

# IANCON 2018: 26th Annual National Conference of the Indian Academy of Neurology

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## **BILATERAL GREATER OCCIPITAL NERVE BLOCK IN TREATMENT OF CHRONIC MIGRAINE: EXPERIENCE FROM A MULTISPECIALTY HOSPITAL IN NORTH INDIA**

**Dr Ruby Chopra, Bathinda;  
Prof Debashish Chowdhury, New Delhi**

Greater occipital nerve (GON) block is the most widely used peripheral nerve block for different primary headache disorders. It is cheap, minimally invasive, has no side effects, is associated with a reasonable duration of pain relief and reduces pill burden and toxicity of abortive and prophylactic medication. There is no Indian data on the use of GON block for treatment of primary headaches.

A study was therefore conducted with patients attending Neurology OPD from December 2016 to April 2018 who were diagnosed with chronic migraine according to ICHD 3 $\beta$ . Response was estimated by reduction in headache days as compared to baseline. It was categorized as complete (100%) if there was no headache in 1 month after GON block, significant (76-99%), moderate (50-75%) and mild (<50%).

At 1-month follow-up, complete response was noted in 42.7% patients, significant in 13.8% patients, moderate in 18% patient, and mild in 4.2% patients. Twenty out of 94 patients (21.3%) did not respond. Average time to develop pain relief after block was  $3.5 \pm 3.18$  days (range 1-15 days). It was concluded that GON block is an effective treatment option in chronic migraine with or without MOH. Presence or absence of OT does not affect the response to GON block. Severity of pain, duration of migraine history, and presence of comorbid psychiatric disorders do not affect response. Side effects are mild and self-limiting.

## **STEM CELL THERAPY IN STROKE: A META-ANALYSIS**

**Dr Amit Kumar, New Delhi**

There are limited therapeutic options available for the treatment of stroke, with limited time window. Pre-clinical research suggests that stem cells potentially modulate multiple pathways involved in endogenous

neurogenesis, angiogenesis, immune modulation, neural plasticity, secretion of growth factors, etc. Translation of these advances into meaningful therapeutic options is required. A meta-analysis was conducted with the aim to assess the effectiveness and safety of cell therapies, studied as monotherapy in adult patients with stroke and published in English language. Trials investigating the use of stem cell therapy in adult patients who had experienced a stroke and in any phase from acute to chronic phase, were included.

Trials investigating combination therapies including stem cells with other therapies were excluded. This review and meta-analysis provides evidence for the safety, feasibility and preliminary efficacy of cell therapies for stroke. There is substantial heterogeneity due to differences in stroke type, route of intervention, timing of intervention, cell types, dose, etc. Further progress in this field will require execution of well-designed phase 2/3 clinical trials with high quality.

## **DIFFERENTIATING CLUSTER HEADACHE AND SIDE-LOCKED MIGRAINE: A CLINIC-BASED STUDY FROM NORTH INDIA**

**Dr Amit Shankar Singh, Chandigarh;  
Prof Debashish Chowdhury, New Delhi**

- Although migraine and cluster headache (CH) are considered 2 different entities with different features, overlap does exist between them.
- Probably the excessive activity of the trigeminal autonomic reflex in this subset of migraine patients is the cause of overlap.
- It is possible that they both share a common pathophysiological step, probably a functional alteration in hypothalamic or brainstem circuits.
- Similarities between CH and side-locked migraine (SLM): Side-locked headaches; Comparable severity of headaches; Common location of headache (orbito-temporal); Throbbing character of pain.
- Differences in CH and SLM: Male preponderance in CH; Duration of attacks - less in CH, more in

SLM; Restlessness (universal in CH); Differences in CAS - Florid ipsilateral CAS in CH in terms of severity, consistency and number.

### **COMPARISON OF EFFICACY AND SAFETY OF AMITRIPTYLINE WITH GABAPENTIN IN MIGRAINE PROPHYLAXIS: RANDOMIZED DOUBLE-BLINDED DOUBLE DUMMY TRIAL**

**Dr Satish J Wagh, Puducherry**

Migraine is a chronic incapacitating neurovascular disorder. In the United States, only 1 in 5 (19.6%) eligible patient currently receives migraine specific preventive care. Both amitriptyline (AMT) and gabapentin (GP) are effective in migraine prophylaxis. AMT and GP have similar efficacy and side effect profile. Migraine prophylaxis does not affect adiponectin levels. Higher responder rates of both drugs indicate that: AMT may be re-considered as first-line therapy (presently second-line); GP may be evaluated as a novel migraine prophylactic medication.

