CCP News

Newsletter of the Ceylon College of Physicians

March 2019

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Compiled and edited by:

Dr Achala Balasuriya
Dr Kishara Gooneratne

Ceylon College of Physicians
341/1, Kotte Road
Rajagiriya, Sri Lanka
Phone: +94 (0)11 2888146 or 3094140
Fax: +94 (0)11 2888119 E-mail: office@ccp.lk

President's message

Dear Fellows and Members,

The first quarter of the year is drawing to a close and I am happy to inform you that the foundation for the year's activities has been firmly laid.

We conducted the first regional meeting in Matale which was a resounding success. The educational programme for the nursing officers was greatly appreciated by them, their enthusiasm was rewarding to note. I thank Dr Zarook Sahabdeen, VP and President of the Matale Clinical Society and the Council members of the College Drs Madhuwanthi Hettiarachchi, Dinithi Fernando and Shehan Silva for their commitment and dedication in organising the event and the team that represented CCP for their enthusiasm and support in delivering a very successful academic programme.

The Matale meeting was preceded by the first regional Young Physicians Forum for the year. This was conducted at the Teaching Hospital Kandy and six of our Associate Members made interesting presentations on varied topics. As a new feature in the CCP Newsletter for 2019, we share some of these with you and we hope you will find the contents useful in your work.

The submission of abstracts for the 52nd Anniversary Academic Sessions and the orations for 2019 is now open and I invite all of you to submit your work. It will be a good opportunity to share local data with fellow physicians and to discuss these with the international faculty who will be joining us. The submissions must be made online.

For the successful completion of all these activities, the Council members were ably supported by the CCP office staff. It was a "baptism by fire" to our pre-interns Drs Ravindu Kodithuwakku and Udara Perera as they worked tirelessly to ensure that many deadlines are met simultaneously. As a Team, the CCP has done well during the first quarter of 2019.

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President's message

The Sinhala and Tamil New year will dawn in a week and I wish all of you a very happy and a successful New Year!

With best wishes,

Professor Chandanie Wanigatunge
President
Ceylon college of Physician

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YPF Kandy

The YPF Kandy was held on the 5th of March at the Kandy Teaching Hospital Postgraduate Auditorium. There were six interesting presentations from Associate Members (senior registrars). This event was very well attended by trainees, junior doctors, consultants from Kandy and Peradeniya Teaching Hospitals together with a delegation of Council Members of the CCP. There were over 120 participants.

This event was sponsored by cipla.

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Lupus Nephritis

Dr B M D B Basnayake, Senior Registrar in Nephrology, Teaching Hospital Kandy

Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease that can affect any organ. It is more prevalent in women than men. It affects the kidneys in about 50% of patients. The Clinical involvement of kidney in SLE is called Lupus Nephritis (LN) and is a major risk factor for morbidity and mortality and 10% of patients with LN will develop End Stage Renal Disease(ESRD). Importantly, 10 year survival improves from 46% to 95% if disease remission can be achieved.

SLE arises in individuals with an appropriate genetic background who are exposed to certain environmental triggers. Carriers with HLA-DR4 and DR11 are protected against LN. Conversely HLA-DR3 and DR15 confers an increased risk of LN. Propensity to develop LN increases when the expressions of neutrophil-associated genes are increased. Neutrophil activation is preceded by an increase in interferon (IFN) and plasmablast-related transcripts and is followed by upregulation of other myeloid cells and proinflammatory transcripts. The disease initiates preclinically with an IFN response and differentiation of B cells into plasmablasts, and progresses to tissue-specific and systemic inflammation as neutrophils and myeloid cells activate. The C system is generally activated in LN and may directly mediate kidney injury through the terminal pathway, or indirectly increase renal inflammation by recruiting leukocytes to the kidney.

Proteinuria is seen in almost all patients (100%). Other clinical manifestations include nephrotic range proteinuria/nephrotic syndrome (50%), microscopic hematuria (80%), macroscopic hematuria (5%), urinary RBC casts (30%), other urinary cellular casts (30%), renal insufficiency (60%), rapid decline in kidney function (15%), hypertension (30%) and tubular abnormalities (70%).

