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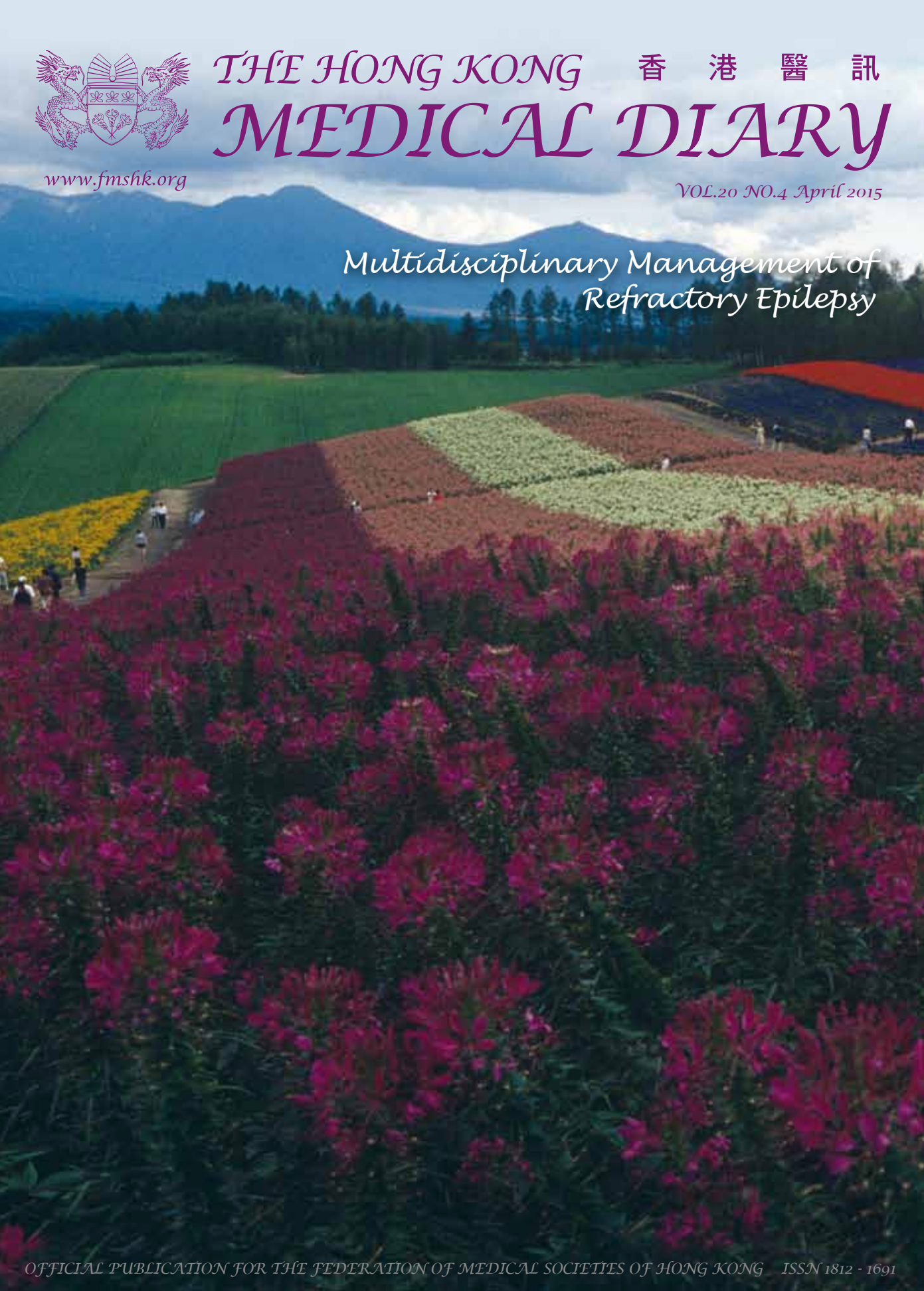
Multidisciplinary Management of Refractory Epilepsy



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HK-FY-MM-14J-03

Contents

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The Cover Shot

A Wide Perspective

Prior to 'stitching' and iPhonography, to take a panoramic picture was exciting but challenging. Using an ultra wide-angle lens with cropping might work but with the noticeable distortion, it seldom works in my hands. Then I got hold of Hasselblad XPan II with an aspherical 30/5.6. It captures the scene on 2 frames of conventional 35 mm films producing an aspect ratio of about 8:3. Soon it becomes my good companion when I go for scenic shots.

This Cover Shot was taken at Hokkaido on Kodak E100VS. The colours of the terrain are orchestrated but appealing to tourists, adults and children alike. The picture is chosen for its purple motif. March 26th is the annual ***Purple Day*** dedicated to increasing awareness of epilepsy. People around the world would wear purple on this day and host events in support of the condition.

Dr Dawson FONG *Specialist in Neurosurgery*

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Editorial

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Editor

Dr Mario WK CHAK

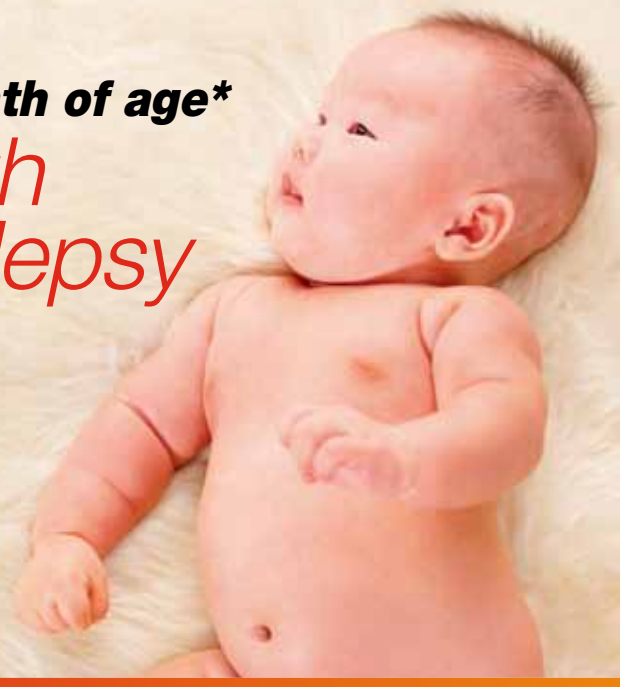
Multidisciplinary Management of Refractory Epilepsy

Despite the discovery of new antiepileptic drugs, there are still approximately one third of patients with epilepsy that remain resistant to pharmacotherapy. Apart from having frequent unpredictable seizure attacks and side effects of polypharmacy, these patients could also suffer with developmental and cognitive dysfunction, psycho-behavioural comorbidities as well as social stigma. In Hong Kong, refractory epilepsy imposes a significant clinical, economic and psycho-social burden to our society.

Managing these "intractable" or "medically refractory" or "drug resistant" epilepsy is challenging and requires a multi-disciplinary team approach with the collaboration and input of various expertise in a specialised tertiary centre to provide a comprehensive assessment and evaluation with the aim to have an in-depth understanding of the patient's epilepsy aetiology and to optimise their outcome. This means we not only need to focus on seizure control, but also the developmental, cognitive and social psycho-behavioural aspect of the patient. With the recent advance in Epileptology, Neuroimaging and Neurophysiology, there is a breakthrough in surgical and dietary treatment of medically refractory epilepsy resulting in a better clinical outcome. I am glad that we have invited different experts to share about their valuable experience in managing refractory epilepsy patients with peers in Hong Kong. As a Paediatric Neurologist, apart from relying on the antiepileptic drugs, it is time for us to know how to evaluate these refractory epilepsy patients by using various locally available technologically advanced investigations, and how to counsel patients on the different treatment modalities including surgical and dietary treatment. Dr Dawson Fong, an experienced Neurosurgeon will enlighten us on Resective Epilepsy Surgery and how to co-registrate different structural and functional brain imaging into a brain navigation system, as well as how to use functional cortical mapping with either intra-operative Electrocorticography or extra-operative intracranial monitoring to optimise surgical outcome. Dr KY Yam, also an experienced Neurosurgeon will enlighten us on the effectiveness of using Vagus Nerve Stimulator in Epilepsy and potential side effects. Ms Carmen Yeung, a hospital Dietitian will discuss how to use the Modified Atkins Diet in Epilepsy. Dr Venus Tam, a Child Psychiatrist will discuss the Common Psychiatric Co-morbidities in Paediatric Epilepsy and its management. I sincerely hope that you all find these articles interesting and useful in your clinical practice.

Keppra®
levetiracetam

NOW is indicated for infants from 1 month of age* with epilepsy



As adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation

INTEGRATED SAFETY INFORMATION

Contraindications Hypersensitivity to the active substance or other pyrrolidone derivatives or any of the excipients. **Warnings and Precautions** Discontinuation It is recommended to withdraw KEPPRA gradually (e.g. in adults and adolescents weighing ≥50 kg: 500 mg decreases twice daily every 2- 4 weeks; in children and adolescents weighing < 50 kg: dose decrease should not exceed 10 mg/kg twice daily every 2 weeks; in infants (< 6 months): dose decrease should not exceed 7mg/kg twice daily every 2 weeks). Paediatric population The tablet formulation is not adapted for use in infants and children under the age of 6 years and initial treatment in children weighing <25 kg. Available data in children did not suggest impact on growth and puberty. However, long term effects on learning, intelligence, growth, endocrine function, puberty and childbearing potential in children remain unknown. The safety and efficacy of levetiracetam has not been thoroughly assessed in infants with epilepsy aged less than 1 year. Only 35 infants aged less than 1 year with partial onset seizures have been exposed in clinical studies of which only 13 were aged < 6 months. Renal or hepatic impairment The administration of KEPPRA to patients with renal impairment (especially elderly ≥ 65 years) may require dose adjustment. In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection. Depression and/or suicidal ideation Suicide, suicide attempt and suicidal ideation have been reported in patients treated with anti-epileptic agents (including levetiracetam). A meta-analysis of randomized placebo-controlled trials of anti-epileptics medicinal products has shown a small increased risk of suicidal thoughts and behavior. The mechanism of this risk is not known. Therefore patients should be monitored for signs of depression and/or suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should any symptoms of depression and/or suicidal ideation or behavior emerge. **Adverse Reactions** The following adverse events have been reported with a frequency of ≥1/100 to 1/10 (common) and ≥1/10 (very common). Nasopharyngitis, anorexia, depression, hostility/aggression, anxiety, insomnia, nervousness/ irritability, somnolence, headache, amnesia, convulsion, dizziness, tremor, balance disorder, lethargy, veretigo, cough, abdominal pain, diarrhoea, dyspepsia, nausea, vomiting, rash, asthenia/fatigue.