### **TRANSITION FROM CHILDHOOD TO ADULTHOOD IN LENNOX-GASTAUT SYNDROME - COGNITIVE AND THERAPEUTIC OUTCOMES**

**Dr Nitin K Sethi, New York**

- There are very few well-performed studies. Impairments are not always necessarily permanent. The outcomes can vary. Babies who have West syndrome and children who have Dravet syndrome (severe myoclonic epilepsy in infancy) usually will have long-term cognitive and behavioral problems.
- Lennox-Gastaut syndrome (LGS) also often has a poor prognosis. Children with Landau-Kleffner syndrome have a variable prognosis; some regain speech while others have permanent speech impairment. Cognitive and behavioral outcome of at least some children with these syndromes can be influenced greatly by early effective treatment with either antiepileptic medication or surgery.
- Antiepileptic drugs, ketogenic diet, vagus nerve stimulation and epilepsy surgery are effective for seizure control in LGS patients, but not necessarily for improvement in cognitive and behavioral outcomes.
- The cause is more than just seizures (likely underlying genetic causes of cognitive and behavioral deficits). Multidisciplinary treatment is the need: adult neurologist/epileptologist, neuropsychologist, psychiatrist, social workers, special needs school/teachers, family and friends.

### **N-METHYL-D-ASPARTATE ENCEPHALITIS - OUR EXPERIENCE WITH DIAGNOSTIC DILEMMAS, CLINICAL FEATURES AND OUTCOME**

**Dr SR Chandra, Bengaluru**

A total of 29 cases were observed by the team. Surprisingly, only three were males. Their age group ranged from 3 to 31 years and the mean age was 17 years. Age-wise distribution showed maximum incidence in 12-18 years age group. Referral diagnosis in the patients ranged from viral encephalitis in five, catatonia in six, attention-deficit disorder in two, autism spectrum disorder in three, rheumatic chorea in two, autoimmune encephalitis in five, psychiatric illness unspecified in five, rabies in one and schizophrenia in one.

Of the 29 patients, 20 reported minor respiratory infection preceding the problem by 4-10 days. One patient had global developmental delay with congenital heart disease, one patient had hydronephrosis that was operated 4 years ago, and one patient was bitten by dog and received anti-rabies vaccine 30 days before symptom onset. All patients had psychiatric symptoms.

Severe mania-like features were seen in one and schizophreniform symptoms in one, severe panic in nine, unexplained anxiety in 11, catatonia in six, mutism in one, biting self and others in one, and delusions and hallucinations in seven. Neurological features observed in patients were hemiplegia and aphasia in one, mutism in one, seizures in 21, cognitive decline in 29, and chorea in three.

Two patients had benign ovarian teratoma. EEG showed slowing of background in 23 patients, epileptiform discharges in nine, and extreme delta brush in 11. MRI was normal in seven cases. Though reported normal, signal changes in limbic structures were observed in five cases. All others showed clear-cut features of limbic encephalitis. None had any other tumors.

Cerebrospinal fluid (CSF) test showed moderate antibody titers with less than 10% of transfected cells showing two to three plus granular cytoplasmic fluorescence, and serum test showed very high titers of up to 40-60% in seven cases, reverse in 12 cases, and both were moderately positive in 10 cases.

During follow-up at 6 months, only two patients remained positive in serum test. CSF was not tested during follow-up. N-methyl-D-aspartate (NMDA) antibody-related encephalitis seems to be more commonly present with a rapid-onset neuropsychiatric syndrome in children and young girls. Autonomic

involvement was not seen in this cohort as against the literature. Immunotherapy with a single responsive drug was sufficient in most of the patients. Majority of patients are left with cognitive behavioral sequelae and hence, high-degree of suspicion is essential for early diagnosis and treatment. Some of the aggressive and panicky behavior of the patients can even mimic the potentially fatal diagnosis of rabies and needs caution.

Investigators suggest that to the best of their knowledge, this review is the first to report self-mutilating behavior in NMDA encephalitis.

### **NEW-ONSET UNPROVOKED SEIZURES**

**Dr Chaturbhuj Rathore, Vadodara**

New-onset unprovoked seizures are common with an incidence of 60/1,00,000 person-years. Nearly 20% of patients with apparent new-onset seizures have other diagnoses. Many of these patients have previously unrecognized minor seizures. Careful assessment of clinical details, EEG and MRI are required to assess the recurrence risk and the need for drug therapy. Symptomatic etiology and abnormal EEG are two most important risk factors for seizure recurrence after the first unprovoked seizure. Early drug treatment reduces the risk of immediate recurrence by 50% without affecting the long-term prognosis. Therapy needs to be individualized and majority of patients do not wish to start drug treatment after proper counseling.