If kidney involvement is suspected, a kidney biopsy should be considered. Renal biopsy is important to define the nature of renal involvement. Although immune complex mediated GN is the common cause of kidney disease in SLE, there are other mechanisms that result in renal injury which can only be diagnosed with a biopsy (Eg: ATN/ AIN, TMA (24%), lupus podocytopathy (1.3%)).

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Lupus Nephritis

There are six histological patterns in LN. Repeat renal biopsies in LN are controversial, but emerging data suggest serial biopsies may inform ongoing treatment decisions & predict long term renal prognosis.

A retrospective descriptive study involving 351 patients attending TH Kandy Nephrology Unit was carried out from January 2010 to November 2018. There were 309 (88.03%) females and 42 (11.96%) males. Female: male ratio was 7.3: 1. Mean age at initial presentation was 29.73 (age range 11 – 70 years). Proteinuria was evident in almost all patients (96.3%). Anemia (hemoglobin <12g/dl) and thrombocytopenia (<150 × 109/ L) was noted in 82.05% and 10.8% of patients, respectively. Around 20% of patients had high serum creatinine (>130umol/L). ANA reports were available in 209 patients and was positive in 190 (90.9%) and negative in 19 (9.09%) patients. Of 53 patients with Ds DNA tested, 43 (81.13%) patients were test positive and 10 (18.86%) patients were test negative. Both ANA and Ds DNA negativity was noted only in 3 patients. Commonest histological pattern was LN class IV (65.8%), followed by LN class II (15%), LN class III (11.6%), LN class V (5.6%), LN class I (1.13%) and class VI (0.5%).

Standards of care include, remission induction, maintenance therapy, adjunctive therapy (blood pressure control, Hydroxychloroquine, Aspirin/ anticoagulation, lipids and cardiovascular risk modification drugs).

Pregnancy should be planned and LN should be stable, inactive with a uPCR of less than 50g/mgCr for the preceding six months before conception. There is a need to switch teratogenic drugs such as MMF to Azathioprin (at a dose not exceeding 2mg/kg/day). HCQ, calcineurin inhibitors and steroids are safe. In a disease flare steroid treatment needs to be intensified with or without AZA. Therapy should not be tapered during pregnancy and includes at least three months postpartum.

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Acute pulmonary embolism

Dr M. J. M. Nawshad, Senior Registrar in Cardiology, TH Kandy

Introduction

Acute pulmonary embolism has been a dilemma for physicians. It has a high annual incidence. The diagnosis is often missed and sometime only identified during a postmortem. Diagnosing acute pulmonary embolism is important as it can reduce the mortality by commencing anticoagulation therapy in a timely manner.

Pathophysiology

Understanding the pathophysiology is important to investigate as well as to treat the patient with pulmonary embolism. As major emboli blocks the main pulmonary artery it increases the resistance and right ventricular afterload in the pulmonary circulation. This will increase the pressure in the right ventricle (RV) causing RV dilatation and tricuspid insufficiency. Increased RV myocardial strain causes RV ischemia and subsequently, reduces the RV output. Low RV output reduces the Left ventricular (LV) preload and LV output. Low cardiac output leads to shock and reduces the RV coronary perfusion which worsens the RV ischemia and RV output. Death occurs due to cardiogenic shock and RV ischemia.

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Acute pulmonary embolism

Clinical presentation

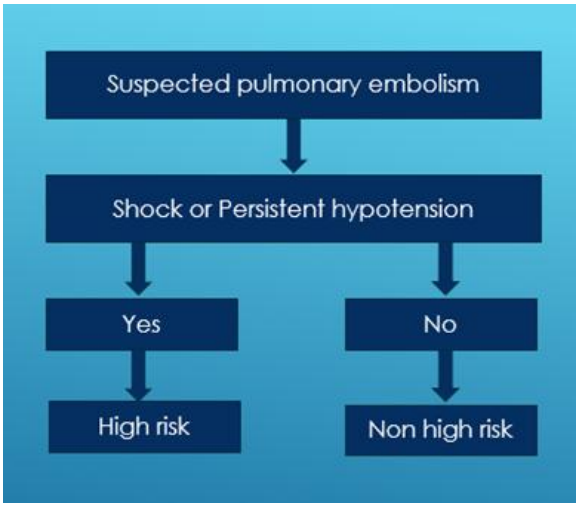
Clinical presentation varies according to the severity of pulmonary embolism. Acute pulmonary embolism commonly presents as an acute shortness of breath, other symptoms include pleuritic type chest pain, tachypnea, hemoptysis and cough. Massive embolism may cause syncope. On examination tachycardia and clear lung fields may be evident. Usually a massive embolism will present with persistently low systolic blood pressure of less than 90mmhg or cardiogenic shock.

