Imperial College
London

Imperial Pituitary Masterclass Meeting

Monday 16th September 2019

IMPERIAL PITUITARY MASTERCLASS MEETING 2019

6 EXTERNAL CPD CREDITS
ROYAL COLLEGE OF PHYSICIANS LONDON

Venue: Charing Cross Hospital, Imperial College Healthcare NHS Trust, London

08.30 - 09.00 Registration.

09.00 - 09.15 **Welcome.**
Dr Niamh Martin.

SESSION 1.

Chairs: Dr Benjamin Whitelaw (Kings College Hospital NHS Foundation Trust) and Dr Alison Wren (Chelsea and Westminster Hospital NHS Foundation Trust).

09.15 – 09.45 *Late effects of cancer treatment on the pituitary.*
Dr Claire Higham (The Christie NHS Foundation Trust, Manchester).

09.45 - 10.00 Case presentation. *A difficult case of Cushing's disease – what next?* S. Samarasinghe, N. Mendoza, R. Nair, D. Peters, S. Akavarapu, N. Martin K. Meeran, E. Hatfield. (Imperial College Healthcare NHS Trust, London).

10.00 - 10.15 Case presentation. *Rare presentation of pituitary granulomatosis with polyangitis*. R. Banatwalla, N. Sithamparanathan, R. Herring, D. Russell-Jones. (Royal Surrey County Hospital, Guildford).

10:15 – 10.45 *Imaging the pituitary*
Dr Anastasia Gontsarova (Imperial College Healthcare NHS Trust, London).

10.45 – 11.15 BREAK.

SESSION 2.

Chairs: Dr Nicola Bridges (Chelsea and Westminster Hospital NHS Foundation Trust) and Dr Jeremy Cox (Imperial College Healthcare NHS Trust London).

11.15 - 11.45 *Pituitary disease in children and young people*
Prof Paul Dimitri (Sheffield Children's NHS Foundation Trust).

11.45 - 12.00 Case presentation. *Management of diabetes insipidus during hyperhydration therapy associated with chemotherapy – a therapeutic challenge.* P. Dimitri, V. Lee, J. Devaraja. (Sheffield Children's NHS Foundation Trust).

12.00 - 12.15 Case presentation*. Langerhans cell histiocytosis with cranial diabetes insipidus: a challenging presentation.* N. Ahmed, S. Wong, A. Nyunt, G. Sreemantula, T. Dacruz. (Glan Clywd Hospital, Wales).

12.15 – 12.45 *New approaches in the differential diagnosis of diabetes insipidus.*
Prof Mirjam Christ-Crain (University of Basel, Switzerland).

12.45 - 13.45 LUNCH.

SESSION 3.

Chairs: Dr Dan Darko (London Northwest University Healthcare NHS Trust) and Mr Nigel Mendoza (Imperial College NHS Trust London).

13.45 - 14.30 *Debate. Biopsy is an underused diagnostic tool in sellar-region disease.*

For the motion: Mr Nick Thomas (Kings College Hospital NHS Foundation Trust, London).

Against the motion: Dr Stuart Ritchie (Western General Hospital, Edinburgh).

14.30 - 14.45 Case presentation. *Deceptive presentation of a pituitary mass.* Z. Banu, N. Dorward, D. El-Sharkawi, T.T. Chung. (University College London Hospitals NHS Foundation Trust, London).

14.45 – 15:00 Case presentation. *Pituitary plasmacytoma presenting as a mimic of pituitary apoplexy – demonstrating the value of obtaining a histological diagnosis.* E. Ahmad, N. Chandhyoke, T. Hampton, A.King, N. Thomas, B. Whitelaw. (Kings College Hospital NHS Foundation Trust, London).

15:00 - 15:30 BREAK.

SESSION 4.

Chairs: Dr Katherine McCullough (Royal Surrey County Hospital) and Mr Ramesh Nair (Imperial College NHS Trust London).

15.30 – 16:00 *Getting It Right First Time (GIRFT) in the management of pituitary disease – what have we learnt?* Prof John Wass (Oxford University).