### **ACUTE ISCHEMIC STROKE**

**Dr Elavarasi A, Puducherry**

- Acute stroke therapy has developed hugely in 22 years since alteplase was approved.
- New kids on the block, like tenecteplase, are promising.
- Mechanical thrombectomy has revolutionized stroke therapy.
- Multimodal imaging has changed the way we look at and treat stroke.
- Aspirin is still the KING.
- Many trials in therapy and rehabilitation are on the way.

### **NEUROLOGY OF SICKLE CELL ANEMIA**

**Prof Vijay K Sharma, Singapore**

- Sickle cell disease is one of the most common disorders of blood caused by a genetic mutation, causing the production of abnormal hemoglobin

within the red blood cells (RBCs). This abnormal hemoglobin (HbS) causes distortion of the RBCs (sickling), making them prone to rupture. This leads to anemia (sickle cell anemia) and blocking of blood vessels causing tissue damage, especially in the brain (stroke) and abdomen (crisis).

- Sickle cell anemia primarily affects Africans and African-Americans. Very limited information is available for this disease in India. It has been reported from certain belts in Tamil Nadu, Kerala and central India. Since most of the complications of this disease are preventable, there is an urgent need to understand the features of Indian sickle cell disease so that locally appropriate models of care may be developed.

### **OCCURRENCE OF MEMORY DYSFUNCTION AND BRAIN LESIONS IN PATIENTS WITH CHRONIC MIGRAINE**

**Dr Ashish Kumar Duggal, Dr GA Khwaja, Dr Meena Gupta, Dr Debashish Chowdhury; New Delhi**

Previous hospital-based studies have shown that migraineurs perform poorly on tests of attention, verbal and visual memory, executive function and psychomotor speed. According to this study that assessed the occurrence and pattern of memory dysfunction, occurrence and character of brain lesions on neuroimaging in patients with chronic migraine (CM), more than 50% of migraine patients reported impaired daily functioning and cognitive symptoms. Ten percent of CM patients had abnormal cognitive tests and most important factor was overuse of medication. Patients with CM had poor performance on working memory, attention, delayed verbal recall and visual retention. Patients with low CR were more prone to develop MOH. Therefore, patients with migraine must be advised to maintain a healthy lifestyle and avoid other risk factors in order to minimize additional brain insults.

### **INDIGENOUS DEVELOPMENT OF ECoG ELECTRODES**

**Dr JK Radhakrishnan, Bengaluru**

- Prevalence of epilepsy in India is 5.59-10 per 1,000. For seizures that do not respond to antiepileptic medications, surgery is considered as the established option.
- Electrocorticography (ECoG) electrodes are needed in surgery of refractive epilepsy, for direct recording of electrical activity from cortical surface of the brain. At present, ECoG electrodes are imported, and their cost is prohibitive (one

1 × 4 strip electrode costs Rs. 18-24 thousand). Development of indigenous electrodes, which are accurate and safe, with a far less cost, will enable more patients to afford the surgical procedure. Development of indigenous 1 × 4 strip electrodes has been completed. Its impedance values are comparable to imported ECoG electrodes. All the materials/components used for the electrode fabrication are biocompatibility certified. The cost of indigenous ECoG electrode works out to about one-fifth the cost of imported electrode.

- ⇒ Novelty claims of this indigenous electrode are:
  - Tear-shaped sensing electrodes, to give a sense of the electrode-array orientation in X-ray images taken pre-surgery and during surgery.
  - Multi-strand, insulated and biocompatible conducting wire ribbon, instead of single strands of conducting wires, for ease of fabrication/assembly of the electrode array.
  - Enhanced electrical contact between the electrode and the conducting wire by using a combination spot-welding and adhesive.

#### **SPECTRUM OF PSYCHIATRIC COMORBIDITIES IN ADULT MIGRAINE PATIENTS: LARGEST SERIES OF 470 PATIENTS FROM INDIA**

Dr Dilip Nagarwal,  
Dr Debashish Chowdhury; New Delhi

Psychiatric comorbidities, especially depression and anxiety, have been well documented in patients with migraine. Limited data exists on a comparative study of the spectrum and distribution of psychiatric comorbidities (Psy-CoM) in migraine from India. A study was thus conducted with migraine patients diagnosed by ICHD 3β criteria who were evaluated for psychiatric comorbidities. Nearly two-thirds of migraine patients had at least one psychiatric comorbidity. In all, 62.4% patients had Psy-CoM. CM patients had greater occurrence and combinations of Psy-CoM than episodic migraine (EM) patients (1.4 vs. 1). Depression is the commonest psychiatric comorbidity in both episodic and chronic migraine patients. EM and CM patients did not differ when compared for severity scores of depression, anxiety and OCD although CM patients had greater proportion of moderate-to-severe depression than EM (34% vs. 25%). All migraine patients, especially CM patients, must be evaluated and adequately treated for Psy-CoM as these may have great bearing on headache outcome.