Please refer to the full prescribing information for further information and prior to administration.

ABBREVIATED PRESCRIBING INFORMATION

Name of medicinal product: Keppra® **Qualitative and quantitative composition:** Tablets 250 mg / 500 mg / 100 mg; Oral Solution 100 mg/ml; Concentrate for solution for infusion 100 mg/ml **Indication:** As monotherapy in the treatment of partial onset seizures with or without secondary generalisation in patients from 16 years of age with newly diagnosed epilepsy OR as adjunctive therapy in the treatment of partial onset seizures with or without secondary generalisation in adults, children and infants from 1 month of age with epilepsy (except for concentrate for solution for infusion 100 mg/ml should only be used in adults and children from 4 years of age), myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy, primary generalised tonic-clonic seizures in adults and adolescents from 12 years of age with Idiopathic Generalised Epilepsy. **Dosage and Route of Administration:** Levetiracetam therapy can be initiated with either intravenous or oral administration. Conversion to or from oral to intravenous administration can be done directly without titration. The total daily dose and frequency of administration should be maintained. Film-coated tablets and Oral solution may be taken with or without food and the daily dose is administered in two equally divided doses. Concentrate for solution for infusion is for intravenous use only and the recommended dose must be diluted in at least 100 ml of a compatible diluent and administered intravenously as a 15-minute intravenous infusion. There is no experience with administration of intravenous levetiracetam for longer period than 4 days. Levetiracetam concentrate is an alternative for patients (adults and children from 4 years of age) when oral administration is temporarily not feasible. **Adults** Monotherapy Adults and adolescents from 16 years of age Initial dose 250 mg twice daily, then increase to an initial therapeutic dose of 500 mg twice daily after 2 weeks. May increase by 250 mg twice daily every 2 weeks depending upon the clinical response. Max. dose 1500 mg twice daily. Add-on therapy Adults (≥ 18 years) and adolescents (12 to 17 years) weighing ≥50 kg Initial therapeutic dose 500 mg twice daily (can be started on the first day of treatment). May adjust by 500 mg twice daily every 2 - 4 weeks depending upon the clinical response. Max. dose 1500 mg twice daily. **Children** Monotherapy No data available. Add-on therapy Infants aged from 6 months of age, children and adolescents weighing < 50 kg Initial therapeutic dose 10 mg/kg twice daily. Depending upon the clinical response and tolerability, the dose can be increased up to 30 mg/kg twice daily. Dose changes should not exceed adjustments of 10 mg/kg twice daily every 2 weeks. Dose in children weighing ≥50 kg is the same as in adults. Infants aged from 1 month to less than 6 months Oral solution is the formulation to use in infants. Initial therapeutic dose 7 mg/kg twice daily. Depending upon the clinical response and tolerability, the dose can be increased up to 21 mg/kg twice daily. Dose changes should not exceed adjustments of 7 mg/kg twice daily every 2 weeks. The lowest effective dose should be used. **Contraindications:** Hypersensitivity to the active substance or other pyrrolidone derivatives or any of the excipients. **Warnings and Precautions:** Discontinuation It is recommended to withdraw KEPPRA gradually (e.g. in adults and adolescents weighing ≥50 kg: 500 mg decreases twice daily every 2- 4 weeks; in children and adolescents weighing < 50 kg: dose decrease should not exceed 10 mg/kg twice daily every 2 weeks; in infants (< 6 months): dose decrease should not exceed 7mg/kg twice daily every 2 weeks). Paediatric population The tablet formulation is not adapted for use in infants and children under the age of 6 years and initial treatment in children weighing <25 kg. Available data in children did not suggest impact on growth and puberty. 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There are no adequate data available from the use of levetiracetam in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for human is unknown. As with other antiepileptic medicinal products, physiological changes during pregnancy may affect levetiracetam concentration. Decreased in levetiracetam plasma concentrations has been observed during pregnancy. This decrease is more pronounced during the third trimester (up to 60% of baseline concentration before pregnancy). Appropriate clinical management of pregnant women treated with levetiracetam should be ensured. Discontinuation of antiepileptic treatments may result in exacerbation of the disease which could be harmful to the mother and the foetus. Lactation Levetiracetam is excreted in human breast milk. Therefore, breast-feeding is not recommended. **Ability to perform tasks that require judgement, motor or cognitive skills:** No studies on the effects on the ability to drive and use machines have been performed. Due to possible different individual sensitivity, some patients might experience somnolence or other central nervous system related symptoms, especially at the beginning of treatment or following a dose increase. Therefore, caution is recommended in those patients when performing skilled tasks, e.g. driving vehicles or operating machinery. Patients are advised not to drive or use machines until it is established that their ability to perform such activities is not affected. **Adverse Reactions:** Nasopharyngitis, infection, thrombocytopenia, leukopenia, neutropenia, pancytopenia, anorexia, weight decreased or increased, depression, hostility/aggression, anxiety, insomnia, nervousness/irritability, suicide attempt, suicidal ideation, psychotic disorder, abnormal behavior, hallucination, anger, confusional state, affect lability/mood swings, agitation, completed suicide, personality disorder, thinking abnormal, somnolence, headache, amnesia, convulsion, dizziness, tremor, balance disorder, lethargy, memory impairment, coordination abnormal/ataxia, paresthesia, disturbance in attention, choreoathetosis, dyskinesia, hyperkinesias,diplopia, blurred vision, veretigo, cough, abdominal pain, diarrhoea, dyspepsia, nausea, vomiting, pancreatitis, liver function test abnormal, hepatic failure, hepatitis, rash, alopecia, eczema, pruitus, toxic epidermal necrolysis, Steven-Johnson syndrome, erythema multiforme, injury, muscular weakness, myalgia, asthenia/fatigue. **Overdosage:** Somnolence, agitation, aggression, depressed level of consciousness, respiratory depression and coma were observed with KEPPRA overdoses. After an acute overdose, the stomach may be emptied by gastric lavage or by induction of emesis. There is no specific antidote for levetiracetam. Treatment of an overdose will be symptomatic and may include haemodialysis. The dialyser extraction efficiency is 60% for levetiracetam and 74% for the primary metabolite.

Please read the full prescribing information prior to administration. Full prescribing information is available on request from GlaxoSmithKline Ltd, 23/F, Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong

Abbreviated Prescribing Information based on PI version 03

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*except for concentrate for solution for infusion 100 mg/ml should only be used in adults and children from 4 years of age.

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HKRX/LTM/0006/13(11/2015)

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HELP PATIENTS COPE WITH PERSONAL HYGIENE **AND OTHER BASIC ACTIVITIES OF DAILY LIFE**

EXELON PATCH 10 cm² showed superior efficacy to placebo over 24 weeks

EXELON PATCH 10 cm² significantly improved **Activities of Daily Living (ADLs),** such as the ability to **groom** and **dress**[1]

ITT-LOCF=intention to treat–last observation carried forward.

- EXELON PATCH 10 cm² showed superior efficacy to placebo as measured by improvement in the Alzheimer's Disease Cooperative Study-Activities of Daily Living (ADCS-ADL) scale and global functioning over 24 weeks ($P<.05$)[1]

EXELON® Patch 5
EXELON® Patch 10
EXELON® Patch 15

Important note: Before prescribing, please consult full prescribing information.
Presentation: Exelon Patch 5 contains 9 mg rivastigmine. The release rate is 4.6 mg/24 h.
Exelon Patch 10 contains 18 mg rivastigmine. The release rate is 9.5 mg/24 h.
Exelon Patch 15 contains 27 mg rivastigmine. The release rate is 13.3 mg/24 h.
Indication: Symptomatic treatment of mild to moderately severe Alzheimer's dementia.
Dosage: In patients with mild to moderately severe dementia associated with Alzheimer's disease.: Initiation and re-initiation of therapy should start with one Exelon Patch 5 each day. If well tolerated, it may be increased after a minimum of 4 weeks of treatment to one Exelon Patch 10 each day which is the recommended effective dose. Patients treated by Exelon capsules or oral suspension with a maintenance dose of 3 to 6 mg/day may be switched to Exelon Patch 5. A patient on a stable and well tolerated dose of 9 mg/day Exelon capsules or oral suspension can be switched to Exelon Patch 10. If the oral dose of 9 mg/day has not been stable and well tolerated, a switch to Exelon Patch 5 is recommended. A patient on a dose of 12 mg/day Exelon capsules or oral suspension can be switched to Exelon Patch 10. . A minimum of 6 months of treatment and good tolerability with the previous dose should be observed before titrating up to higher doses.
Method of administration: Transdermal patches should be applied once a day to clean, dry, hairless, intact healthy skin on the upper or lower back, upper arm or chest, in a place which will not be rubbed by tight clothing. It is not recommended to apply the transdermal patch to the thigh or to the abdomen due to decreased bioavailability of rivastigmine observed when the transdermal patch is applied to these areas of the body.
The transdermal patch should not be applied to skin that is red, irritated or cut. Reapplication to the exact same skin location within 14 days should be avoided to minimise the potential risk of skin irritation.
Contraindications: Known hypersensitivity to rivastigmine, other carbamate derivatives, or other ingredients of the formulation. Previous history of application site reactions suggestive of allergic contact dermatitis with rivastigmine transdermal patch.
Precautions/Warnings: Medication misuse and dosing errors with Exelon transdermal patch (e.g. not removing the old patch when putting on a new one and the use of multiple patches at one time) have resulted in serious adverse reactions; some cases have required hospitalization, and rarely led to death. Patients and their caregivers must be instructed on important administration instructions for Exelon transdermal patch. ♦If treatment is interrupted for longer than three days, treatment should be re-initiated with Exelon Patch 5. Gastrointestinal adverse effects have been observed at initiation of therapy and shortly after dose increase. ♦Caution in case of prolonged vomiting or diarrhoea (risk of dehydration). ♦Extrapyramidal symptoms may be exacerbated by cholinomimetics and worsening of parkinsonian symptoms (particularly tremor) has been observed in patients treated with oral rivastigmine. Adverse effects may respond to removing the patch. If they persist, the daily dose should be temporarily reduced to the previous well-tolerated dose. ♦Patient's weight should be monitored during therapy with Exelon Patch. ♦As with other cholinomimetics, caution is recommended in patients with sick sinus syndrome, conduction defects (sino-atrial block, atrio-ventricular block), gastroduodenal ulcerative conditions, history of or current respiratory disease, urinary obstruction, and seizures in predisposed patients. ♦In case of disseminated skin hypersensitivity reactions with the use of rivastigmine, treatment should be discontinued. Use of rivastigmine patch may lead to allergic contact dermatitis, in this case treatment should be discontinued and patients should be switched to oral rivastigmine only after negative allergy testing and under close medical supervision. Some patients sensitized by exposure to rivastigmine patch may not be able to take rivastigmine in any form. ♦Caution in patients with clinically significant hepatic impairment ♦Caution in patients with body weight below 50 kg: carefully titrate and monitor these patients for adverse reactions (e.g. excessive nausea or vomiting) and consider reducing the dose if such adverse reactions develop. . Exelon should not be used during pregnancy unless clearly necessary. Women on Exelon should not breast-feed.
Interactions: Caution in case of concomitant use with cholinomimetic drugs, anticholinergic medications, succinylcholine-type muscle relaxants during anaesthesia.
Adverse reactions: Very common: **nausea.**
Common: vomiting, anorexia, decreased appetite, anxiety, depression, insomnia, dizziness, headache, diarrhoea, dyspepsia, abdominal pain, urinary incontinence, application site reactions (erythema, pruritus, oedema), fatigue, asthenia, weight decrease, urinary tract infection.
Uncommon: dehydration, agitation, delirium, hallucinations, aggression, cerebrovascular accident, syncope, somnolence, psychomotor hyperactivity, cardiac arrhythmia (e.g. bradycardia, supraventricular extrasystole), gastric ulcers, gastrointestinal haemorrhage, hyperhidrosis, contact dermatitis, malaise.
Rare: hypertension, application site hypersensitivity, pruritus, rash, erythema, urticaria, blister, dermatitis allergic, fall.
Very rare: tachycardia, atrioventricular block, atrial fibrillation, pancreatitis, seizure, worsening of Parkinson's disease.
Not known: restlessness, sick sinus syndrome, hepatitis, abnormal liver function tests, disseminated cutaneous hypersensitivity reactions.
Additional adverse reactions observed with Exelon capsules/oral solution: severe vomiting associated with oesophageal rupture (very rare); angina pectoris, myocardial infarction, duodenal ulcers (rare); tremor, confusion (common).
Packs and prices: Country specific.
Legal classification: Country specific.
Ref : EMA June 2013