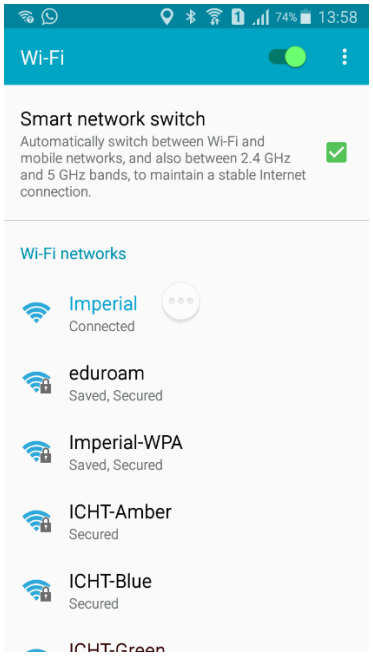
16.00 - 16:15 Case presentation. *Should SHBG be measured in every patient before diagnosing hypogonadotrophic hypogonadism?* M. Phylactou, A. Abbara, P.C. Eng, S.A. Clarke, D. Papadopoulou, C. Izzi-Engbeaya, C.N. Jayasena, A.N. Comninos, J. Todd, S. Howard, T. Tan, W.S. Dhillo (Imperial College London & Queen Mary University of London).

16.15 - 16:30 Case presentation. *Prolactinoma causing visual disturbance in pregnancy – a multidisciplinary management conundrum.* S. Azam, R. Scott, C. Izzi-Engbeaya, S. Jarvis, S. Samarasinghe, A. Comninos, N. Hill, R. Nair, E. Hatfield, N.Martin and K. Meeran. (Imperial College Healthcare NHS Trust, London).

16.40 **CLOSING REMARKS AND FEEDBACK.**

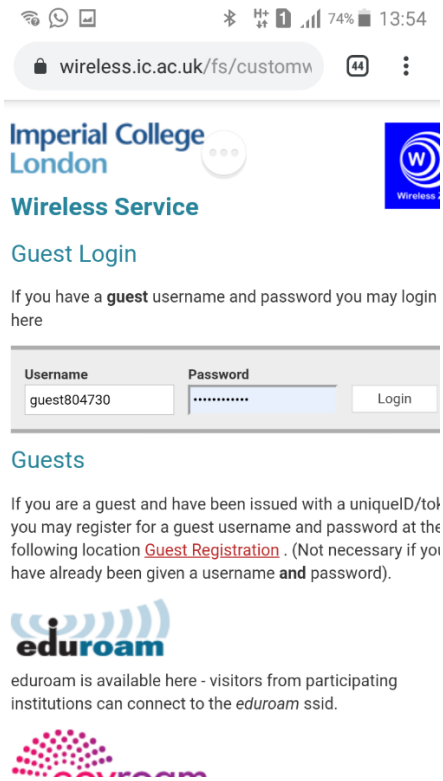
Wireless Instructions

Find “Imperial” (open) on your list of connections.



Open a web page. A guest login page will appear.

Put in guest804730 as the username, and Pituitary1 as the password.



Research to compare different steroids for replacement in patients with adrenal insufficiency.

Funded by NHS National Institute for Health Research

At present, there is no evidence in support of any of the different steroids used in patients with primary or secondary adrenal failure.

Although the primary reason for the use of prednisolone once daily instead of hydrocortisone at Charing Cross was the huge difference in price in 2014 (Amin et al, 2014), it has become clear over the last five years that many patients prefer prednisolone once daily. The price of hydrocortisone has now fallen, but patients who have switched to once daily prednisolone are very reluctant to switch back and preliminary data is encouraging (Smith et al, 2017; Choudhury et al 2019). In addition, the DREAM study suggests that late doses of hydrocortisone may affect clock genes and might also have an effect on the immune system and hence thrice daily hydrocortisone might be harmful, especially an evening dose (Muller et al, 2018). It is thus possible that in addition to being cheaper and more convenient, when used at the correct dose, prednisolone has fewer undesirable effects than hydrocortisone thrice daily. The plasma profile of once daily prednisolone matches the natural circadian rhythm of plasma cortisol levels better than any other steroid (Williams et al, 2016).