#### **SPINAL INTRAMEDULLARY TUMOR AND ITS MIMICKERS: AVOIDING MASLOW'S HAMMER**

Dr Suresh Nair, Trivandrum

Differential diagnosis for intramedullary spinal lesions: Demyelinating disorders (MS, TM, NMO, ADEM); tumor (astrocytoma, ependymoma, hemangioblastoma, metastases); vascular (ischemia, spinal AVM); inflammatory (vasculitis, sarcoidosis); infection (herpes-VZV, HIV-VM-TB, bacteria, toxofungus).

According to a study by Lee and coworkers that elucidated characteristics that would identify patients with atypical, non-neoplastic intramedullary spinal cord lesions as harboring non-neoplastic lesions before surgical intervention, the most consistent clue was absent or minimal spinal cord expansion on the preoperative magnetic resonance images. Surgeons must not work with Maslow's hammer. A mind with Crabtrees bludgeon will avoid Maslow's hammer. How to avoid Maslow's hammer? Always consider demyelinating diseases in the differential diagnosis of enhancing intramedullary lesions. Surgeons should never ever have Dunning Kruger effect: A cognitive bias in which unskilled individuals suffer from illusory superiority, mistakenly rating their ability much higher than accurate. This is attributed to a metacognitive inability to recognize own ineptitude.

#### **BREAKTHROUGH SEIZURES: WHAT WE KNOW?**

Dr Shyam K Jaiswal, Hyderabad

The UK Driver and Vehicle Licensing Agency defines a breakthrough seizure as the first seizure after a minimum of 12 months seizure freedom while on treatment. The risk of seizure recurrence following breakthrough seizure has been reported to be more likely among the following patients: Those who require polytherapy in comparison to those who need monotherapy; took longer to achieve 12-month remission and increased their dose after breakthrough seizure. Factors related to poor adherence in epileptic patients: Not taking prescribed medicine by choice; forget to take medication; poor tolerance; poor purchasing capacity, especially in developing countries; nonavailability of drugs in pharmacy in the place of domicile. It is important to get it right because breakthrough seizures can have devastating consequences for patients (loss of job or driving license, low self-esteem, loss of independence). A link has been seen between seizure frequency and levels of anxiety and depression, perceived impact of epilepsy, perceived stigma and marital and employment status.

# ESICON 2018: 48th Annual Conference of Endocrine Society of India

NOVEMBER 15-18 | MAYFAIR CONVENTION, BHUBANESWAR

## INTERESTING CASE SCENARIOS IN ENDOCRINOLOGY

Dr CM Batra, New Delhi

- Pituitary metastasis from thyroid – Only 22 cases had been reported till 2012. From 2013 to 2017, 12 more cases of pituitary metastasis have been reported but none from carcinoma thyroid.
- Pituitary metastasis from follicular carcinoma thyroid – Only 11 reported cases from world literature and none from India.
- In pituitary metastasis from follicular carcinoma thyroid, the tumors are larger, more invasive and anterior pituitary deficiency is rare. Diabetes insipidus does not occur.
- The prognosis of pituitary metastasis is poor and only one case of intrasellar metastasis has been cured so far. There is no neuroradiological imaging which could lead to a sure diagnosis.
- A rare case of pituitary metastasis from follicular carcinoma thyroid was presented.
- The treatment in this case was FNAC thyroid, total thyroidectomy; biopsy of the tissue; whole body RAI scan and <sup>131</sup>I therapy. Radiotherapy of residual sellar and suprasellar mass was also done, following which the patient was referred to AIIMS.
- The patient was recommended for Tg, TgAb and TSH every 6 months and MRI brain every year. RAI therapy after rh-TSH was repeated 6 times in 6½ years.
- The treatment was successful and the patient continues to live after 10 years.
- In such cases, the treatment outlined above is probably the best approach.
- Surgical treatment is difficult to perform, increases morbidity and does not increase survival.
- Thyroglobulin and thyroid transcription factor 1 are the tumor markers that confirm a thyroid malignancy, while cytokeratin 7 and focal staining for cytokeratin 19 confirm epithelial malignancy.