References: 1. Wimbad B, Cummings J, Andreasen N, et al. A six-month double-blind, randomized, placebo-controlled study of a transdermal patch in Alzheimer's disease—rivastigmine patch versus capsule. Int J Geriatr Psychiatry. 2007;22:456-467.

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Multidisciplinary Refractory Epilepsy Evaluation Programme

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded 1 CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 April 2015.

Magnitude of problems of refractory epilepsy in Hong Kong

According to a local population-based epidemiological survey of epilepsy by telephone interview, the crude prevalences of active epilepsy and seizure disorders in Hong Kong had been estimated to be 3.94/1000 and 8.49/1000 respectively[1]. Another local prospective study conducted by a university hospital found that the period prevalence of epilepsy in Chinese children in 1997 was estimated to be 4.5 per 1000 children aged < 19 years[2]. In another study which was conducted by a regional hospital, the prevalence rate of active epilepsy for children under 15 years of age was 1.52 per 1000[3]. 14% of these epilepsy children were found to be medically intractable, which is defined as uncontrolled seizures with an average frequency of at least 1 seizure per month over a period of 2 years or more, despite treatment with at least 3 different anti-epileptic drugs, singly or in combination[4]. Traditionally, intractability is defined as therapeutic failure of three antiepileptic drugs. However, several prospective case series have shown that a high likelihood of medical intractability can be identified after two unsuccessful trials[5]. Recently, a task force of the International League against Epilepsy proposed that drug-resistant be defined as the failure to achieve seizure freedom after adequate trials of two tolerated, appropriately chosen and administrated antiepileptic drugs (whether as monotherapy or in combination)[6]. The rationale behind this is that after an unsuccessful trial of two antiepileptic drugs, the likelihood of achieving seizure freedom will be very low.

How important is it to be medically refractory? Mortality, Morbidity and Quality of Life

Sudden unexplained death in epilepsy patients (SUDEP) is 40 times more likely among patients who continue to have seizures than in those who are seizure free[7]. Both a case control study and a surgical study suggest that seizure frequency is the most important factor in determining the risk for sudden unexplained death in epilepsy patients[8,9]. Moreover, patients with refractory epilepsy also have a higher chance to have nonfatal seizure related injuries, disability and decreased quality of life including unemployment, social isolation, poor academic achievement, as well as excessive dependency[8,10].

Beware of apparent refractory: Incorrect diagnosis of seizure classification leads to inappropriate drug choice

Failure to recognise an idiopathic generalised epilepsy syndrome could lead to inappropriate use of antiepileptic drugs, for example, use of Carbamazepine in Juvenile Myoclonic Epilepsy could aggravate seizures; by stopping this culprit drug and switching to an appropriate drug could make the seizures easily controllable.

Inadequate drug dosage and drug frequency

Inadequate drug dosage or frequency of antiepileptic drugs could lead to persistent poor seizure control which could be improved after optimising the drug dosage and frequency.

Other Correctable factors

Other correctable factors that need to be considered include: poor drug compliance and any other triggering factors for seizures such as sleep deprivation, alcohol, drug abuse etc.

Paroxysmal Non-epileptic Disorders or Events

A detailed history and description of events by witnesses, as well as analysing the events by videotape recording is mandatory to make a correct diagnosis. In-patient Long term Video EEG recording could also help to distinguish psychogenic non-epileptic disorders and other non-epileptic events such as syncope, movement and sleep disorders from genuine seizure disorder, hence avoiding misdiagnosis and unnecessary treatment.

How to evaluate a patient with refractory epilepsy ? Is he/she a potential candidate for epilepsy surgery?

The ILAE Commission on Classification and Terminology has revised terminology in classification of aetiologies of epilepsy, as "structural/metabolic" , "genetic" or "unknown" causes, and replace previously used terms of "idiopathic", "cryptogenic" and "symptomatic"[11]. The aim is to encourage clinicians to try their best to find out the patients' epilepsy underlying aetiologies and to manage individual epilepsy patient accordingly.

Patient Birth and Developmental History

The patient's detailed background history is important which includes any antenatal and peri-natal insult, any important past history such as, prolonged febrile convulsions, brain injury, CNS infection etc. The developmental history is also essential including any delay in achieving the developmental milestones and any developmental regression which may indicate epileptic encephalopathy.

Seizure Semiology could hint Ictal Onset Zone

A detailed description of the seizure especially, any aura during seizure onset is vitally important, for example, any motor or sensory symptoms, any auditory or visual hallucination, any dysphasia, any unprovoked fear, epigastric aura, Déjà vu etc. The above specific aura could hint seizure onset from specific brain regions, for instance, primary motor, primary sensory, auditory, occipital, lateral temporal language cortex, amygdala, mesial temporal cortex etc.

Interictal EEG recording and Long term Video EEG Monitoring

An interictal EEG recording including sleep is mandatory[12]. Any refractory epilepsy patient is also recommended to have Long Term Video EEG monitoring which combines both an EEG and video recording. By capturing the patient's clinical events to determine whether the recurrent clinical event is epileptic or non-epileptic. By analysing the seizure semiology and EEG pattern, we could classify the seizure and epilepsy syndrome and guide an appropriate treatment. Furthermore, Video EEG is also an important tool in pre-surgical evaluation and help to find out where is the focal seizure onset. Serial studies may be necessary to document consistency or progression, especially in infants and young children[12].

An MRI with a specified epilepsy Protocol

It is essential for each patient with refractory epilepsy to have a detailed Magnetic Resonance Imaging to look for any structural abnormality. If a previous MRI scan showed no abnormality, it is worth-while to repeat an MRI with epilepsy protocol to look for occult lesions. The common recommended protocols should include thin slice T1 weighted gradient recalled echo sequence, T2-weighted and fluid attenuated inversion recovery (FLAIR) sequence[13]. Special MRI sequences may be required in the first 2 years of life because of immature myelination, and serial scans may be necessary to identify abnormalities during early postnatal brain development[12]. Occasionally, a computed tomography (CT) scan is indicated to look for any calcified lesion.

Age appropriate Neuropsychological / Neuropsychiatric Assessment

Paediatric epilepsy surgery candidates both in temporal and extratemporal lobe epilepsy have a high incidence of neurodevelopmental and mental health disorders[14,15]. One study showed a high degree of correlation between intellectual impairment and age of onset of epilepsy; eight-two per cent of children whose epilepsy onset occurred under the age of one year showed intellectual dysfunction[16]. Therefore, age-appropriate neuropsychological/developmental assessments are a mandatory aspect of the pre- and postsurgery evaluation. A neuropsychiatric evaluation is also recommended[12].

Functional Brain Imaging for patients with Difficulty in localisation of seizure onset

The Single Photon Remission Computer Tomography (SPECT) scan measures blood flow in the brain. During a seizure (i.e. Ictal SPECT), blood flow increases in the region of the brain where the seizure begins. In-between seizures (i.e. Interictal SPECT) the blood flow to the brain where the seizure begins will be decreased. Therefore, by measuring the blood flow during SPECT scans, one could determine where the seizure originates and indicates the epileptogenic focus. An Ictal SPECT could be performed with simultaneous Video EEG recording to allow more early detection of electro-clinical seizure onset and hence early radio-isotopes injection. Substraction ictal SPECT co-registration with MRI (SISCOM) improves the sensitivity and the specificity of SPECT in localising the seizure focus for epilepsy surgery. Concordance between SISCOM localisation and the site of surgery is predictive of postsurgical improvement in seizure outcome[17].

FDG-PET could show the distribution of glucose metabolism in different regions of the brain. The region of focal hypometabolism in FDG-PET, if in concordance with seizure semiology, EEG and MRI findings may localise the region of the epileptogenic focus.