Risk factors

Strong predisposing risk factors are bone fracture, knee replacement, major surgery, spinal cord injury, malignancy and thrombophilia. The use of oral contraceptives has also increased the risk. Pregnancy, postpartum and travelling over long distances also increase the incidence of acute pulmonary embolism.

Initial risk stratification

Initial risk stratification is important to arrange further investigations and management. Shock or persistent hypotension is identified as, a reduction in systolic blood pressure (SBP) < 90 mmHg, or a drop in SBP >40mmHg for more than 15 min which is not due to other causes.



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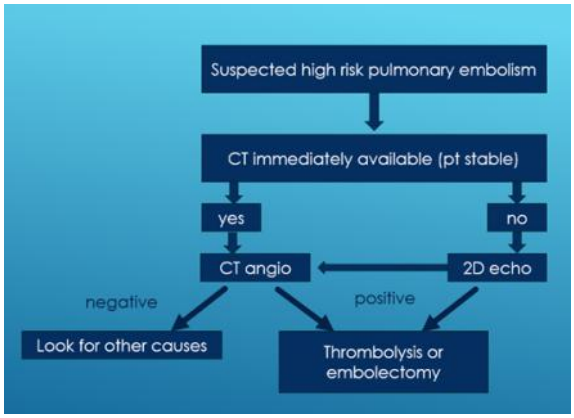
Acute pulmonary embolism

High risk pulmonary embolism

First line investigation for high risk pulmonary embolism is the CT pulmonary angiogram where the thrombus can be visualized. CT has the added advantage of being able to detect other diagnoses other than pulmonary embolism. Next line investigation is the 2D echocardiogram. Echo can show the presence of features due to right ventricular strain (McConnell sign – RV free wall hypokinesia with apical sparing). Other features visible through echo are tricuspid regurgitation and IVC congestion. Sometimes dilated pulmonary arteries with proximal pulmonary artery thrombi may be visible. ECG will also show features of right ventricular strain with RBBB, tachycardia and rarely S1Q3T3 pattern.



Non high risk pulmonary embolism

The clinical probability score of PE can be assessed with the modified Well's score or a revised Geneva score. If the probability is low, with a negative D- Dimer, it excludes the possibility of pulmonary embolism. If the clinical probability is high, a CT angiogram should be done to confirm the diagnosis. Other supportive investigations can be done, such as positive troponin and Pro-BNB, which will indicate right ventricular ischemia and failure. CXR-PA may show Westermarck and Hampton signs. The VQ scan is largely replaced by CT but it is useful in eliminating the possibility of pulmonary embolism. USS Doppler of the lower limb and abdomen will give a clue as to the source of thrombi.

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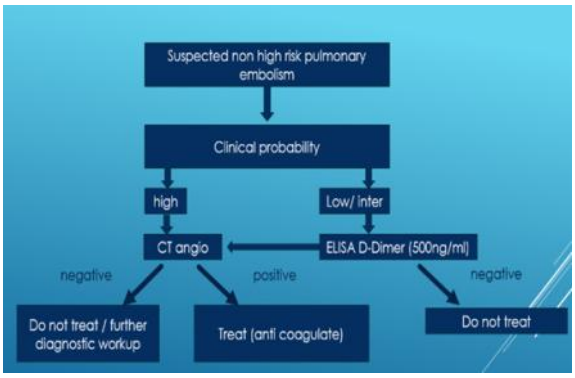

Therapeutic strategies in pulmonary embolism

Hemodynamic stabilization should be achieved, for the treatment of hypotension fluid resuscitation and noradrenaline is the drug of choice. Oxygen supplementation can be administered for the reversal of hypoxemia. Prevention of thrombus growth can be treated by starting heparin or LMWH when embolism is suspected (level C evidence). Restoration of pulmonary blood flow can be achieved through thrombolysis. Alteplase, Urokinase and streptokinase can be used for thrombolysis. Percutaneous catheter (PC) directed therapy such as PC directed thrombolysis, thrombus fragmentation and aspiration are other options. Non high risk patients should be treated with LMWH, Heparin or Fondaparinux and should be started on long term prophylaxis with Warfarin to prevent recurrence. Patients should continue on warfarin for a minimum of three months and may need to extend the treatment depending on the persistence of risk factors. A IVC filter may have to be considered in patients who are unable to continue warfarin.

