 1997 and again in 1999. However, she was not 'cured' and underwent a bilateral adrenalectomy at Hammersmith Hospital in 1999. Her post-operative ACTH was 300ng/L. In 2002, she developed Nelson's Syndrome with hyperpigmentation, elevated ACTH between 2000-6000ng/L and pituitary MRI scan showed a larger recurrent right-sided pituitary adenoma invading the cavernous sinus encasing the carotid artery. Visual Fields were normal. Annual pituitary MRI scans have shown no change. Her only medications are Thyroxine, Hydrocortisone and Fludrocortisone replacement and she has regular periods. The patient had a successful spontaneous pregnancy with the birth of a baby boy in April 2005 and is keen to have another child later this year. Although her ACTH level fluctuates between 3000-6000 ng/L, her latest MRI scan in October 2005 shows no change. Given the findings on her MRI pituitary and raised ACTH, would the panel offer this lady radiotherapy or would the panel wait until she has completed her family and then offer her radiotherapy?

5. Should Informed Consent For Transphenoidal Surgery Include The Fact That The NHS May Not Support Gonadotrophin Deficiency Postoperatively And That Surgery Might Render Patients Irreversibly Infertile?
K Meeran, N Neary and E Hatfield
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine, London

A 21 year old presented with typical features of Cushing's syndrome and had transsphenoidal surgery. She remained well until 2003 (aged 24) when her Cushing's recurred, and she faced surgery again. She was told that "the whole pituitary might have to be removed and that this may leave her infertile, but that this would not be a problem as she would be able to have fertility treatment". She was told that age was on her side, and that it would be easy for her to conceive as "they would balance my hormones". She already had a 3-year old child. She required transsphenoidal surgery a third time before being told that the surgery was a success. She was told again that the "hormones lost in surgery would be artificially replaced through medication" and that she would need fertility assistance. He was then referred to us at Charing Cross for follow up when she moved to London. She has desperately been trying for another pregnancy for 7 years. Her local PCT does not cover treatment for anyone who has had a previous pregnancy and she thus remains on HRT only. Patients should be fully informed before transsphenoidal surgery, and this should include being told that they may be rendered irreversibly infertile, and that the NHS may not support gonadotrophin replacement postoperatively. Would the panel consider bilateral adrenalectomy earlier in young women who have not completed their family?
(The patients' full story can be seen in the January 2006 LAPPS newsletter).

6. Management Options Of Static Non-Functioning Chiasmal Lesions
C Ward and J Norris
Neurosurgery Department, Hurstwood Park Neurological Centre, Haywards Heath, West Sussex

This case presents an opportunity to discuss the management options for chiasmal lesions in the absence of pituitary or progressive visual dysfunction. A 27-year old right-handed woman presented in 2002 with headaches, lethargy and intermittent blurred vision for over 4 years. She was found to have defective colour vision with bitemporal pallor of the optic discs and a left non-congruous hemianopia. She had no relevant past medical history. Imaging revealed an extensive hypothalamic region lesion, extending into the third ventricle with calcification in the right basal ganglia. This cystic mass causing expansion of the optic chiasm was thought to represent hamartoma, glioma or craniopharyngioma. Hormonal and biochemical profile was normal. Serial MRIs have revealed no change in the mass from 2002. There has been a slight deterioration in visual function, MRI awaited and evaluation in management strategies.

7. A Difficult TSHoma: Potentially Life Threatening?
T Peng Yeow, J Ahlquist and M Powell.
Southend Hospital and National Hospital for Neurology and Neurosurgery, Queen Square, London.