## APPROACH TO SHORT STATURE

Dr Jayaprakash P, Kochi

- Shortness is defined as, “below 3rd percentile or 2 SD below the mean”; excessively short for MPF or TH; or growth velocity <25th percentile over 1 year.
- Various growth charts are available: Growth standards, growth references, WHO charts, CDC charts, Agarwal charts, Khadilkar charts. Physical examination includes height, weight, height age, weight age, midparental height, target height, US:LS, arm span and examination of head, eyes, neck, mouth, hand, SMR and systems.
- Immediate evaluation is required in following cases - Severe short stature: height >3 SD below the mean; Height >1.5 SD below MPH; Height >2 SD below the mean and a height velocity over 1 year >1 SD below the mean for chronological age; Decrease in height SD of >0.5 over 1 year in children over 2 years of age.
- CDGP: Children born with normal weight and length; growth decelerates in 2nd and 3rd year to reach below 3rd percentile; puberty and growth spurt delayed; bone age delayed; males fail to achieve tanner G2 by 14 years and females B2 by 13 years.
- Pubertal assessment is recommended for all children more than 6 years of age. Bone age gives information about skeletal maturity, correlates closely with SMR, informs about growth potential and helps in prediction of adult height. IGF-I assays are dependent on age, puberty, bone age and nutrition; they have low sensitivity but high specificity in younger age.
- IGFBP3 assays are constant, with higher levels, no BP interference, valuable at young ages and not dependent on nutrition. GH provocation tests exclude hypothyroidism. Long-acting GH preparations comprise of depot formulations, PEGylated formulations, Prodrug formulations, Noncovalent albumin-binding GH compound and GH fusion proteins.

## GAMMA CAMERA AND SPECT IMAGING IN ENDOCRINOLOGY

Dr Ishita Sen, Delhi

Conventional nuclear medicine techniques can be tools for problem solving in Endocrinology. Investigations should be tailored to answer specific clinical query. Regular interaction between Nuclear Medicine and Endocrinology departments is essential to develop optimum strategies.

Routine screening of asymptomatic diabetics for silent ischemia is not recommended. Stress myocardial perfusion imaging (MPI) has high sensitivity for detecting silent ischemia. Positron emission tomography (PET) coronary flow rate may be useful to detect nonocclusive coronary artery disease (CAD).

According to the ACCF/AHA guidelines, asymptomatic diabetics over age 40 should be screened for coronary heart disease (CHD) with coronary artery calcium (CAC) scan. For those with CAC score <400, medical therapy can be considered and for those with a score >400, stress imaging study should be considered.

## NEURORADIOLOGY: PRACTICAL TIPS FOR ENDOCRINOLOGISTS

Prof Niranjan Khandelwal, Chandigarh

- Sellar dimensions on plain radiograph – Anteroposterior diameter: 17 mm (range 5-16 mm); depth: 13 mm; width: 16 mm (range 10-15 mm); area on lateral view: 130 sq.mm; volume: 1,092 cumm (mean 599 cumm).
- Elster's rule for pituitary gland height on MRI (maximum height in mm) – Infants and children: 6; men and postmenopausal women: 8; women of childbearing age: 10; women in late pregnancy and postpartum: 12.
- Imaging approach – Recognize the normal sellar/parasellar region contents; determine the abnormality/lesion; place the abnormality in the appropriate space (sellar/parasellar) – Lesion epicenter; characterize the lesion based on imaging features (solid, cystic, mixed, calcifications, etc.); make a set of imaging differentials.
- MRI protocol – *Cavernous sinus*: T2WI brain; FLAIR brain; pre and post-contrast 3D T1 SPGR/MPRAGE; 3D heavily T2 weighted (CISS/SPACE); T2 cor (optional); T1 FS cor post gad (optional). *Sella*: T1FS sag pre/post gad; T2 sag; T1 cor pre/post gad; T2 cor; dynamic (microadenomas).

- Arachnoid cyst – Lack of fenestration of Lilliequist membrane; may occur secondary to adhesions; asymptomatic/hydrocephalus/hypopituitarism/seizures; smooth cyst, no enhancement.
- Tuber cinereum hamartoma – Slow growing heterotopias; precocious puberty/gelastic seizures; nonenhancing, non-calcified, isointense to grey matter, bright on T2; sessile/pedunculated.
- Pituitary hypoplasia – Absent/thread-like stalk; small adenohypophysis; ectopic posterior pituitary bright spot.
- Persistent craniopharyngeal canal – Congenital skull base defect; Sellar floor to nasopharynx; Associations: hamartomas, duplication of pituitary gland/stalk, callosal dysgenesis, facial dysmorphisms.
- Tolosa Hunt syndrome – Idiopathic steroid responsive inflammation; painful ophthalmoplegia; enhancing soft tissue at orbital apex, may extend along tentorium.