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Motor Complications in Parkinson Disease

Dr Pubudu Amarasena ,Senior Registrar in Neurology, Teaching Hospital Kandy

Parkinsonism is a collection of typical symptoms first described by Dr. James Parkinson in his essay titled "The Shaking Palsy" published in 1817. Idiopathic Parkinson disease is implicated in 80% of patients with Parkinsonism. Clinical features of IPD can be divided into motor symptoms, non-motor symptoms and complications or adverse effects of treatment. The cardinal motor symptoms include tremor, bradykinesia, rigidity, loss of postural reflexes, flexed posture and freezing. Non-motor features include disorders of mood and affect with apathy, anhedonia and depression, cognitive dysfunction and hallucinosis, as well as complex behavioural disorders.

Motor complications occur due to treatment with Levodopa (L-Dopa). These can be broadly categorized into motor fluctuations and dyskinesias. These can be sub classified according to the timing as 'OFF – state', 'ON-state' and 'Transitional state' complications (Table 1).

OFF state	ON State	Transitional State
'Wearing off Phenomenon	Peak dose dyskinesia	Beginning of dose worsening
Dose Failure / Partial Response	ON – Period Freezing	End of dose rebound
OFF - Period Freezing	Delayed ON response	Diphasic Dyskinesia
OFF – Period Dystonia		

Table 1: Motor Complication in Parkinson Disease

Wearing off phenomenon includes predictable wearing off (regular occurrence of symptoms at the end of a levodopa dose), unpredictable wearing off (sudden recurrence of symptoms unrelated to the timing of the next levodopa dose), and ON-OFF fluctuations (rapid, abrupt transitions from ON-state to OFF-state). Management of predictable wearing off is by maintaining a minimum effective level of L-Dopa throughout the day, which can be achieved by reducing the dosing interval up to 4 hours and adding a COMT inhibitor or a dopamine agonist and subsequently a MAO-B inhibitor. Unpredictable wearing off is managed by optimizing the L-Dopa dose and frequency and adding a dopamine receptor agonist. Rescue therapy for sudden OFF-states includes subcutaneous Apomorphine injections and soluble forms of L-Dopa.

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Dose failures includes delayed responses, partial responses and no responses to L-Dopa, which occur mainly due to erratic absorption of L-Dopa. These can be minimized by enhancing absorption by taking L-Dopa 30 minutes before or 2 hours after meals, avoiding high protein meals, increasing gastric motility using peripherally acting antiemetics, treating constipation, avoiding anticholinergics and treating Helicobacter pylori infection if present.

Freezing is a transient inability to initiate of continue voluntary movement, which can occur in both OFF and ON states. Management is by reducing OFF periods. Selegiline and Amantadine has shown some benefit.

Transitional state complications include beginning of dose worsening and end of dose rebound, which are difficult to treat. Adding an additional L-Dopa dose can be considered, but with the increased risk of dyskinesia.

Dyskinesia include peak-dose dyskinesia, diphasic dyskinesia and OFF-period dystonia. Peak-dose dyskinesia occur at the best 'ON' response and are typically choreiform movements which are managed by reducing individual L-Dopa doses, using regular L-Dopa instead of controlled-release preparations and avoiding COMT and MAO-B inhibitors. Amantadine or Clozapine can be used to treat dyskinesia. Diphasic dyskinesia occurs at the beginning of dose and at the end of dose and are stereotypical alternating dystonic or ballistic kicking movements. These can be treated by adding a dopamine receptor agonist and using rescue treatment for acute episodes. OFF period dystonia occurs mostly when waking up and reducing OFF periods is beneficial while Botulinum toxin (BOTOX) injections, anticholinergics and muscle relaxants are also used.