A 37-year-old man with tachycardia was found to have thyrotoxicosis, and biochemistry indicated that this was due to a TSH-secreting pituitary adenoma (TSH 9.99 mU/L, free T4 46 pmol/L). The fT4 level was confirmed by equilibrium dialysis and alpha subunit was elevated at 2.05 U/L (normal < 1.0), supporting the diagnosis. MRI demonstrated a large multi-lobar pituitary mass, extending superiorly behind a prefixed chiasm to the third ventricle and back to the level of the pons. He had no visual symptoms, but a mild left homonymous hemianopia by perimetry. Carbimazole 40mg daily prior to pituitary surgery led to normalization of the fT4 level (48 to 19 pmol/L) but a rise in TSH (9.99 to 23.36 mU/L). At transsphenoidal surgery the tumour was unusually firm; despite debulking there was no biochemical improvement. Histology confirmed TSH positive pituitary adenoma. Repeat transsphenoidal surgery was again difficult, leading to panhypopituitarism with diabetes insipidus; after surgery he had significant residual tumour and persistent thyrotoxicosis (TSH 7.89 mU/L, fT4 36.7 pmol/L). Treatment with Carbimazole consistently results in doubling of his TSH level. His present treatment includes Sandostatin LAR, pituitary radiotherapy and replacement therapy. Prolonged thyrotoxicosis has resulted in osteoporosis. This man with a sight threatening pituitary tumour and uncontrolled hyperthyroidism poses a treatment dilemma. Biochemically, his TSH secreting adenoma demonstrates a behaviour reminiscent of Nelson's syndrome. Treatment with Carbimazole consistently causes a negative feedback rise of TSH level, and may potentially increase his tumour size and worsen his vision. However, his persistent hyperthyroidism is potentially life threatening.

8. The Endocrine Management Of A Patient With Neurosarcoidosis
ECI Hatfield and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

A 33 yr old male, with a diagnosis of Neurosarcoid, presented with loss of libido, reduced frequency of shaving, and fatigue. Investigations confirmed hypogonadotrophic hypogonadism, cortisol and GH deficiency. The patient was managed with high dose Prednisolone, subsequently titrated to maintenance dose, and replacement testosterone. Subsequent investigation, 1 yr later, confirmed recovery of gonadal and cortisol axis, but not GH axis. (ITT peak cortisol 613, GH 3.4 IU/L). The patient scored highly on the AHGDA questionnaire (24). He was commenced on GH replacement. 2 months later, the patient had a relapse of the neurosarcoid, an MRI showing leptomeningeal enhancement of brain stem and optic chiasm. This responded to immunosuppressive therapy (pulsed IV methylprednisone followed by azathioprine 75 mg od). 6 months after starting GH the patient felt much better, and a repeat AGHDA reflected this (score 8). He is maintained on 0.2 mg GH od, IGF-1 31.6 (NR 13-64). The patient is currently in remission from his neurosarcoid and awaiting repeat assessment of his GH and cortisol axis. NICE guidelines require a set improvement in the AGHDA score for the patient to continue on long term GH replacement, which this patient fulfilled. However, it is difficult to interpret the follow up AGHDA score, in view of the patient's relapsing neurosarcoid and subsequent treatment for this, occurring at the same time. Of note his presenting problems of gonadal and cortisol deficiency have recovered and it is possible that his GH deficiency may recover, but assuming it does not, how do we evaluate the true response to GH replacement in this patient?

Pituitary Workshop 3 - Acromegaly

1. Acromegaly- A Dilemma in Treatment
C Johnston
Dept of Endocrinology, Hemel Hempstead Hospital

A 53-year old woman has at least a 10-year history of classic symptoms including surgery for hyperhydrosis and carpal tunnel. On examination she has classic clinical features. Investigations confirm elevated basal GH 14.5mu/l and IGF1 130nmol/l with failure to suppress to oral glucose load (0 min 12.5, 30 /8.5, 60 /14.3, 90 /15.5, 120 /16.4mu/l) Remainder of pituitary function is normal: FT4 15pmol/l, TSH 0.98mu/l, FSH 66iu/l, LH 31iu/l, cortisol 263 nmol/l, prolactin 218mu/l. She is Hepatitis C Positive