## THERANOSTICS IN ENDOCRINOLOGY – CURRENT PERSPECTIVE

Dr CS Bal, New Delhi

- Theranostics refers to the treatment strategies that combine diagnostic testing with targeted therapy, which is the epitome of personalized medicine.
- Radioiodine imaging in Ca thyroid – Post-surgery assessment; post-therapy scanning for confirming staging; assessment of radioiodine ablation after 6-12 months; restaging when there is clinical, biochemical or radiological suspicion of recurrence.
- Theranostic radioiodine imaging (Dx-WBS) can provide detailed biological status for each cancerous lesion and helps in predicting the therapeutic response of every lesion to <sup>131</sup>I treatment. Based on the imaging, ineffective <sup>131</sup>I treatment can be avoided.
- Theranostic approach – Dx-WBS followed by RAI therapy: Unlike fluorodeoxyglucose (FDG) diagnostic imaging studies, radioiodine imaging can forecast response to therapy. It can also potentially alter the decision to treat or not to treat with <sup>131</sup>I.
- In recurrent differentiated thyroid cancer (DTC), empiric therapy with RAI should be reserved for those with significantly elevated Tg (or rapidly rising levels) without a structural target amenable to directed therapy.

- Suspecting recurrence – About 20% patients will have elevated Tg levels up to 1 year after near-total thyroidectomy (NTT). Only one-third will have structural disease, rest will remain disease free and often have a decreasing Tg over time; Measurement of serum Tg coupled with neck ultrasound has become the cornerstone of surveillance strategies; Chest CT scan can detect pulmonary metastases in 80-90% cases, being able to detect lesions between 3 and 6 mm; FDG/PET is usually performed in case of elevated Tg with negative WBS; FDG PET scan can offer additional information in about 10% of these patients.
- Localized radioiodine refractory DTC can be treated with – Surgery; stereotactic external beam therapy; ablation (thermal, laser, alcohol); embolization (chemoembolization, radioembolization).

### HYPERPROLACTINEMIA AND INFERTILITY

**Dr Muthu Kumaran Jayapaul, Chennai**

Pathological hyperprolactinemia may cause defective ovulation and reduced fecundability. Known physiological and pharmacological causes of hyperprolactinemia must be considered and a detailed medical history must be obtained. Abnormal prolactin (PRL) secretion is usually related to an idiopathic hypothalamic dysfunction or to the presence of a pituitary adenoma. Clinical examination and blood biochemistry, including tests for pregnancy and renal and thyroid function, are all important. It is also important to determine the serum FSH in order to pick up an unknown primary ovarian insufficiency in the women seeking pregnancy.

Hyperprolactinemic anovulation – Diagnostic work-up: Measure TSH, T3 and T4 (to exclude hypothyroidism); Among women with menses, measure PRL and progesterone in the supposed luteal phase (during at least 2 cycles); Among women with oligomenorrhea, measure FSH and PRL on two different occasions; MRI to be performed in all hyperprolactinemic women. For a reliable study of the abnormal luteal phase, repeated post-ovulatory plasma progesterone assays and the precise measurement of the luteal phase length are the key to treatment.

### ROLE OF PET-CT IMAGING IN ENDOCRINOLOGY

**Dr Kanhaiyalal Agrawal, Bhubaneswar**

- Radiology vs. Nuclear Medicine – Radiology (X-ray, CT) gives a transmission image and is associated

with increased radiation dose. Nuclear Medicine gives an emission image and is associated with decreased radiation dose.

- PET tracers – Differentiated Ca: <sup>18</sup>F-FDG, <sup>68</sup>Ga-DOTATATE, <sup>68</sup>Ga-PSMA; Medullary Ca: <sup>18</sup>F-FDG, <sup>68</sup>Ga-DOTATATE, <sup>18</sup>F-DOPA; Anaplastic Ca: <sup>18</sup>F-FDG.
- Flip-flop phenomenon – Tumors with functional differentiation of iodine uptake have low glucose metabolism and low FDG avidity; Tumors without functional differentiation of iodine uptake show high glucose metabolism and high FDG avidity.
- A study revealed that the diagnostic accuracy of FDG PET in radioiodine negative thyroid cancer may vary depending on serum Tg levels at imaging. The sensitivity of PET/CT according to Tg levels was 28.6% when stimulated Tg was 2-5, 57.1% when it was 5-10, 60% when it was 10-20 and 85.7% when Tg was >20 ng/mL.
- High FDG uptake suggests more dedifferentiation, aggressive tumor, poorer prognosis and reduced survival.
- A study evaluated the role of <sup>68</sup>Ga-DOTANOC PET-CT in DTC patients with negative <sup>131</sup>I-WBS along with serially increasing serum Tg, and compared the same with <sup>18</sup>F-FDG PET-CT. Per-patient sensitivity and specificity of <sup>68</sup>Ga-DOTANOC PET-CT was 78.4%, 100% and for <sup>18</sup>F-FDG PET-CT was 86.3%, 90.9%, respectively.
- FDG PET in disease recurrence – A meta-analysis analyzed data on the diagnostic performance of <sup>18</sup>F-FDG PET, and PET/CT in detecting recurrent medullary thyroid carcinoma. Pooled detection rate (DR) on a per patient-based analysis was 59%. It stated that DR of FDG PET and PET/CT increases in patients with higher calcitonin and carcinoembryonic antigen (CEA) values and lower calcitonin doubling time (CTDT) and CEA doubling time (CEADT) values.
- <sup>18</sup>F-DOPA PET in recurrent MTC – Sensitivity of 47-83% depending on calcitonin levels; the sensitivity is higher than FDG and <sup>68</sup>Ga-somatostatin analog PET/CT. However, FDG PET is a better indicator of survival.
- Indications of imaging in NET – Staging: Evaluation of metastases and localization of primary tumor; Re-staging: residual tumor, recurrence; Evaluation of receptor status and therapy monitoring. In a systematic review and meta-analysis, somatostatin