Resistant motor fluctuations are treated using device-assisted methods including deep brain stimulation, infusional Levodopa-carbidopa intestinal gel and continuous apomorphine injections.

In summary, the management IPD is not universal and needs to be tailor-made to suit each individual depending on the response to treatment and the presence of complications.

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Motor Complications in Parkinson Disease

References

1. *Burn, D. (2013). Oxford Textbook of Movement Disorders. Oxford University Press, pp.83-92.*
2. *Hess CW, Okun MS. Diagnosing Parkinson Disease. Continuum (Minneapolis, Minn). 2016;22(4 Movement Disorders):1047-63*
3. *Morgan JC, Fox SH. Treating the Motor Symptoms of Parkinson Disease. Continuum (Minneapolis, Minn). 2016;22(4 Movement Disorders):1064-85*
4. *Freitas ME, Hess CW, Fox SH. Motor Complications of Dopaminergic Medications in Parkinson's Disease. Seminars in neurology. 2017;37(2):147-57*
5. *Dietrichs E, Odin P. Algorithms for the treatment of motor problems in Parkinson's disease. Acta neurologica Scandinavica. 2017;136(5):378-85*

Hypopituitarism: What we know and don't know?

Dr Dhulashiha Jegavanthan, Senior Registrar in Endocrinology. Teaching Hospital Kandy

Pituitary is the master gland in our body, anatomically having two lobes which secrete hormones which are essential for growth and development. The anterior pituitary secretes Growth Hormone (GH), Luteinizing hormone (LH), Follicle stimulating hormone (FSH), Thyroid stimulating hormone (TSH), adrenocortical stimulating hormone (ACTH) and Prolactin. The posterior pituitary secretes Oxytocin and Anti Diuretic Hormone (ADH).

Hypopituitarism is defined as deficiency of one or more hormones of the pituitary gland which can result from diseases of the pituitary gland or hypothalamus.

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Hypopituitarism: What we know and don't know?

It is mandatory to diagnose a hypopituitarism early as possible to avoid complications of hormonal deficiencies which can be even life threatening. If we consider the prevalence of hypopituitarism it is estimated to be 45 cases per 100 000, with an incidence of about four cases per 100 000 per year in the western world. However we don't have our own data for the Sri Lankan population, though there are many patients presenting with hypopituitarism in our day to day practice.

Aetiologically hypopituitarism can be caused by any illness affecting the hypothalamus or pituitary gland. It can be due to congenital disorders, genetic mutations, tumors involving hypothalamus or pituitary, surgical procedures or radiation. There are disorders are due to inflammation, infarction as well as infiltration and causes include Sarcoidosis, Langerhan Cell Histiocytosis and Haemochromatosis. In addition to the above causes pituitary abscess, snake bite, HIV infection, Sheehan syndrome, road traffic accidents are also found to cause hypopituitarism in tropical countries like Sri Lanka.

Clinical features of hypopituitarism differ according to the particular hormonal deficiency which the patient has and the age at presentation; if there is a pan-hypopituitarism in a child he may present with short stature and delayed puberty or adrenal crisis. Similarly an adult may present with fertility issues or menstrual abnormalities. Therefore a careful history and examination including height, weight, tanner staging, visual assessment and features of hyper-secretion of a single hormone are paramount.

Once there is a suspicion regarding a single or multiple pituitary hormonal deficiency, the evaluation should be further carried out by assaying the anterior pituitary hormones. This should necessarily contain both trophic and target hormones. For example a normal TSH with low FT4 still implies a central hypothyroidism as there is an inappropriately normal TSH response to a low FT4. In addition if the patient has osmotic symptoms, an evaluation for central diabetes insipidus also should be carried out.

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Hypopituitarism: What we know and don't know?

List of anterior pituitary hormone assay:

- LH/FSH
- Serum fasting testosterone or oestradiol
- Serum 9am cortisol
- TSH and FT4
- Serum prolactin
- IgF1 levels.

Depending on above findings dynamic tests should be carried out.