At present, there is no evidence to support the use of either drug. We really need data to inform our future practice and to this end the NIHR have adopted three trials, one of which you can take part in through your NIHR Clinical Research Network.

Once your site is enrolled, the study is very simple although it needs someone to lead each site. Patients need to be stably replaced on either hydrocortisone or prednisolone for the preceding four months. When seen, the locally available markers of steroid exposure such as bone turnover markers, glucose, Hba1c and lipids, weight, BMI, waist and hip measurements, blood pressure and the results of an SF36 well-being questionnaire need to be recorded. They are then switched to an equivalent dose of the alternate drug for a further four months and the data collected again at the end of that period. Checking for an appropriate dose can be supported by prednisolone levels if desired.

If you would like to take part in this study, please e-mail steroids@imperial.ac.uk

References:

Amin A, Sam, A and Meeran K. Glucocorticoid replacement. BMJ 2014: 349: g4843.

Smith DJF, Prabhudev H, Choudhury S, Meeran K. Prednisolone has the same cardiovascular risk profile as hydrocortisone in glucocorticoid replacement. Endocr Connect. 2017;6(8):766-772.

Choudhury S, Machenahalli P, Tan T, Meeran K. Inadvertent treatment of hypoadrenalism with prednisolone in pemphigus: A case report. Clin Case Rep. 2019;7(5):987-989.

Muller L, Quinkler M. Adrenal disease: Imitating the cortisol profile improves the immune system. *Nat Rev Endocrinol*. 2018;14(3):137-139.

Williams EL, Choudhury S, Tan T, Meeran K. Prednisolone replacement therapy mimics the circadian rhythm more closely than other glucocorticoids. *J Appl Lab Med*. 2016;1(2):152-161.

Case presentation. ***A difficult case of Cushing's disease – what next?***

S. Samarasinghe, N. Mendoza, R. Nair, D. Peters, S. Akavarapu, N. Martin K. Meeran, E. Hatfield. (Imperial College Healthcare NHS Trust, London and Frimley Health NHS Foundation Trust).

A 57-year-old lady was referred to local endocrinology services with an incidental finding of a 17 mm pituitary macroadenoma on dedicated pituitary MRI. Initial pituitary function tests and 24-hour urine free cortisol (UFC) were normal. Repeat MRI almost 4 years later showed the adenoma had shrunk, now measuring 12 mm. Subsequently, she developed type 2 diabetes mellitus and hypertension, with violaceous abdominal striae but no evidence of proximal myopathy. Her BMI was 34 kg/m^2. An overnight dexamethasone suppression test showed failure to suppress 9 am cortisol (307 nmol/L; normal <50 nmol/L); 24-hr UFC was elevated at 390 (NR 50 – 270 nmol/24 hrs). A low dose dexamethasone suppression test (LDDST) confirmed failure to suppress cortisol (T=0 538 nmol/L and T=48h 227 nmol/L) with a baseline ACTH of 59 ng/L.

She was referred to our tertiary centre for review and further investigations. A repeat LDDST confirmed failure to suppress cortisol (T=0 425, T=48h 186 nmol/L) and elevated midnight salivary cortisol 3.6 nmol/L (<2.6). Inferior petrosal sinus sampling demonstrated a basal central:peripheral ratio of ACTH>2 and stimulated central:peripheral ratio >3 on the right, excluding ectopic ACTH secretion. Following discussion at the pituitary MDT, she was scheduled for endoscopic trans-sphenoidal adenohypophysectomy, started on metyrapone (250 mg tds) and prophylactic tinzaparin. Histology was consistent with a corticotroph adenoma. Unfortunately, post-operative cortisol remained elevated (day 4 394 nmol/L, day 8 cortisol 1132 nmol/L). Metyrapone was restarted at 250 mg BD. Review of post-operative imaging did not show any obvious residual tumour but given her rising serum cortisol levels, the patient underwent repeat endoscopic trans-sphenoidal surgery. Histology from the second surgery showed reactive changes only. Post-operative cortisol remained detectable (day 4 cortisol 145 nmol/L, day 10 429 nmol/L). A cortisol day curve (four weeks post-operatively) showed detectable cortisol and loss of diurnal variation (199, 324, 218, 363 nmol/L). Further definitive treatment options, including bilateral adrenalectomy were discussed with the patient. However, prior to any decision, another cortisol day curve was performed (10 weeks post-operatively) (187, 87, 51, 114 nmol/L) (baseline ACTH 22.2ng/L).