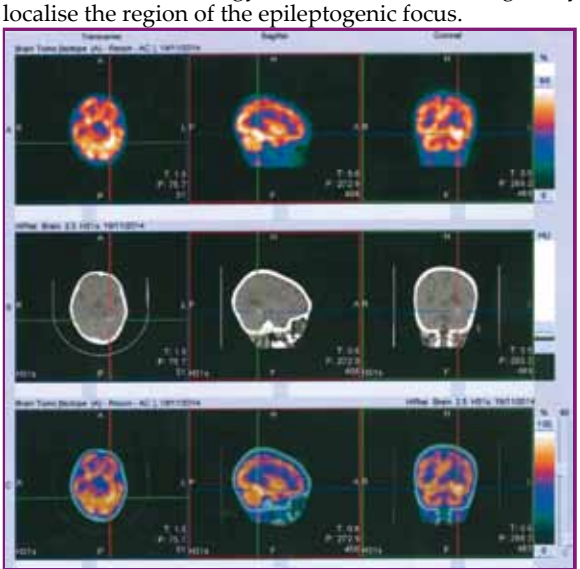

Figure 1. Patient with left inferior temporal calcified cortical dysplasia which showed hyperperfusion during clinical seizure in Ictal SPECT scan

How to find and localise an epileptogenic lesion? Electro-clinico-anatomical-functional correlation

Not all MRI findings are relevant and are epileptogenic. The patient's brain imaging findings should be correlated with the seizure semiology and EEG findings to look for any epileptogenic brain lesion. If the patient's seizure semiology and Video EEG show a focal seizure onset, and indicate localisation related epilepsy, but the structural brain imaging is unrevealing and non-localising, the patient could be referred to have functional neuroimaging such as positron emission tomography (FDG-PET) or single photon emission

computed tomography (Ictal SPECT) which could help to localise any subtle epileptogenic lesion, for example, Type II B Focal Cortical Dysplasia with Balloon Cells.

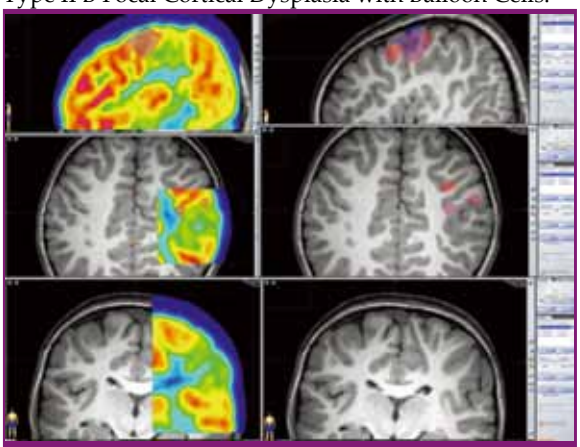

Figure 2. Co-registration of FDG-PET and MRI Brain showed the focal regional hypometabolism over right parietal lobule turn out to be Focal Cortical Dysplasia in histology

According to the Nice Guidelines, the indications for referral to tertiary services for further assessment:

If seizures are not controlled and/or there is diagnostic uncertainty or treatment failure, children, young people and adults should be referred to tertiary services as early as possible for further assessment.

Referrals should be considered when one or more of the following criteria are present:

1. the epilepsy is not controlled with medication within 2 years
2. management is unsuccessful after two drugs
3. the child is aged under 2 years
4. a child, young person or adult experiences, or is at risk of, unacceptable side effects from medication
5. there is a unilateral structural lesion
6. there is psychological and/or psychiatric co-morbidity
7. there is diagnostic doubt as to the nature of the seizures and/or seizure syndrome

- Behavioural or developmental regression or inability to identify the epilepsy syndrome in a child, young person or adult should result in immediate referral to tertiary services.
- Children, young people and adults with specific syndromes such as Sturge–Weber syndrome, the hemispheric syndromes, Rasmussen's encephalitis and hypothalamic hamartoma should be referred to a tertiary epilepsy service.
- Psychiatric co-morbidity and/or negative baseline investigations should not be a contraindication for referrals to a tertiary service.
- The tertiary service should include a multidisciplinary team, experienced in the assessment of children, young people and adults with complex epilepsy, and has adequate access to investigations and treatments by both medical and surgical means.
- The expertise of multidisciplinary teams involved in managing complex epilepsy should include psychology, psychiatry, social work, occupational therapy, counselling, neuroradiology, clinical nurse specialists, neurophysiology, neurology, neurosurgery and neuroanaesthesia. Teams should have MRI and video telemetry facilities available to them.[18]

Functional Plasticity and Early Epilepsy Surgery in Children

The child' brain is unique and is capable of reorganisation of neurologic functions after an insult or surgery. Early surgery is recommended since functional plasticity in a developing brain could enhance the rate of recovery from seizure-related damages and from possible postsurgical neurologic deficits[19,20]. This functional plasticity is particularly important to the recovery of linguistic competence in infants and very young children and has a positive effect to facilitate neurologic reorganisation after epilepsy surgical treatment[20]. In a recent study of memory outcome of temporal lobe epilepsy surgery, there were no significant pre- to postoperative decrements in memory. In contrast, gains in verbal episodic memory were seen after right temporal lobe surgery, and visual episodic memory improved after left temporal lobe surgery, indicating a functional release in the un-operated temporal lobe after seizure reduction or cessation[21]. Studies on a group basis demonstrated that postoperative developmental trajectories would at least be maintained. A gain in development is shown in long term follow-ups[22].

How to choose? Continue trial of Anti-epileptic Drugs vs Surgical Treatment

When compared with continued medical treatment, a randomised control study showed that surgical treatment had a higher chance to let patients with refractory temporal lobe epilepsy become seizure free[23]. Children having undergone temporal lobe resections were more likely to achieve seizure freedom than in those with extratemporal lobe resections. According to the audited result of a local paediatric referral centre, 84% patients were reported to be seizure free after Temporal Lobe Epilepsy Surgery versus 50% patients with Extra-temporal Lobe Epilepsy Surgery[24]. When the patients became seizure free after epilepsy surgery, their antiepileptic drugs would be gradually wean off, but not all would guarantee success. A local study showed that 47% of children after resective temporal lobe epilepsy surgery could be cured with both seizure and medication free[24]. Apart from the cessation or reduction of seizures, one study showed that epilepsy surgery in children would significant improve development, psychosocial function and overall health related quality of life[25].

How to choose? Resective Epilepsy Surgery vs Vagus Nerve Stimulator or Ketogenic Diet

Resective epilepsy surgery should be the first treatment of choice for medically refractory lesional partial epilepsy as this has the highest chance of producing remission. From the experience of one of the local referral hospitals, resective epilepsy surgery of the epileptogenic focus could be curative

by achieving seizure free in 50-84 per cent of selected refractory epilepsy children and adolescents.[24] Further Antiepileptic drug trials, vagus nerve stimulation, and ketogenic diet can reduce seizure frequency and improve quality of life but are more likely to be palliative, rather than the curative treatment option[26].

Ketogenic Diet Programme

The Ketognic Diet is designed to mimic the biochemical effect of starvation. The Nice guidelines recommend to refer children and young people with epilepsy whose seizures have not responded to appropriate antiepileptic drugs to a tertiary paediatric and adult epilepsy specialist for consideration of the use of a ketogenic diet[27]. The ketogenic diet is found to be more effective in patients with symptomatic generalised epilepsy. The ketogenic diet is the treatment of choice for seizures in Glucose transporter type I deficiency[28]. In a local small case series, the Ketogenic diet was found to be effective (>50% seizure reduction) in refractory epilepsy with Ohtahara' syndrome and other Neuro-metabolic Disorders e.g. Mitochondrial Cytopathy Complex I & IV deficiency, Succinic Semi-aldehyde Dehydrogenase Deficiency, but not so effective in patients with underlying cortical dysplasia[29].

Vagus Nerve Stimulator

According to the Nice Guidelines, Vagus nerve stimulation is indicated for use as an adjunctive therapy in reducing the frequency of seizures in children, young people and adults who are refractory to antiepileptic medication but who are not suitable for resective surgery. These include children, young people and adults whose epileptic disorders are dominated by focal seizures (with or without secondary generalisation) or generalised seizures.[30]

In a small local case series, apart from achieving seizure reduction in terms of frequency and duration, one patient had significant reduction in duration of post-ictal drowsiness[23], hence improved the patient's well-being.

Conclusion:

The goal of any multi-disciplinary refractory epilepsy evaluation programme is to improve the patient's quality of life by maximising the patient's seizure freedom and minimising the treatment side effects by optimising medical treatment and offering epilepsy surgery or the ketogenic diet to the suitable patients.