If serum cortisol is low proceed with:

- serum ACTH
- Insulin Tolerance Test/ Glucagon tolerance Test (gold standard)
- Or Short Synacthen Test

If serum IgF 1 is normal with high suspicious of GH deficiency (which can be negative in 40% of deficient patients) it is advised to proceed with:

- Insulin Tolerance Test/ Glaucogon tolerance test
- Or Combined GHRH with arginine/ GHRP

Following blood investigations other supportive investigations like X-ray non dominant hand for bone age assessment, metabolic screening to aid future management and MRI Pituitary to find out the exact cause should be arranged.

Once the diagnosis of hypopituitarism is made, the cause should be treated if possible (e.g. tumour excision) or hormone replacement should be arranged.

Cortisol is replaced with oral hydrocortisone 20mg in divided doses to mimic the normal diurnal variation of body cortisol. A sick day rule is advised. Similarly central hypothyroidism is treated with levothyroxine 1.6 mcg/kg dose to target FT4 in the mid normal range.

Thirdly if patient has growth hormone deficiency with short stature, recombinant growth hormone injections can be given with aiming at a height increment of 5cm/year. In adults with normal height and GH deficiency can be similarly treated with GH injections to improve their quality of life with monitoring of QoL-AGHDA score.

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Finally once the desired height is achieved the gonadal hormone replacement can be commenced which in turn improves quality of life, bone health and to a certain extent sexual function. If fertility is desired gonadotrophins pulses are given to achieve endogenous sex hormone levels. It should be always kept in mind that the gonadal hormone replacement should always be preceded by growth hormone replacement in needed patients to prevent premature closure of the epiphysis.

"A timely diagnosis and proper management of hypopituitarism will lead to a successful life with better quality".

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Regional meeting Matale

Compiled by Dr Shehan Silva, Consultant Physician, NIMH

The first regional meeting of the CCP was held in collaboration with the Clinical Society of Matale District General Hospital on the 6th March 2019 at the hospital premises. The event as per tradition consisted of two parallel sessions for doctors and nurses separately.

Two modules, namely the anaphylaxis and acute kidney injury modules were presented in the doctors programme. The lectures covered topics of leptospirosis, cardiac arrhythmias, newer drugs in management of diabetes mellitus and obstructive sleep apnea. The lecture on 'Medicines use: maximizing benefits and minimizing harm' by the president of the CCP was a noteworthy presentation.

The nurses program covered topics on management of critical patients, dengue monitoring, nutritional therapy, oxygen therapy, insulin therapy and the use of inhalers.

Both these sessions were well attended by health professionals of the Matale hospital and from other smaller health institutions in the district. The program was sponsored by Zydus and Cipla.

An excerpt of the lecture on 'Medicines use: maximising benefits and minimising harm' by Prof Chandanie Wanigatunge is as follows:
'The clinician must focus on prescribing the right medicine in the right dose and dosage form at the right time through the right route of administration with the right information dispensed on the right person. Moreover, he must consider that the disease that he has to manage in context of other comorbidities and patient's psychosocioeconomic aspects. Generic drugs are expected to demonstrate therapeutic equivalence in producing similar clinical effects both in terms of therapeutics and side effects. Therapeutic equivalence is comprised of pharmaceutical and biological equivalence. Pharmaceutical equivalence implies similar amounts of active substances in similar dosage and administration meeting comparable standards. Biological equivalence is an indirect method to ensure uniformity of standards of efficacy and safety. Any short acting generic is acceptable if they are properly manufactured, stored and administered. Brand substitution is not recommended for most extended/ sustained release preparations as they may not show therapeutic equivalence'

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Regional meeting Matale

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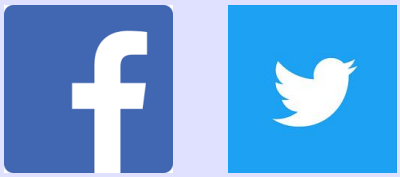
Forthcoming events

April

- April 2: Young Physicians' Forum: at the ClinMARC auditorium, National Hospital of Sri Lanka
- April 5: Council meeting, at the College Office
- April 18: MTI- 'Medical training initiative' interview: at the College Office

May

- May 3: Maternal medicine Specialty Update: at the ClinMARC auditorium, National Hospital of Sri Lanka
- May 10: Council meeting: at the College office
- May 14: Young Physicians' Forum: at the ClinMARC auditorium, National Hospital of Sri Lanka

Follow us now on 

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