Question for discussion:

- Is this patient now in remission or does she need further definitive treatment?

Case presentation. *Rare presentation of pituitary granulomatosis with polyangitis*.

R. Banatwalla, N. Sithamparanathan, R. Herring, D. Russell-Jones. (Royal Surrey County Hospital, Guildford).

Introduction: Granulomatosis with Polyangitis (GPA) is an ANCA associated multi-system disorder of unknown aetiology. Pituitary involvement is rare[1,2].

Case Study: 38 year old lady accompanied with her partner, presented with severe headaches associated with nausea and vomiting along with recurrent nose bleeds. Past Medical History included well controlled asthma, chronic sinusitis and nasal problems requiring cauterisation. On examination, she had normal visual fields and MRI Pituitary showed a heterogenous cystic Pituitary lesion with thickened pituitary stalk. Differential Diagnosis included lymphocytic hypophysitis, sarcoidosis, pituitary abscess, pituitary vasculitis, IgG4 related disease and necrotic pituitary adenoma. She was commenced on Hydrocortisone 20mg-10mg pending investigations. She went on to develop significant polyuria and polydipsia. The formal Water Deprivation Test confirmed Central Diabetes Insipidus (CDI) and she was started on DDAVP nasal spray. Investigations reported initial ANCA screen negative but Proteinase 3 Antibody Level was elevated. Random Cortisol at 10:00 am was 232 (140-690nmol/l) prior to commencing on Hydrocortisone. The Short Synacthen Test (SST) reported 0 min cortisol at 521nmol/l and 30 minute at 664nmol/l. On trying to withdraw hydrocortisone she felt less well and her repeated vasculitis screen was positive for c ANCA pattern. She underwent serial MRI pituitary scans which did show some reduction in the pituitary lesion. The CT sinuses showed mild mucosal thickening along the nasal floor only, but there was no evidence of active vasculitis or sinusitis. The Insulin Tolerance Test was normal with a peak cortisol level of 645 nmol/L. A formal ENT examination of nasal mucosa failed to identify any abnormality.

Discussion: It is presumed that this represents an ANCA positive GPA of pituitary. Treatment options include biopsy (pituitary) to confirm the diagnosis. High dose steroids/ methotrexate10 mg per week/Rituximab could also be considered[1,2].

Questions for discussion:
1. Is pituitary biopsy required for diagnosis of Pituitary involvement in GPA?
2. Is a pituitary biopsy still a good idea now?

References:

1. S M. Baird et al. Rare presentation of Wegener's granulomatosis in the pituitary gland: Case report and literature review. International Journal of Surgery Case Reports 33 (2017) 24–26.

2. Peters et al. Severe localised granulomatosis with polyangiitis (Wegener's granulomatosis) manifesting with extensive cranial nerve palsies and cranial diabetes insipidus: a case report and literature review. BMC Neurology (2018) 18:59.

Case presentation. ***Management of diabetes insipidus during hyperhydration therapy associated with chemotherapy – a therapeutic challenge.***

P. Dimitri, V. Lee, J. Devaraja. (Sheffield Children's NHS Foundation Trust).

Background:
A 10 year old girl presented with hypernatraemia (Na=176mmol/l), secondary rhabdomyolysis, dehydration and polyuria. Radiological investigations revealed a suprasellar tumour which was confirmed on biopsy to be a non-metastatic germinoma. Further endocrinological investigations confirmed panhypopituitarism with hypodipsia and she commenced desmopressin, hydrocortisone and thyroxine.