References

1. Fong GCY, Kwan P et al. An epidemiological study of epilepsy in Hong Kong SAR, China Seizure 2008; v.17n.5, p.457-464.
2. Wong V. Study of seizure and epilepsy in Chinese children in Hong Kong: period prevalence and patterns. J Child Neurol 2004; 19-25.
3. Karen L Kwong, WK Chak et al. Epidemiology of childhood epilepsy in a cohort of 309 Chinese children. Pediatric Neurol 2001; 24:276-821.
4. Kwong KL, Sung WY et al. Early predictors of medical intractability in childhood epilepsy. Paediatr Neurol 2003; 29:46-52.
5. Kwan P, Brodie MJ et al. Early identification of refractory epilepsy. N Engl J Med 2000; 342:314.
6. Kwan P, Arzimangoglou A, Berg AT, et al. Definition of drug resistant epilepsy consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. Epilepsia 2010; 51:1069.
7. Tomson T. Mortality in epilepsy. J Neurol 2000; 247:15.
8. Sperling MR, Feldman H et al. Seizure control and mortality in epilepsy Ann Neurol 1999;46-50.
9. Mohanraj R, Norrie J, Stephen LJ et al. Mortality in adults with newly diagnosed and chronic epilepsy: a retrospective comparative study Lancet Neurol 2006;5:481
10. Friedman DE, Gilliam FG. Seizure-related injuries are underreported in pharmacoresistant epilepsy: results from a large multicenter study of consecutively enrolled patients using validated quantitative assessments. Epilepsia 2011;52:2181.
11. Anne T. Berg et al. Revised terminology and concepts for organization of seizures and epilepsies: Report of the ILAE Commission on Classification and Terminology, 2005-2009. Epilepsia 2010; 51:676-685.
12. J. Helen Cross et al, Proposed Criteria for Referral and Evaluation of Children for Epilepsy Surgery: Recommendations of the Subcommission for Paediatric Epilepsy Surgery. Epilepsia. 2006;47(6):952-959.
13. Gaillard WD, Chiron C, Cross JH, Harvey AS et al. Guidelines for imaging infants and children with recent-onset epilepsy. Committee for neuroimaging, subcommittee for paediatric neuroimaging ILAE. Epilepsia 2009; 50:2147-53.
14. Mclellan A, Davies S et al. Psychopathology in children undergoing temporal lobe resection a pre and postoperative assessment. Developmental Medicine and Child Neurology 2005; 47:666-672.
15. Colonnelli MA, D'Argenzio L et al. Psychopathology in children before and after surgery for extratemporal epilepsy' Epilepsia 2010.
16. Cormack F, Cross JH et al. The development of intellectual abilities in pediatric temporal lobe epilepsy. Epilepsia 2007; 48:201-204.
17. TJO'Brian et al. Subtraction ictal SPECT co-registered to MRI improves clinical usefulness of SPECT in localizing the surgical seizure focus. Neurology February 1998 vol. 50 no. 2 445-454.
18. Nice Guidelines (CG137) 2004 1.10 Referral for complex or refractory epilepsy 1.10.2-1.10.7.
19. Cossu M et al. Epilepsy surgery in children: Results and predictors of outcome on seizures. Epilepsia 2008; 49:65-72.
20. Roulet-Perez E etal. Impact of severe epilepsy on development: Recovery potential after successful early epilepsy surgery. Epilepsia 2010; 51:1266-76.
21. Skirrow C, Cross JH et al. Temporal lobe surgery in childhood and neuroanatomical predictors of long-term declarative memory outcome. Brain2014; Nov1-14.
22. Frreitag H, Tuxhon et al. Cognitive function in preschool children after epilepsy surgery: rationale for early intervention. Epilepsia 2005; 46:561-567.
23. Engel et al. Early Surgical Therapy for Drug-Resistant Temporal Lobe Epilepsy A Randomized Trail. JAMA 2012; 307:922-930.
24. ChakWKM, KY Yam, TS Fong et al. Clinical audit of seizure outcome and change of number of anticonvulsants after paediatric epilepsy surgery in a regional referral center in Hong Kong from 2001 to Feb 2014.(poster presentation in AOEC 2014 Singapore)p.345.
25. Spencer S, Huh L. Outcomes of epilepsy surgery in adults and children. Lancet Neurol 2008; 7:525-37.
26. Benbadis SR, Tatum WO, Vale FL When drugs don't work: an algorithmic approach to medically intractable epilepsy. Neurology 2000; 55:1780.
27. Nice guidelines (CG137) 2012: 1.12 Ketogenic diet 1.12.1
28. Kossoff EH et al. Optimal clinical management of children receiving the ketogenic diet: Recommendations of the international ketogenic diet study group. Epilepsia 2009; 50:304-17.
29. Chak WKM, Carmen Yeung et al. The clinical audit of effectiveness of seizure control and side effects of using ketogenic diet in refractory paediatric epilepsy: experience of a regional hospital in Hong Kong from 1999 to March 2014. (poster presentation in AOEC 2014 Singapore)p.263.
30. Nice guidelines (CG137) 2012: 1.13 Vagal Nerve Stimulation 1.13.1-1.13.2

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Multidisciplinary Refractory Epilepsy Evaluation Programme" by Dr Mario WK CHAK and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 April 2015. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. "Management of epilepsy is unsuccessful after two drugs" is one of the indication to refer to tertiary service.
2. Psychiatric co-morbidity and/or negative baseline investigations should be a contraindication for referral to a tertiary service.
3. Behavioural or developmental regression or inability to identify the epilepsy syndrome in a child, young person or adult should result in immediate referral to tertiary services.
4. When compared with continue medical treatment, a randomized control study have showed that surgical treatment has a higher chance to let patient with refractory temporal lobe epilepsy become seizure free.
5. Study showed that, apart from cessation or reduction of seizures, epilepsy surgery in children would significant improve development, psychosocial function and overall health related quality of life.
6. Early surgery is recommended since functional plasticity in a developing brain could enhance the rate of recovery from seizure related damage and from possible postsurgical neurologic deficits.
7. Gains in verbal episodic memory were seen after right temporal lobe surgery, and visual episodic memory improved after left temporal lobe surgery, indicating a functional release in the un-operated temporal lobe after seizure reduction or cessation.
8. Resective epilepsy surgery should be the first treatment of choice for medically refractory lesional partial epilepsy as this has highest chance of producing remission.
9. The ketogenic diet is found to be more effective in patient with symptomatic generalized epilepsy.
10. Vagal nerve stimulation is indicated for use as an adjunctive therapy in reducing the frequency of seizures in children, young people and adults who are refractory to antiepileptic medication but who are not suitable for resective surgery.

ANSWER SHEET FOR APRIL 2015

Please return the completed answer sheet to the Federation Secretariat on or before 30 April 2015 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Multidisciplinary Refractory Epilepsy Evaluation Programme

Dr Mario WK CHAK

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Name (block letters):_____ HKMA No.: _____ CDSHK No.: _____

HKID No.: __ __ - __ __ __ __ X X (X) HKDU No.: _____ HKAM No.: _____

Contact Tel No.:_____ MCHK No.: _____ (for reference only)

Answers to March 2015 Issue

New horizon for the management of chronic hepatitis B

1. C 2. B 3. A 4. C 5. D 6. C 7. A 8. C 9. B 10. D

OBITUARY

We will dearly miss **Dr Chiu On PUN (潘昭安醫生)**, our Past President who passed away peacefully on 15 February 2015.

Dr. Pun served as Council Member of Hong Kong College of Cardiology since 1992, and as President from 2007-2009. His genteel and humble disposition will be deeply missed, and his invaluable contribution to the College and momentous role in the development of Cardiology training in Hong Kong will be dearly remembered.

Council Members and staff of the Hong Kong College of Cardiology are saddened by Dr. Pun's passing. His legacy will never be forgotten. We extend our heartfelt condolences to his wife Mary, and the extended family.

The memorial service will be held on 19 April 2015 (Sunday) at 3p.m. at S421, Old Wing, Hong Kong Convention and Exhibition Centre, Wanchai.

Hong Kong College of Cardiology

Resective Epilepsy Surgery

Dr Dawson FONG

Specialist in Neurosurgery

Dr Dawson FONG

Every seizure causes damage to the brain. In young children, it causes learning difficulty and cognitive decline. The Standard Mortality Ratio (SMR), i.e. the ratio of the number of deaths in a population with epilepsy to that in a reference-matched population, is 2 to 3 times greater than that in the general population.[1,2] This difference is mainly attributed to Sudden Unexpected Deaths (SUDEP) the incidence of which varies between 1/1000 person-years among prevalent cases in the community to about 1/250 in specialist centres.[3]

It is therefore our goal to cut down as much as possible the frequency of attacks. In cases where an epileptic focus could be identified, excision of the focus could provide a chance of cure.

Resective epilepsy surgery aims to remove completely the epileptic focus and yet leaving the patient with NO additional neurological deficits. Potential candidates for epilepsy surgery are usually those with medically refractory epilepsy and they would have to go through a whole battery of investigations in order to confirm if there is a definable focus and if so, how it is related to the eloquent functional cortex.

Underlying Pathology

The pathology of epileptic foci can be broadly classified into two groups – atrophy from various causes or intrinsic lesions within the brain such as low-grade tumours, hamartomas, cortical dysplasia or vascular malformations. Benign intrinsic tumours, had they not caused seizures difficult to control, may well be left alone without surgery. But when they are the seed of epilepsy, they deserve a different approach. Most of these are morphologically normal to the naked eye even under the microscope. Yet modern technologies allow surgeons to define these lesions with high accuracies at surgery and to resect them precisely at their borders and not beyond.

Neurophysiological studies

From the understanding of the semiology of the attacks, epileptologists should have a rough idea of the epilepsy. Electro-encephalography (EEG) with scalp electrodes remains an important investigation to see if the pattern fits the semiology. Interictal EEG might give some hints and yet video EEG is more or less the mainstay presurgical study for these potential surgical candidates. Typical attacks could be traced and followed electrically during the whole attack. Results of these studies would lead clinicians to focus on the area in question and from there neuroimaging would follow on.

Neuroimaging

Fig. 1 Neuronavigation image prior to surgery
Objects – Hypometabolic regions on Interictal PET (blue), Hypermetabolic regions on Ictal SPECT (red), Left foot motor cortex (green),
Fibre tracts from DTI – Corticospinal tract (blue), Spinothalamic tract (orange), Optic tract (green)

With the advent of CT and MR, clinicians can now define many of the intrinsic lesions with clarity that the earlier generation could only imagine.

Although CT is not the best modality to study the brain tissue, its ability to reveal fine calcifications could be very useful to define tumours laden with fine calcifications. Examples include gangliogliomas and dysembryoplastic neuroepithelial tumours (DNETs).

MR brought in another quantum leap in its ability to define the fine structural details of the brain. Not only various tumours are visualised, vessels normal and abnormal alike are seen. Because of the ferromagnetic properties of haemosiderin, repeated minor bleedings from lesions like cavernomas are seen with ease and accuracy. Irregular thickness of the grey matter or a blurry margin with the white matter could be picked up as pathognomonic of cortical dysplasia, a very common cause of intractable epilepsy in children. Diffusion Tensor Imaging (DTI) further helps us visualise the fibre tracts within the white matter, telling us the proximity with the lesion. Indeed MR gave a major boost to the popularity of epilepsy surgery for the past 20 years and by now becomes the very first and standard investigation for any patient presented with any form of epilepsy.

Single-photon emission computed tomography (SPECT) and Positron Emission Tomography (PET) give us insight to the epileptic foci from a different angle. Typically these foci are hypermetabolic during ictus and yet in between attacks, hypometabolic. Ictal SPECT and interictal PET are therefore frequently performed to confirm suspected lesions on MR. (Fig. 1)

Neuronavigation

It is fascinating to see the extent of some epileptic foci so clearly on films or the computer screen and yet at surgery after opening the dura, the brain and the lesion look and feel just the same.

Again computer technologies open doors for us. With neuronavigation we can now match the images we obtain prior to surgery to the facial contour of the patient and thus locate the coordinates around the patient's head. With a wand, we could then locate the region of interests from the images exactly on the exposed brain. With 3D reconstruction from thin cut MR images, we obtain nice sulcal map of the brain (Fig. 2) and from the configuration of the sulci, we could locate small lesions in the depths between functional gyri. Since epilepsy surgery is mostly done on the cerebral cortex, there is hardly any CSF leakage and thus brain shift is not a problem for the images to remain relevant at the time of surgery. Thus once we could identify a lesion on images, its anatomical identification at surgery is straightforward. But can we be certain those are all that need to be removed for the surgery to be successful?

Fig. 2 Sulcal map

Functional Localisation and Intracranial Monitoring

In case the lesion is in close proximity with the motor or sensory cortices, we can map out the central sulcus with Somato-sensory Evoke Potential (SSEP) phase reversal and then with cortical stimulation, define the motor cortex.