Unable to perform MRI scan because of claustrophobia. CT with pituitary views shows no abnormality. Options:
1. Proceed to surgery with possibility of cure but would have to identify lesion per-operatively.
2. Open-MRI and proceed to surgery if abnormality found
3. Is the Growth hormone pituitary in origin? ?Petrosal sinus sampling prior to surgery
4. Medical therapy - likely to be curative but young patient ?long-term side-effects
5. Radiotherapy - Long-term risks of pituitary dysfunction and side-effects

2. A Difficult Case Of Acromegaly.
RS Moisey and SM Orme
Endocrinology Department, Leeds Teaching Hospitals NHS trust, St George St. Leeds, LS1 3EX

A 23-year old woman with gross, uncontrolled, progressive acromegaly, despite repeated transsphenoidal surgery, external beam radiotherapy and treatment with cabergoline and Sandostatin LAR. She presented in 2001 with bitemporal hemianopia. She had gross features of acromegaly with a random GH of >100mu/L and IGF-1 >150nmol/L. Imaging confirmed an invasive 4.2 x 3.1cm pituitary tumour. She was deficient in all other anterior pituitary hormones. In March 2002 she underwent transsphenoidal surgery (which confirmed dural invasion of the tumour) with improvement in her visual fields and later that year had external beam radiotherapy. In addition she was placed on Sandostatin LAR 40 mg per month. Despite this she remained symptomatic with progressively elevated levels of GH and underwent further transsphenoidal surgery with photodynamic therapy (PDT) in November 2003. Six months after PDT a repeat MRI showed no reduction in size of the tumour and GH levels had not improved (mean GH on day curve 16.2mu/L, IGF-1 86.8nmol/L). The addition of Cabergoline was not beneficial. She subsequently underwent a third transsphenoidal operation, which resulted in a reduction of tumour bulk and continues on Sandostatin LAR. Despite 3 operations including PDT, external beam radiotherapy and Sandostatin LAR, GH levels have progressively increased (mean GH 10.2µg/L on day curve and IGF-1 level 107.4 nmol/L). She remains significantly symptomatic with sweating and joint pains and is increasingly depressed. Would she benefit from the stereotactic radio-surgery? Is she a candidate for Pegvisomant? Is photodynamic therapy a proven treatment for acromegaly?

3. Acromegaly; Might Primary Medical Management Be Preferable To Surgery?
ECI Hatfield, N Mendoza and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine

A 66-year old lady was diagnosed with Acromegaly (mean GH 16.2 IU/L on OGTT) with otherwise normal pituitary function. MRI scan was contraindicated due to the presence of clips following treatment of a subarachnoid haemorrhage in 1992. Fine-Cut CT suggested slight enlargement of the pituitary fossa but no adenoma was visualised. This case was presented at last year's CPC and the consensus was to offer this patient surgery. However the patient was reluctant to proceed and has been managed with medical therapy, Lanreotide autogel 60 mgs every 6 weeks. Her acromegaly has been well-controlled, recent values IGF-1 24.6 nmol/L (NR 6-36), GH 1.3 IU/L. At her most recent review in January 2006, the patient has expressed willingness to consider surgery. Whilst surgery has been the regarded as the first line treatment for acromegaly, accumulating evidence shows that primary medical therapy can be an effective treatment (1,2). This patient has a presumed microadenoma, which if treated with surgery would have a good cure rate. However, she has an intact pituitary axis and is well controlled on Lanreotide. We would value the panels view on whether we should encourage this patient to have surgery or should she continue to be managed medically.
(Refs: Cozzi R, et al J Clin Endocrinol Metab.2006.Jan. and Feenstra J, et al. Lancet 2005;365:1644-46)

Pituitary Workshop 4 – Craniophayngiomas

1. Management Of Cystic Craniopharyngioma
TM Galliford, E Barrington-Ward, W Dhillo, N Mendoza, K Meeran and JF Todd
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