Problem:
She was started on chemotherapy as the germinoma was not amenable to surgery. Her chemotherapeutic regime consisted of etoposide and ifosfamide, the latter of which required 4L of hyperhydration therapy. Desmopressin was initially omitted to allow adequate diuresis but she subsequently passed 7L of fluid. Oral desmopressin replacement on hyperhydration resulted in erratic sodium control leading to disorientation.

Solution:
We trialled arginine-vasopressin (AVP) infusion to improve her fluid balance and serum sodium. She was catheterised to monitor urine output hourly and to adjust the AVP rate based on this. Based on very limited past literature, a sliding scale was developed to adjust the AVP dose, with an aim to achieve urine output 3-4mls/kg/hr. In the first round of chemotherapy, sodium levels ranged between 123mmol/l to 160mmol/l. In the second phase of ifosamide, the AVP infusion commenced at the outset, allowing tighter control of sodium and urine output.

Conclusion:
AVP infusion during hyperhydration therapy was required to achieve eunatraemia. Doses of AVP may show individual variation and further case series are required to underpin practice.

Questions for discussion:

- Should a standard AVP sliding scale regime be used or should it be personalised to the patient?
- Does anyone have any experiences using AVP infusion in patients on hyperhydration- what were the challenges?

Case presentation*. Langerhans cell histiocytosis with cranial diabetes insipidus: a challenging presentation.*

N. Ahmed, S. Wong, A. Nyunt, G. Sreemantula, T. Dacruz. (Glan Clywd Hospital, Bodelwyddan, Wales).

Abstract:
A 24-year-old male diagnosed case of Central Diabetes Insipidus secondary to Langerhans Cell histiocytosis at the age of 9 years; previously well controlled on Desmospray 10ug bd for 16 years presented with increasing polydipsia and polyuria of 6 litres/day worsening over the past 3-4 months. He found his Desmospray ineffective; even when his Desmospray dose was increased gradually to 20ug bd up to 100 mcg bd gradually over the next clinic visit.

In lieu of his worsening symptoms; U&Es and urinary electrolytes were repeated which came back normal. An MRI Pituitary was done to rule out disease progression of Histiocytosis followed by a repeat skeletal survey. The MRI Pituitary revealed thickened pituitary stalk with stable appearance of the pituitary gland without any interval change; and the skeletal survey was normal as well.

He was then changed from Desmospray to DDAVP melts gradually reaching the maximum dose of 240 mcg tds without much significant symptomatic improvement. Since his renal functions were stable, we added 60-120 mcg DDAVP melts at teatime along with 240 mcg tds of the mentioned dose with the advice that if his urine output suddenly drops or tails off, to decrease oral intake accordingly.

He found some symptomatic benefit but was still having 4-5 Litres of polyuria and hence he was shifted to Desmotabs to a max dose of 1.2 mg daily.

He was seen in the clinic 3 weeks back with persistent symptoms and normal U&Es. Looking at the persistent symptoms he was given a trial of S/c desmopressin reaching a dose of 4mcg/day.
He had a repeat water deprivation test with oral desmopressin which we did to rule out DI/ Primary polydipsia overlap which showed pure Central Diabetes Insipidus. He is still on s/c desmopressin 4 mcg od with subtle improvement in symptoms.

Questions for discussion:

- Why would a relatively stable DI progress symptomatically so rapidly and become unresponsive to high doses of desmopressin and how to manage the same?
- Is there any role of s/c desmopressin in water deprivation test instead of oral desmopressin and if yes what would be the advantage of the same?
- Role of carbamazepine in sensitization of desmopressin? (If severe DI confirmed) v/s use daily s/c desmopressin?