With modern drugs such as remifentanil and propofol, experienced anaesthetists are able to render patients well anaesthetised, without any muscle relaxant and most importantly, with electrical activities unhindered.

Unlike scalp EEG in which the electric potential is very much dampened by the thickness of the intervening skull bone and soft tissue, strip electrodes in direct contact with the brain surface pick up much stronger activities. Silastic strips and grid electrodes with platinum disks placed about 1 cm apart are MR safe and could be used during surgery or be implanted subdurally as the first stage of the surgery for chronic monitoring for a few days. (Fig. 3) For hippocampus or deep-seated lesions, electrical activities could be traced with depth electrodes inserted from the cortical surface. (Fig. 4) With a cortical stimulator, functional areas such as sensory or speech cortices could also be mapped out with the patient awake and constantly giving feedbacks to the epileptologist. Areas epileptogenic, non-functional and thus resectable are worked out as the surgical target. Patients will have another MR and the image used for navigation at the second procedure. (Fig. 5)

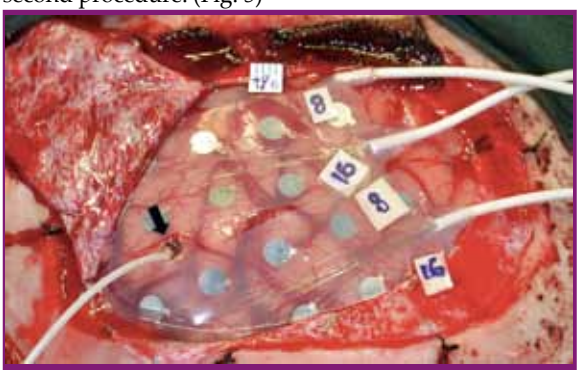

Fig. 3 Subdural and depth electrodes (black arrow) placement for chronic EEG monitoring

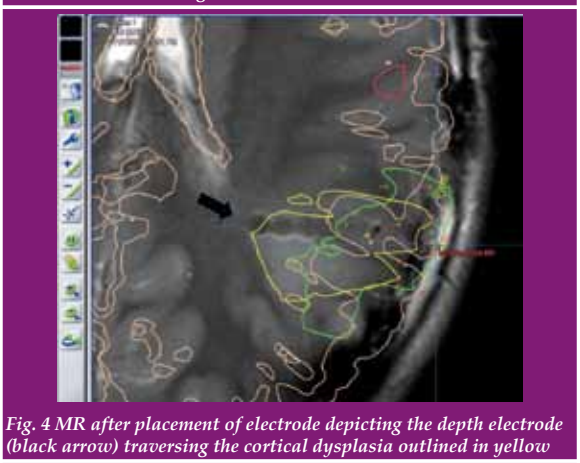

Fig. 4 MR after placement of electrode depicting the depth electrode (black arrow) traversing the cortical dysplasia outlined in yellow

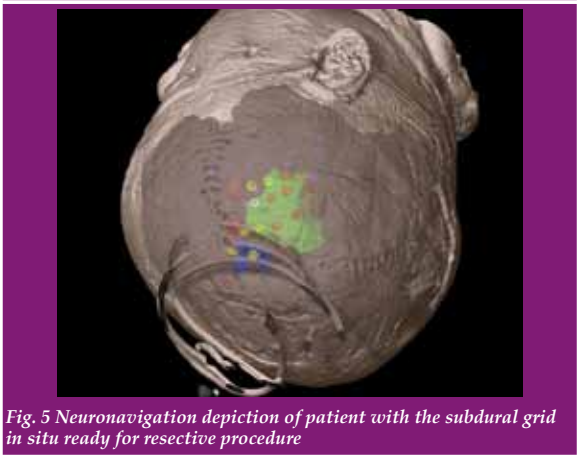

Fig. 5 Neuronavigation depiction of patient with the subdural grid in situ ready for resective procedure

Prior to the actual excision of an epileptic focus, strip electrodes placed within the epileptogenic zone (Fig. 6) could pick up a unique 'signature' of the focus in the form of fast spikes. To see the 'signature' gone at the end of excision gives surgeons a sign of success. (Fig. 7) On the contrary, if the 'signature' persists, surgeons might have to refine the original plan and consider extending the excision.

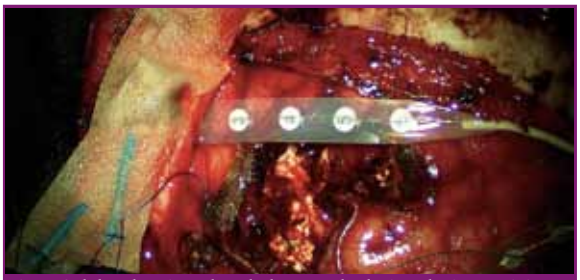

Fig. 6 Subdural strips placed close to the lesion during excision to pick up electrical 'signature' of the focus

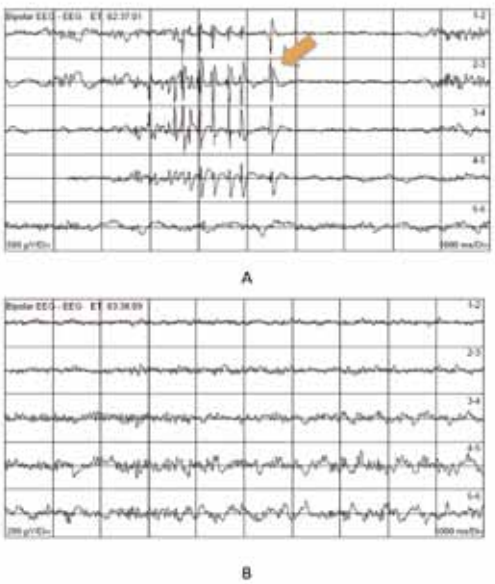

Fig. 7 ECoG bipolar montage showing the 'signature' (yellow arrow). A – prior to excision and B – gone after excision

Outcome

Success of resective epilepsy surgery depends very much on the location of the lesions.

A class 1 RCT of surgery for hippocampal epilepsy found that 64% of those who received surgery were free of disabling seizures compared to only 8% of those on medication alone. The quality of life and social function also significantly improved for those with surgery. Morbidity was infrequent and there was no mortality. For extra-temporal epilepsies, results are less gratifying. Discreteness of the lesions and the proximity to eloquent areas are decisive factors. But still, patients benefit generally - about 45% could achieve Engel's Classification I and 30% totally seizure free, Class I to III together amounting to 75%.[4-6]

Recent audit done by the team at the Tuen Mun Hospital in 2014 showed that 84% of temporal and 50% of extra-temporal lobe epilepsy benefited from resective surgery – quite an encouragement that with appropriate selection, which may be laborious at times, surgery is very rewarding.[7]

Conclusion

This is a group of patients with unsatisfactory medical control and resective surgery can bring forth improvements not only in seizure frequency but also a better quality of life. It is achieved only by a multidisciplinary team approach and a combination of the latest technologies in neuroimaging and neurophysiological monitoring that gives neurosurgeons the highest confidence in achieving a satisfactory epilepsy control without inflicting additional neurological deficit.

References

1. Forsgren L et al. The epidemiology of epilepsy in Europe – a systemic review. Eur J Neurol 2004; 17:141-6
2. Jallon P Mortality in patients with epilepsy Curr Opin Neurol 2004; 17:141-6.
3. Nashef L et al. Risk factors in sudden death in epilepsy (SUDEP). The quest for mechanisms. Epilepsia 2007; 48:859-71.
4. Paolicchi JM et al. Predictors of outcome in paediatric epilepsy surgery. Neurol 2000; 54:642-647.
5. Edwards JC et al. Seizure outcome after surgery for epilepsy due to malformation of cortical development. Neurol 2000; 55:1110-1114.
6. Duchowny M et al. Epilepsy surgery in the first three years of life. Epilepsia 1998; 39:737-743.
7. Chak WKM et al. Clinical audit of seizure outcome and change of number of anticonvulsants after paediatric epilepsy surgery in a regional referral centre in Hong Kong from 2001 to Feb 2014. (poster presentation in AOEC 2014 Singapore) p.345

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Vagus nerve stimulator procedure - effectiveness and side effects

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COS (Neurosurgey)
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Dr Kwong-yui YAM

Introduction

The vagus nerve is part of the autonomic nervous system. The vagus nerve travels inside the carotid sheath between the carotid artery and jugular vein in the cervical region. In the 19th century, doctors noted that applying pressure on the cervical part of the carotid artery and thus on the vagus nerve could stop seizures. Research found that stimulation of the vagus nerve in animals decreases both the frequency and severity of seizures. The results were reproduced in several controlled human trials, which also demonstrated a significant reduction in seizures in terms of frequency, severity and duration of attacks with minimal side effects.[1]

Neuro-anatomy demonstrates that the afferent vagal fibres connect to the nucleus of the solitary tract in the medulla, which in turn projects connections to other brainstem nuclei, including the locus coeruleus and raphe magnus, and therefore modulates norepinephrine, serotonin release and elevates the levels of inhibitory gamma-amino-butyric acid. These neurotransmitters have effects on the reticular, limbic and autonomic centres of the brain. It is postulated that the afferent vagal synapses attenuate seizure activity through neurotransmitter modulation. However, the precise mechanism of action has yet to be elucidated.

Scientists developed the vagus nerve stimulator in 1980s. The machine was in fact a programmable stimulating device like a pacemaker. It consisted of the electrodes, connecting cables and the stimulating device. With the use of a hand held computer device, doctors can adjust the stimulation pattern according to the clinical response of the patients. The first device was implanted in 1988.[2]

Indications for VNS

In 1997, the FDA of USA approved the use of vagus nerve stimulators (VNS) in patients older than 12 with refractory partial epilepsy. Clinical experience also demonstrates efficacy and safety in children. The indications also involve patients with primary generalised epilepsies, Lennox-Gastaut syndrome, Landau-Kleffner syndrome, post-traumatic epilepsy and other seizure disorders that are not suitable for disconnection or resection procedures. VNS becomes an important tool in the treatment of patients with medically refractory epilepsy. This modality is now the most widely used non-pharmacological treatment for drug-resistant epilepsy.

Surgical procedure and its complications

The left vagus nerve is used for stimulation as the right vagus nerve carries more cardiac efferent branches and cardiac side effects are more likely to occur. We perform the implantation of vagus nerve stimulators under general anaesthesia.