**PET Radiotracers in Endocrinology**

Radio-nuclide	Chemical	Radio-nuclide	Chemical
<sup>18</sup> F	Fluorodeoxyglucose (FDG)	<sup>68</sup> Ga	DOTATOC/ DOTATATE/ DOTANOC
<sup>18</sup> F	Dihydroxy-phenylalanine (DOPA)	<sup>68</sup> Ga	DOTA-Exendin 4/ NOTA-Exendin 4
<sup>18</sup> F	Choline	C-11	Hydroxyephedrine
		C-11	Methionine

receptor PET/CT (SMSR PET) was found to have good diagnostic performance for evaluation of NET in the thorax and abdomen. The pooled sensitivity was 93% and specificity 96%.

- Ectopic Cushing syndrome – Pooled detection rates: <sup>18</sup>F-FDG 61.1%; <sup>68</sup>Ga-peptides 70%; <sup>18</sup>F-DOPA 46.7%.

**APPROACH TO A PATIENT OF HYPERCALCEMIA**

**Dr P Velayutham, Coimbatore**

- Hypercalcemia is defined as serum calcium levels more than 2 SD above mean. Serum calcium in normal adults is between 8.6 and 10.4 mg/dL. Severe hypercalcemia refers to serum calcium >14 mg/dL. Hypercalcemic crisis refers to serum calcium >14 mg/dL with neuro, cardiac, renal symptoms.
- For every 1 g/dL drop in serum albumin below 4 g/dL, measured serum calcium decreases by 0.8 mg/dL.
- Corrected calcium = Measured Ca + (0.8 × [4 - albumin]).
- Ambient pH influences protein binding to calcium. Metabolic acidosis – Decreased protein binding ---- increased ionized calcium; metabolic alkalosis – increased protein binding ----- decreased ionized calcium.
- Fall in pH by 0.1 increases serum calcium by 0.4 mg/dL.
- Clinical symptoms of hypercalcemia (acute) – General: Fatigue, weight loss; CVS: Short QT, arrhythmia, syncope; GI: Anorexia, nausea and vomiting, constipation, pancreatitis; Renal: Polyuria, dehydration, AKI, renal stones; Others: Bone pain, irritability, psychosis.
- Lab pitfalls in primary hyperparathyroidism (PHPT) – Low Ca and high phosphorus diet can obscure hypercalcemia; Very low vitamin D status can obscure hypercalcemia; Low vitamin D can be a

manifestation of PHPT; Hypercalcemia can be masked if presentation is with acute pancreatitis; Intact PTH can be high normal in 10-15% of the people with PHPT; High Ca and high iPTH can be seen in 20% familial hypocalciuric hypercalcemia (FHH).

- Correct calcium levels for prevailing serum albumin. PHPT and malignancy account for most of the cases with hypercalcemia. Use of multiple variables helps in arriving at diagnosis easily.
- Hypercalcemic crisis requires urgent medical intervention.