Case presentation. ***Deceptive presentation of a pituitary mass.***

Z. Banu, N. Dorward, D. El-Sharkawi, T.T. Chung. (University College London Hospitals NHS Foundation Trust, London).

A 71-year-old lady was initially referred with a right sided 1.5cm incidental indeterminate adrenal nodule stable in size 2016-18. This was managed with surveillance imaging. Her adrenal nodule seems to be non-secretory with normal UFC twice (32 and 40, normal range 0-125nmol/24hr) but her cortisol was found to be non-suppressed on two occasions.

LDDST	1st Cortisol(nmol/L)	Cortisol (nmol/L)	ACTH (ng/L)
Baseline	526	534	12.1 /13.1
48 hours	243	251	

She had a concurrent history of low grade CD5+ B cell lymphoproliferative disorder which was managed conservatively at the Royal Marsden. She received weekly subcutaneous immunoglobulin for a functional antibody (MBL) deficiency.

Her other medical history included hypertension, osteoporosis, diverticular disease and diet-controlled diabetes.

Her medications included losartan, vitamin D, calcium supplements and yearly zolendronate. On examination, BP was 158/79mmHg, weight 42.7kg. She was a slim lady with no Cushingoid features.

Six months after her initial presentation, she developed fatigue, anorexia, diarrhoea and confusion whilst on holiday. She was later admitted with ongoing diarrhoea, worsening confusion and profound hyponatraemia (Na 117 mmo/L). Her 9am serum cortisol was 324 and 244 nmol/L with TSH 1.7 miu/L(0.27-4.20mU/L). She was treated with fluid restriction and a single dose of tolvaptan and subsequently discharged with a sodium of 130mmol/L. She was readmitted two days later, peri-arrest; her sodium was 116mmol/L and was found to have hypopituitarism with FSH 2.1U/L, LH 0.5U/L, TSH 2.39(0.27-4.20mU/L), FT4 9.9 (12-22pmol/L), Prolactin 2300(102-496mU/L) but serum cortisol was 293nmol/L.

She was initially treated with a high dose hydrocortisone, carbergoline and thyroxine replacement. Her MRI pituitary demonstrated macro-adenoma with no chiasmal compression. Patient made significant clinical improvement on hydrocortisone replacement. Due to her unclear clinical presentation, exuberant response to steroid treatment and her previous non-concordant results of UFC and LDDST, her cortisol was checked with mass spectrometry which excluded assay interference.

A month later, her repeat prolactin was 81mU/L, FSH 21.6 U/L, LH 9.4U/L, therefore cabergoline was stopped. She had a repeat MRI pituitary 3 months later which demonstrated a stable well defined expansile poorly enhanced mass in the sella with mass effect on the pituitary stalk. It was felt that pituitary biopsy was too risky in view of immunodeficiency and a PET CT was recommended by the MDT.

In the meantime, she developed symptoms of sciatica and urinary incontinence but an MRI spine excluded cord compression.

At the Royal Marsden, she underwent a lumbar puncture which revealed clonal B cells with similar immunophenotype to peripheral blood. Her subsequent PET CT showed no evidence

of progression of disease. From the haematological perspective, her low-grade lymphoproliferative disease was considered stable.

Complex discussions occurred between the endocrinologist, haematologist and neurosurgeon for the need of pituitary biopsy.As her clinical picture was not entirely consistent with pituitary macroadenoma, we questioned the nature of the pituitary lesion and therefore a pituitary biopsy was performed.

Her pituitary histology showed CLL/ small lymphyocytic leukemia and the patient is being treated with systemic chemotherapy (Rituximab and Bendamustine) as well as intrathecal methotrexate.

This case illustrated the importance of pituitary biopsy in the management of the patient when things are not quite clear cut.

Questions for discussion:

- The importance of pituitary biopsy in management of this patient.
- The unexplained discrepancy between LDDST and UFC results.
- The “normal” serum cortisol in hypopituitarism.

Case presentation. ***Pituitary plasmacytoma presenting as a mimic of pituitary apoplexy – demonstrating the value of obtaining a histological diagnosis.***

E. Ahmad, N. Chandhyoke, T. Hampton, A.King, N. Thomas, B. Whitelaw. (Kings College Hospital NHS Foundation Trust, London).