After administering prophylactic antibiotics, a 2.5cm transverse skin crease incision is made on the left side of the neck just above the level of the cricoid cartilage from the medial border of the sternocleidomastoid to near the midline. The platysma is opened and the plane medial to the sternocleidomastoid muscle is developed. The carotid sheath is identified and opened, the jugular vein is retracted laterally, and the vagus nerve is usually located in the groove between the jugular vein and carotid artery. The nerve is then exposed for a length of ~ 3–4 cm. Another incision is then made below the clavicle for the pulse generator placement; a pocket is developed above the fascia of the pectoralis muscle. An electrode lead is passed from the neck to the pocket. Electrodes are then placed around the exposed vagus nerve; the lead is attached to the pulse generator. At this point, we have to notify the anaesthestic teams before testing the system as bradycardia, complete atrio-ventricular block or even asystole have been reported. If the device is functioning properly, the pulse generator is placed in the subcutaneous pocket and tacked down with a non-absorbable suture. A protective tension-easing loop of wire is placed in the neck incision and tacked down, usually to the underside of the sternocleidomastoid muscle. The construct is tested again and turned to the off position. The wound is closed in layers.

The surgical procedure is relatively simple and as the surgery does not involve the brain, post-operative complications are relatively trivial. The most common neurological problem following implantation is vocal cord paralysis, occurring in ~ 1% of patients. Patients might have a number of transient symptoms, which include hoarseness, cough, dyspnoea, nausea, and obstructive sleep apnoea. Wound infection is uncommon but may require the removal of the implant and therefore meticulous aseptic technique is mandatory. We usually start stimulating the patients after removal of the stitches seven days post operation. The patients will be followed up regularly and the setting of the stimulation pattern carefully titrated by the epilepsy surgery team led by the neurologist. We can perform brain MRI scans in patients with an implanted VNS.

This is a safe procedure when a modified MRI protocol is followed.[3]

Seizure control

The majority of the studies published on the efficacy of VNS showed that around 35 to 50% of patients have demonstrated a seizure frequency reduction of exceeding 50% of their baseline level. The seizure free rate was only around 2% to 5%. However up to 30% of them showed no worthwhile benefits. The clinical outcomes can be observed in various epileptic disorders but we cannot identify or predict any particular subset of patients having more favourable responses. The clinical response will become more prominent after prolong stimulation. There seems to be a reasonable reduction in the utilisation of health care services and the time spent on epilepsy-related tasks after 6-12 months. Further improvements in seizure reduction can be observed 1 year after VNS.[4,5,6]

Studies have shown that almost half of the patients can reduce their drug therapy by either lowering the dose or taking a less number of drugs. The seizure control or the quality of life was not compromised in this group of patients.[7]

The battery of the stimulator usually lasts for 4 -6 years and battery life depends on the stimulation pattern. Around 70% of implanted patients will have it replaced and for the rest who have no clinical benefits they can either leave the machine behind or have it explanted. The electrodes are usually left behind, as dissection around the scarred vagus nerve may compromise its function.

Conclusion

Vagus nerve stimulation is a well-tolerated procedure and is effective in the management of drug resistant epilepsy. The therapeutic effects show no disparity among adults and paediatric patients. The results seem long lasting and improve gradually with time. Improvement is also observed in other domains and measures such as mood, attentiveness, learning and quality of life. VNS appears to have a positive effect in a subset of patients suffering from intractable epilepsy. Though the procedure can be invasive and the device expensive, VNS may be the only solution that can alleviate the suffering of this unfortunate group of patients.

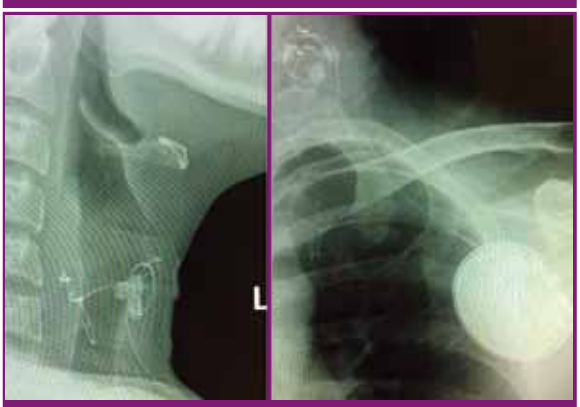
References

1. Ben-Menachem E, Manon-Espaillat R, Ristanovic R, Wilder BJ, Stefan H, Mirza W, et al.
Vagus nerve stimulation for treatment of partial seizures: 1. A controlled study of effect on seizures. First International Vagus Nerve Stimulation Study Group. Epilepsia 35:616–626, 1994
2. Penry JK, Dean JC: Prevention of intractable partial seizures by intermittent vagal stimulation in humans: preliminary results. Epilepsia 31:2 Suppl S40–S43, 1990
3. Rösch J, Hamer HM, Mennecke A, Kasper B. 3T-MRI in patients with pharmacoresistant epilepsy and a vagus nerve stimulator: A pilot study. Epilepsy Res. 2015 Feb; 110:62-70.
4. Orosz I, McCormick D, Zamponi N, Varadkar S, Feucht M, Parain D, Griens R, Vallée L, Boon P, Rittey C, Jayewardene AK, Bunker M, Arzimanoglou A, Lagae L. : Vagus nerve stimulation for drug-resistant epilepsy: a European long-term study up to 24 months in 347 children.
Epilepsia; 55(10): 1576-84. 2014 Oct
5. Wheeler M, De Herdt V, Vonck K, Gilbert K, Manem S, Mackenzie T : Efficacy of vagus nerve stimulation for refractory epilepsy among patient subgroups: a re-analysis using the Engel classification. Seizure. 20(4) : 331-5. 2011 May
6. Spanaki MV, Allen LS, Mueller WM, Morris GL III: Vagus nerve stimulation therapy: 5-year or greater outcome at a university-based epilepsy center. Seizure 13:587–590, 2004
7. Bernstein A, Barkan H, Hess T: Vagus nerve stimulation therapy for pharmacoresistant epilepsy: effect on health care utilization. Epilepsy Behav 10:134–137, 2007

Figure 1. Vagus Nerve Stimulator (VNS) by courtesy of the Cyberonics, Inc.

Figure 2. Surgical incisions for implantation of VNS

Figure 3. Putting the electrodes onto the vagus nerve



Figures 4 & 5. X ray showing the implanted VNS and the tension releasing loops.

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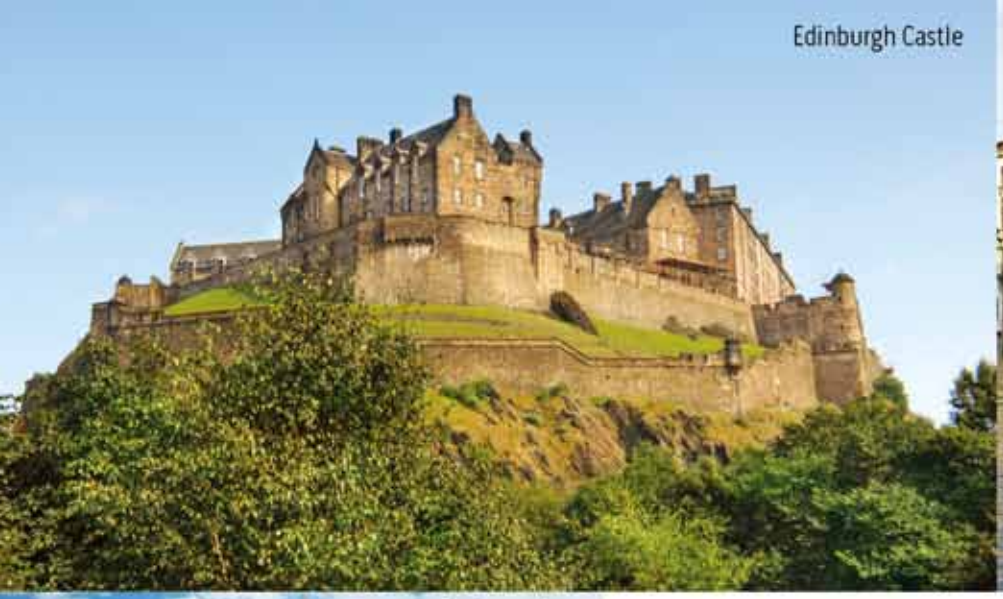

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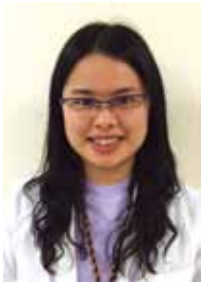
Modified Atkins Diet for refractory epilepsy, does it work as effective as ketogenic diet?



Ms Carmen YEUNG

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The Modified Atkins Diet (MAD) was created at the Johns Hopkins Hospital as an attempt to create a more palatable and less restrictive dietary treatment primarily for children with behavioural difficulties and adolescents that parents and neurologists were reluctant to start on the traditional Classical Ketogenic Diet (KD). MAD was designed to mimic ketosis while providing similar but unlimited quantities of high fat and protein foods.

Diet composition

The composition of the MAD was elaborated upon in a prospective, crossover-design evaluation with detailed 3-days food record provided by parents[1]. The MAD was similar in fat composition to a 0.9:1 ketogenic ratio (fat : carbohydrate and protein), with approximately 65% of the calories from fat sources. This is certainly less fat than a classical 4:1 KD (90% fat) but more than a typical normal diet at a ratio 0.3:1(35% fat) (Figure 1). In children, the carbohydrates are limited initially to 10 grams per day (10 grams carbohydrate means a tablespoon of rice or half a banana or a cup of milk), with planned increases after 1 month to 15 grams, then 20 to 30grams per day after 1 month. All carbohydrates are allowed, in contrast to the low glycaemic index treatment which restricts carbohydrates to those with a glycaemic index less than 50[2]. Carbohydrates can be given throughout the day or at one meal. It allows fibres to be ignored from the total carbohydrate count, but not sugar alcohols. The diet is modified from the Atkins Diet as the induction phase of the diet limiting carbohydrates, and fat is encouraged, however weight loss is not the goal for epilepsy control unless nutritionally indicated.

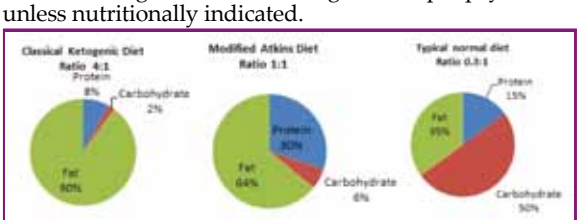

Figure 1: Composition of ketogenic diet, modified Atkins diet and normal diet

How to start MAD

Currently there is no consensus for all countries on how the modified Atkins diet is administered. There are differences in the amount of carbohydrate prescribed per day; how to give adequate fat; whether or not to measure protein. The daily carbohydrate allowance ranges from 10 to 30 grams. It may be reduced to optimise seizure control[3,4].