**DIAGNOSIS AND MANAGEMENT OF PHEOCHROMOCYTOMA**

**Prof Karel Pacak, USA**

- Pheochromocytomas (PHEOs) are chromaffin – neural crest cell tumors characterized by catecholamine production and catecholamine metabolites (metanephrines/methoxytyramine) secretion.
- About 23 genes are involved in the pathogenesis of PHEO. Nearly 27-35% are inherited (germline mutations), 30-39% have somatic mutations. About 7% have fusion genes.
- All patients with a catecholamine producing PHEO must receive α/β adrenoceptor blockade. Metanephrines are a gold standard in the biochemical diagnosis of PHEO. Metanephrines are produced and released continuously independent of pulsatile catecholamine secretion.
- Catecholamines cannot be used for PHEOs <7-10 mm. About 30% of PHEOs do not secrete catecholamines. Additionally, some PHEOs produce only dopamine which is not usually measured.
- Clonidine test distinguishes increased sympathetic activity (false-positives) from PHEO (true-positives).
- Methoxytyramine, tumor size and succinate dehydrogenase subunit B (SDHB) are independent predictors of metastatic PHEO. <sup>68</sup>Ga-DOTATATE PET/CT has a better performance in patients with PHEOs as compared to other imaging modalities. Metabologenomics has a potential role in PHEO diagnosis and treatment.
- Hypoxia-inducible factor (HIF) signaling seems to play an important role in the development of PHEOs and paragangliomas (PGLs), thus suggesting novel therapeutic approaches for the treatment of these tumors. Precision medicine seems to have a potential role in the management of PHEOs.



## News and Views

### **ICMR to Undertake a Nationwide Surveillance of Fruit Bats to Gauge Nipah Virus Threat**

The Indian Council of Medical Research (ICMR)-National Institute of Virology (ICMR-NIV) will undertake a nationwide surveillance of fruit bats to gauge Nipah virus threat. The move follows the presence of Nipah virus in fruit bats (*Pteropus giganteus*) during the recent outbreak in Kerala, following which 17 people succumbed to the pathogen in May-June 2018.

"In the recent outbreak in Kerala, ICMR-NIV had shown 23% positivity of Nipah virus in the *Pteropus* bats while screening throat and cloacal (rectal) swabs of the mammals captured near the index case's house," scientist Devendra Mourya, Director, ICMR-NIV told TOI. The study also becomes vital as there is no information on the presence of the virus in fruit bats in the country, except West Bengal, Assam and Kerala, which are considered the hotspots of the deadly disease. Experts said the crucial intelligence on the presence of the virus in other areas would help in giving alerts, increase preparedness and contain the human-to-human transmission of the virus to save lives. "About 20 states, including Maharashtra, will be covered in the first phase. The site selection activities have begun in 16 states from January... (TOI, January 13, 2019)

### **Updated Guidelines for Treatment of Migraine**

The American Headache Society (AHS) has published an updated position statement for treatment of migraine online December 10, 2018 in the journal *Headache*. The statement recommends use of evidence-based treatments when possible and appropriate; start with a low-dose and titrate slowly; reach a therapeutic dose if possible; allow for adequate treatment trial duration; establish expectations of therapeutic response and adverse events and maximize adherence. Neuromodulation may be useful for patients who prefer nondrug therapies or who respond poorly, cannot tolerate or have contraindications to pharmacotherapy.

### **Health Hazards from Exposure to Cement Common in Construction Workers**

Men and women laborers at construction sites who handle cement or are exposed to it are at high risk of contracting skin infections owing to the harmful

chemicals it contains, a new study conducted by the All India Institute of Medical Sciences (AIIMS), New Delhi has found. The study, conducted by the AIIMS Department of Dermatology and Venereology along with Sweden's Lund University, with key researchers being Dr Kaushal Verma and Dr Magnus Bruze, found that major concentrations of chemicals like hexavalent chromium in cement can lead to skin problems like dermatitis, eczema, rashes and burning sensation, among others. (*India Today, January 13, 2019*)

### **Whole Body Examination not Necessary to Diagnose Scabies**

According to a study published December 27, 2018 in the journal *PloS Neglected Tropical Diseases*, compared to a full body examination, examination limited to hands, feet and lower legs had 90% sensitivity for detecting scabies. Body regions with highest yield were the hands (sensitivity compared to whole body examination, 51.2%), feet (49.7%) and lower legs (48.3%).

### **A Healthy Diet Precludes the Need of Vitamins or Nutritional Supplements for Most People**

Most people do not need to take vitamins or nutritional supplements as they can get all the nutrients they need by eating a healthy diet, according to a new patient page "Vitamins and Nutritional Supplements What Do I Need to Know?" published online January 7, 2019 in *JAMA Internal Medicine*. It includes information and answers to questions about vitamins and nutritional supplements that patients often have.

### **Takotsubo Syndrome not as Benign as Thought to be**

A systematic review and meta-regression study has shown relatively high rates of life-threatening complications such as acute heart failure (HF) with shock (19%) and malignant arrhythmias (10%), with in-hospital death occurring in 1.8% of cases of Takotsubo syndrome. One percent of the survivors had a recurrent episode. Long-term total mortality in each study was significantly associated with older age, physical stressor and the atypical ballooning form of Takotsubo syndrome. These findings are published January 3, 2019 in the *Journal of the American College of Cardiology: Heart Failure*.