A previously well 51-year-old female presented to her district general hospital with sudden onset headache, diplopia, decreased vision and right ptosis. The clinical presentation was interpreted as pituitary apoplexy and CT head demonstrated findings consistent with a pituitary macroadenoma. She was treated with stress doses of hydrocortisone and transferred to her regional pituitary service at King's College Hospital.
On examination her visual acuity was 6/60 in the right eye, 6/20 in the left eye, mild swollen optic discs bilaterally, right complete 3rd nerve palsy and bilateral sixth nerve palsy.
Biochemistry was consistent with hypopituitarism and the effect of hydrocortisone treatment: TSH 0.18 (0.3-5.5m IU/L), Free T3 2.1 (3.5-6.5pmol/l), Free T4 8.7 (9.5- 25pmol/l), FSH 1.4 IU/L, LH <0.8 IU/L, Oestradiol 47 pmol/l, Prolactin 1189 pmol/l, Cortisol 1385 (130-580 nmol/l), GH 0.30ug/l, IGF1 32.7 (12.1- 31.8 nmol/l).
Imaging demonstrated a 5cm sella and right parasellar lesion, reported as probable macroadenoma (59 x 33 x 28mm) invading into the right cavernous sinus with compression of right optic nerve and erosion of anterior skull base.
She underwent transsphenoidal surgery within 48 hours of presentation. Post-operatively, neurological symptoms improved apart from bilateral 6th nerve palsy and mild right ptosis.
Histology showed pituitary plasmacytoma with CD56 positivity and Ki67 95%. FDG PET Scan demonstrated intensely metabolically active bone disease associated with the fractures of the left humerus and right clavicle and widespread involvement of other bones as well. A bone marrow biopsy confirmed Plasma Cell neoplasm.
Skull base radiotherapy (5 fractions) was given followed by 6 cycles of Cyclophosphamide, Revlimid and Dexamethasone (CRD) treatment. Subsequently BEAM autologous transplant was performed and the patient went into complete remission.
There was gradual improvement in the 6th nerve palsy and ptosis. Pituitary function normalised with normal cortisol and growth hormone response shown on insulin stress test.

Discussion:
The current UK guidelines on apoplexy advocate conservative management in many cases and do not mention the value of histological assessment of apoplexy cases, to exclude a neoplastic condition mimicking apoplexy. The unusual diagnosis of pituitary plasmacytoma requires specific systemic treatment but the diagnosis could have been missed and was achieved only by surgical biopsy.

Question for discussion:

- Should UK apoplexy guidelines be amended to state that surgery (to obtain histology) is an important aspect of apoplexy management in cases which are non-resolving or show any atypical features?

Case presentation. ***Should SHBG be measured in every patient before diagnosing hypogonadotrophic hypogonadism?***

M. Phylactou, A. Abbara, P.C. Eng, S.A. Clarke, D. Papadopoulou, C. Izzi-Engbeaya, C.N. Jayasena, A.N. Comninos, J. Todd, S. Howard, T. Tan, W.S. Dhillo (Imperial College London & Queen Mary University of London).

A 19-year-old British-Asian man presented with a two-year history of gynaecomastia. He had no other symptoms of hypogonadism. On examination, BMI was 28kg/m^2 and he had post-pubertal-sized testes (20mls) with normal secondary sexual characteristics.

Hypogonadism was confirmed by two morning fasting total testosterone levels of 4.7 and 5.2 (RR 9.2-31.6nmol/L). Haemoglobin was normal (152g/L) and serum oestradiol was <100pmol/L. He had inappropriately normal serum gonadotrophin levels: LH 1.2 (RR 1.2-7.8iU/L), FSH 2.1 (RR 2.0-5.0iU/L) consistent with hypogonadotrophic hypogonadism. Other pituitary hormone levels and MRI pituitary were normal. In view of his biochemical hypogonadism, he was started on testosterone replacement therapy. A DEXA scan following six years of testosterone replacement showed Z scores of -2.1 in the spine and -1.3 in the hips. Seminal fluid analysis was normal on several occasions and he had fathered a child.