This 30-year-old female presented, in New Zealand, with headaches and secondary amenorrhoea at the age of 16. Bilateral quadrantinopic visual field defects were present and following investigation she was diagnosed with panhypopituitarism secondary to cystic craniopharyngioma. Hormonal replacement was commenced and she has subsequently undergone four transsphenoidal debulking operations following

tumour re-growth and visual field disturbances. Although visual field defects have always resolved post-surgery, she has developed diabetes insipidus. Surgery was last performed in November 2004 and visual fields are currently normal. Replacement therapy with hydrocortisone, thyroxine, Prempak C and Desmopressin is adequate, however she complains of tiredness and has biochemical evidence of GH deficiency with AGHDA score of 18. Latest pituitary MRI in November 2005 shows a small amount of ill-defined enhancement of tissue within the pituitary fossa that is thought to represent post-surgical scarring. Should this patient be considered for radiotherapy and what is the panel's preferred management of GH deficiency in cases of craniopharyngioma?

2. Recurrent Cystic Craniopharyngioma
A Banerjee, J Turner, W Dhillo, N Mendoza, A Falconer and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

SL presented at the age of 30 in 1993 with a two-month history of visual loss. CT scan showed a large suprasellar cyst. This was managed by craniotomy and histology confirmed a diagnosis of cystic craniopharyngioma. She made a complete recovery and subsequently became pregnant. In 1997 she again presented with visual loss and was found to have a recurrence of her suprasellar cystic lesion. Which was managed on this occasion by transsphenoidal decompression. This was complicated by diabetes insipidus and hypoadrenalism. In 2004 there was further recurrence and she was treated with endoscopically assisted, image guided, transsphenoidal aspiration of cyst followed immediately by external beam radiotherapy (54Gy in 30 fractions). Twelve months later the patient remains well and the latest imaging demonstrates only a small residual cyst. Should we have considered drainage and radiotherapy earlier?

3. GH Deficiency In Craniopharyngioma
S Baldeweg and M Powell
National Hospital, Queen Square

Abstract to follow

4. A Boy With Craniopharyngioma.
V Nermithan and S Chakrabarty
Southend General Hospital, Prittlewell Chase, Westcliff-on–Sea, Essex.

12-year old male presented with complains of continuous frontal headache, tinnitus and intermittent early morning vomiting of 3 weeks duration. Tinnitus and dizziness was intermittent, lasting for many hours. There was no history of fever, trauma, loss of consciousness or abnormal movements. On examination, he had bilateral papilloedema and bilateral loss of temporal fields of vision. His height was in the 2nd to 9th centile but on questioning had growth failure for the past two years. Rest of the systemic examination was unremarkable. CT scan showed craniopharyngioma and a degree of proximal hydrocephalus. He was referred to the GOSH where he underwent stereotactic aspiration of a large craniopharyngioma cyst. Visual field reverted to normal but the headache continued for a further month. Postoperatively he was started on dexamethasone and monitored for diabetes insipidus and hyperglycaemia. Presently he is on hydrocortisone maintenance dose and his pituitary function is due to be assessed in the next couple of weeks.

Pituitary Workshop 5 – Issues in Radiotherapy

1. Multi-Focal Neurological Signs After Pituitary Radiotherapy.
S Shaw, J Ahlquist* and J Benjamin
Department of Neurosurgery, Essex Neurosciences Centre, Oldchurch Hospital, Romford and *Southend Hospital, Westcliff on Sea, Essex.

A 48-year old gentleman presented with a 12-month history of visual impairment. He had markedly reduced visual acuity bilaterally, a right temporal field defect and was also hypopituitary. MRI showed a pituitary macroadenoma causing chiasm compression. Following transsphenoidal surgery there was good improvement in the left eye. Histology confirmed an adenoma with focal ACTH immunopositivity. Residual tumour was present on follow-up MRI; pituitary radiotherapy was arranged 6 months after

surgery and was tolerated well. A standard three-field plan was used with 50Gy in 30 fractions given over 6 weeks. 2 months following radiotherapy he re-presented with a rapid onset of visual deterioration and diplopia over a few days. He had a mild right ptosis and left facial weakness. He also demonstrated abnormal extra-ocular movements not in keeping with specific cranial nerve palsies but typical of an inter-nuclear ophthalmoplegia. MRI demonstrated focal abnormalities in the dorsal pons, left middle cerebellar peduncle and both temporal lobes. Extensive neurological investigations showed nothing to suggest an inflammatory, infective, demyelinating, malignant or vasculitic pathology. The clinical features slowly improved over the following months without any specific therapy. Review of the radiotherapy plans indicated that all of the abnormal regions fell within the radiation fields. We suggest that he suffered an idiosyncratic response to pituitary radiotherapy.

2. Meningioma Treated With Stereotactic Fractionated Radiotherapy
NM Neary, ECI Hatfield, JJ Turner, ND Mendoza and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit
Imperial College Faculty of Medicine.

A 36-year old female nurse presented to the endocrine clinic with a history of irregular periods, proptosis of the right eye and deteriorating vision. She was found to have an elevated serum prolactin level 1127 mU/l (NR<625) and evidence of secondary hypothyroidism but with adequate cortisol reserve. Thyroxine replacement was commenced. An MRI scan showed an extensive skull based tumour extending around the right cavernous sinus consistent with meningioma. Given that total excision was not possible and the potential risks of surgery outweighed the benefits, conservative management with close surveillance was advised. The patient sought a second opinion, and was treated with stereotactic fractionated radiotherapy in Australia and warned that she could develop hypopituitarism. An MRI scan in the UK 6 months later showed that the tumour was unchanged in size. Clinically there was improvement in proptosis and acuity in the right eye. She also reported symptoms of oestrogen deficiency. The prolactin had normalised and gonadotrophin failure was confirmed on an LHRH test. There was evidence of cortisol deficiency and GH deficiency on an insulin tolerance test one year after radiotherapy. She is currently on hydrocortisone and thyroxine replacement. HRT has been withheld because of the possibility that the tumour is progesterone or oestrogen receptor positive. GH replacement has not been offered due to possible risk of tumour progression. The patient is currently well and would like children in the future. Do the panel feel that stereotactic fractionated radiotherapy was appropriate and are there any current treatment options? Would the panel offer this patient HRT?

3. Management Of GH Replacement In A Patient With Growth Of Residual Tumour
ECI Hatfield, N.Mendoza and K Meeran
Charing Cross and Hammersmith Hospitals Endocrine Unit, Imperial College Faculty of Medicine.

A 37-year old man presented with a 6-month history of frontal headache and reduced visual acuity in the right eye. An MRI scan revealed a pituitary macroadenoma with suprasellar extension and optic chiasm compression, and lateral extension into the left cavernous sinus. His pituitary axis was intact, with normal prolactin levels and transsphenoidal surgery was arranged. Post operatively the patients visual fields improved and an MRI scan showed a marked reduction in size of the pituitary adenoma, but with residual tissue. Pituitary function testing confirmed an intact cortisol axis, but thyroid, testosterone and growth hormone deficiency. A repeat MRI at 1year post op showed no change in size of the residual tumour. The patient had severe symptoms of fatigue, despite adequate cortisol reserve, thyroxine and testosterone replacement, and scored highly on the AGHDA questionnaire (17). He was commenced on GH replacement, (0.2 mg Genotropin), IGF-1 levels rose from 17.3 to 40.9 (NR 13-64) and the patient felt symptomatically improved. However, a further MRI scan 3 months after starting GH replacement showed a slight increase in size of the residual adenoma. GH has been discontinued and a repeat MRI at 6 months showed no interval change in the residual adenoma. The patient remains symptomatic with fatigue and is very keen to restart GH (0.1mg initially) and follow up with regular MRI scans.
Clearly the growth of residual tumour may be unrelated to the GH replacement. What is the preferred management when there is tumour growth whilst on GH? If there is further growth, should the patient be considered for further surgery (+/- radiotherapy) early given that he wishes to continue on GH?