He was re-evaluated following 7yrs of testosterone therapy. Both pituitary-function tested with a 100mcg GnRH test, and hypothalamic-function tested with a kisspeptin-54 challenge test, were consistent with responses of healthy men. His sex hormone binding globulin (SHBG) was found to be consistently low at 6 (RR 15-55nmol/L). His calculated free testosterone level by the Vermeulen equation was found to be borderline at 0.251 (RR >0.225nmol/L). His father's SHBG was also found to be very low at 4nmol/L (father's BMI 24 kg/m^2) consistent with a rare inherited SHBG mutation (analysis pending).

Conclusion:
The interpretation of serum gonadotrophins relies on the initial determination that testosterone levels are consistent with hypogonadism. Endocrine Society guidance suggests that SHBG does not need to be measured unless the testosterone level is borderline, or conditions that could affect the SHBG level exist. This case highlights the potential for misclassification of gonadal function if unexpectedly low SHBG levels are not considered when evaluating patients presenting with possible hypogonadism.

Questions for discussion:

- Is there sufficient evidence to confirm that this man is hypogonadal?
- Should SHBG be measured in every patient before diagnosis of hypogonadism?

Case presentation. ***Prolactinoma causing visual disturbance in pregnancy – a multidisciplinary management conundrum****.*

S. Azam, R. Scott, C. Izzi-Engbeaya, S. Jarvis, S. Samarasinghe, A. Comninos, N. Hill, R. Nair, E. Hatfield, N.Martin and K. Meeran. (Imperial College Healthcare NHS Trust, London).

A 33 year old primip presented to the local ophthalmic hospital at 34+4 weeks' gestation with two weeks of blurred vision. Examination revealed a bitemporal hemianopia and reduced visual acuity. She was previously fit and well, and a pre-eclampsia screen was negative.

An MRI scan demonstrated a haemorrhagic pituitary lesion extending into the suprasellar cistern with mild compression of the optic chiasm. Pituitary function tests showed a raised prolactin 3844mU/l, isolated hypothyroxinaemia (TSH 2.16miU/l, fT4 8.4pmol/l), evening cortisol of 264nmol/l, LH 0.2iU/l, FSH <0.1iU/l and oestradiol 63676pmol/l. She was commenced on cabergoline 500mcg after discussion between the endocrine and neurosurgical teams in an immediate medical attempt to relieve pressure on the optic chiasm. In view of her low T4 she commenced thyroxine 50mcg and prednisolone 5mg for safety.

However, after 10 days of cabergoline treatment, despite a reduction in prolactin to 1140mU/l, a significant quadrantanopia and acuity defect remained. With the need for neurosurgery increasing, and after discussion with the obstetric team, she underwent induction of labour. She had a successful vaginal delivery at 36+2 weeks gestation.

As the bitemporal quadrantanopia persisted postpartum (with continued elevation of prolactin at 1232mU/l), she underwent stereotactic endoscopic transphenoidal hypophysectomy 6 days post-partum. This completely resolved her visual field and acuity defect. Five days post-operatively her prolactin was 191mU/l, 9am cortisol 230nmol/l, TSH 0.54iU/l and fT4 16.6pmol/l. She was therefore weaned off thyroxine and cortisol. Histology demonstrated a sparsely granulated lactotroph staining adenoma with Ki67 of 2%.

This case demonstrates the multidisciplinary challenges in the management of pituitary lesions in pregnancy. Clinical acumen is essential, as well as cautious interpretation of pituitary hormone levels in the absence of robust, trimester-specific reference ranges for pituitary hormones. Decisions require consideration of the risks and benefits to both mother and fetus, and demand an effective multidisciplinary approach.

Questions for discussion:

- Is there always a role for trial of cabergoline in pituitary adenomas causing visual compromise in pregnancy?
- How are decisions made to balance the risks and benefits of prioritising obstetric delivery in comparison to immediate neurosurgical management?