In practice, as protein is not limited it is unlikely that minimum requirements will not be met. Household measures are used rather than accurate weighing of foods as energy intake is not strictly controlled. The carbohydrate intake of the child's diet is reduced and that fat intake increases gradually over 1-2 weeks until the diet prescription is achieved.

Efficacy of MAD

A study showed, the efficacy of MAD was surprisingly high, with 13 (65%) having at least a >50% seizure reduction at 6 months, half of whom (35%) had >90% seizure reduction using an intent-to-treat analysis. When given the option to continue the diet beyond the 6-months study period, 14 of 16 completing the study chose to remain on the MAD[5]. A similar design study from South Korea of 14 children aged 2-14 years demonstrated slightly less likelihood of a >50% seizure reduction (43%), however, a higher incidence of >90% seizure reduction (36%) [6].

Several children in a prospective study had planned increases in carbohydrate limits as the study progressed without resultant worsening of seizure frequency. To further test a hypothesis that carbohydrate limits were not critical, a randomised, prospective study compared 10 grams versus 20 grams per day of carbohydrates at MAD onsets, with a crossover to the opposite limit after 3 months[7]. The hypothesis was proven correct at the 3- months crossover time point; increasing carbohydrates did not worsen seizure control despite improving tolerability and decreasing carbohydrates did not improve seizure frequency. However, there was a surprisingly higher incidence of >50% seizure reduction at 3 months with an initial carbohydrate limit of 10 grams per day (60% vs. 10%, p = 0.03). This study suggests that a strict carbohydrate limit is important, but only during the first 1-3 months.

There have now been 100 reported children and adults started on the diet in eight publications worldwide. Forty-five (45%) have had 50-90% seizure reduction, and 28 (28%) > 90% seizure reduction, which is remarkably similar to the traditional KD. Further adult and paediatric studies are underway[8].

Side effects

The MAD appears to be tolerable with limited adverse events in studies up to date. An approximately 25-50mg/dl increase in total cholesterol was noted in both the Johns Hopkins paediatric and adult studies[1,3,7], which

was statistically significant and included an increase in LDL cholesterol in the latter two. Triglyceride did not increase in the adult study[1]. The only other significant laboratory abnormally found was blood urea nitrogen (BUN), likely a result of increased protein intake, although serum creatinine does not appear to increase[4]. Weight loss can occur in children and adults who are overweight predominantly and may be desired.

Overall, the long term side effects of the MAD have not been established, unlike the KD[4]. Considering the increased protein and decreased fat, one suspect the risk of growth impairment, kidney stones, dyslipidaemia, and gastro-oesophageal reflux will be reduced in comparison to the KD[8]. Should this be demonstrated in long-term studies, switching children on the KD to the MAD after several years of therapy may be practical.

Discontinuing the MAD

In general, MAD should be slowly tapered off until ketones are lost, similar to the KD. During the step down diet, carbohydrate will be increased by 10 grams per day for every 2 weeks, until the child reaches 60 grams per day (i.e. takes 12 weeks). If seizures worsen, withhold first and to be reassessed by neurologist and dietitian. After 2 weeks of reached 60grams of carbohydrate intake, may start switching daily meals each week, one at a time, for more "regular" meals[9]. For example, for 1 week, give a lunch with rice, fruits, but not high fat or protein. The next week, give both lunch and breakfast this way. The third and final week, the child will be off the diet.

Conclusion

Although MAD is less restrictive than KD, it is still not an easy diet to maintain. Asian countries have different food cultures with higher carbohydrates and less fat composition than those of customary Western diets. MAD may be applied as an effective therapeutic modality for refractory epilepsy.

References

1. Kossoff EH, Rowley H, Shinha SR, Vining EPG. (2008a) A prospective study of the modified Atkins diet for intractable epilepsy in adults. Epilepsia 49: 316-319
2. Pfeifer HH, Thiele EA. (2005) Low glycemic index treatment: a liveralized ketogenic diet for treatment of intractable epilepsy. Neurology 65:1810-1812
3. Kossoff EH, McGrogan JR, Bluml RM, Pillas DJ, Rubenstein JE, Vining EP. (2006) A modified Atkins diet is effective for the treatment of intractable pediatric epilepsy. Epilepsia 47:421-424
4 Kossoff EH, Freeman JM, Turner Z, Rubenstein J. Ketogenic Diets. (2011) Treatment for epilepsy and other disorders. 5th edn. New York: Demos Publishing.
5. Kossoff EH, Krauss GL, McGrogan JR, Freeman JM. (2003) Efficacy of the Atkins diet as therapy for intractable epilepsy. Neurology 61: 1789-1791
6. Kang HC, Lee HS, You SJ, Kang DC, Ko TS, Kim HD. (2007) Use of a modified Atkins diet in intractable childhood epilepsy. Epilepsia 48:182-186.
7. Kossoff EH, Turner Z, Bluml RM, Pyzik PL, Vining EP. (2007) A randomized, crossover comparison of daily carbohydrate limit using the modified Atkins diet. Epilepsy Behav 10:432-436
8. Kossoff EH, Dorward JL (2008) The modified Atkins diet. Epilepsia. 49(Suppl 8) 37–41.
9. Worden LT, Turner Z, Pyzik PL, Rubenstein JE, Kossoff EH (2011) Is there an ideal way to discontinue the ketogenic diet? Epilepsy Research 95,232-236.

Common psychiatric co-morbidities in paediatric epilepsy and their management

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Introduction

Epilepsy is the most common paediatric neurological disorder (0.5 – 1% of all children from birth to 16 years of age). Children with epilepsy were known to have an increased prevalence of mental health disorders.

In the Isle of Wight study in 1970, Rutter et al.[1] reported that 7% of children in the general population exhibited a mental health problem compared with 12% of children with non-neurological physical disorders. Significantly, higher rates were reported in epilepsy: 29% in children with uncomplicated and 58% in those with complicated epilepsy (i.e. structural brain abnormalities and seizures). In another UK epidemiological investigation conducted by Davies et al. in 1998[2], similar findings were reported. Psychiatric disorders were found in 9.3% of the general population aged 5 to 15 years, in 10.6% of those with a chronic medical disorder, and increased rates in epilepsy, including 26% in uncomplicated epilepsy and 56% in complicated epilepsy.

The most common psychiatric co-morbidities in children with epilepsy include attention deficit hyperactivity disorder (ADHD), anxiety and mood disorders and autistic spectrum disorder (ASD). The epidemiology, clinical presentation and management of the above mentioned disorders are to be discussed in this article.

Attention Deficit Hyperactivity Disorder (ADHD)

Compared with the estimated 2-16% of school-aged children in the general population with ADHD[3,4], rates of ADHD in children with epilepsy range from 30 to 40% with predominately inattentive subtype of ADHD, making ADHD the most common behavioural problem that is associated with paediatric epilepsy[5]. Another unique phenomenon in this population is the disappearance of usual gender differences in the prevalence of ADHD. Without epilepsy, ADHD is seen in school-aged children with a male to female ratio of 2-3:1; but the ratio is 1:1 when co-morbid with epilepsy[6]. In most cases, ADHD precedes the first seizure.

Symptoms of inattention and distractibility present challenges to clinicians attempting to differentiate ADHD from seizures. Sub-syndromal problems with attention are perhaps associated with subclinical EEG abnormalities or non-convulsive seizures. Other attention issues that complicate diagnosis may be side-effects of anti-epileptic drugs, pre-ictal auras or post-ictal confusion. Specific seizure types, namely, absence seizures, may be very difficult to be distinguished from state abnormalities of ADHD[7].

The clearest course of diagnosis of ADHD in people with epilepsy is through history-taking. Typical ADHD symptoms occur in multiple settings such as at home or at school and are usually only mitigated by high degrees of structure. Epilepsy may be less predictable, and symptoms may be more prominent in peri-ictal periods. Fidgeting and impulsivity are less common and organisation ability may not be affected.

For ADHD, multiple rating scales, such as Child Behaviour Checklist (CBCL), Conners Parent/ Teacher Rating Scale and ADHD Rating Scale, have been developed to effectively measure the presence and severity of ADHD. They can be used as screening tools in people with epilepsy.

As some anti-epileptic medications may adversely affect attention and concentration[8], it is important to optimise seizure control and minimise poly-pharmacy and drug-drug interactions.

Previously, methylphenidate has been said to lower seizure threshold and many clinicians avoid the use of stimulants. However, recent studies have shown that this concern may be unfounded.

Stimulant medications do not appear to have prominent effects of pathways for gamma-aminobutyric acid (GABA), glutamate and aspartic acid, or at sodium or calcium channels, which have been associated with the pathophysiology of epilepsy. Although no large scale clinical trials have been done, several case series and small trials have been done with methylphenidate (MPH). The largest open-label trial, with 119 children with epilepsy and ADHD, found no increase in seizures with MPH treatment[9]. Another large cohort study showed that cases with epilepsy and ADHD treated with MPH had initial response rate 86%[10]. A small post hoc review of clinical trial data as well as retrospective review showed no increase in seizures in patients treated with atomoxetine.

A qualified consensus among existing studies suggests that when epilepsy is well controlled, i.e. less than one seizure a month, addition of MPH does not lead to an increase in seizures. However, in children with uncontrolled seizures, caution needs to be exercised[11] after balancing the risk/ benefit profile. Behavioural therapy and parent education about ADHD are also very important in the management.

Anxiety and Mood disorders

The prevalence rates of anxiety disorders in paediatric epilepsy range from 5 to 49%[12] and those of depression vary from 23% to 33%[13]. In terms of frequency in adolescence, the anxiety disorder with the highest lifetime prevalence rate is specific phobia (19.9%), with social phobia (8.5%) and separation anxiety (7.6%) coming in at a close second and third[14].

The diagnosis of anxiety and depression is mainly clinical and their manifestations are largely similar in children with epilepsy compared with those without epilepsy. However, symptoms of depression and anxiety may be associated with the temporal relationship of seizures (pre-ictal, ictal, post-ictal or inter-ictal). Moreover, most anti-epileptic drugs can cause symptoms of depression in young people with epilepsy. If an anti-epileptic drug with mood stabilising properties is discontinued, symptoms of a mood disorder which was in remission due to the effects of anti-epileptic drugs can return. The side-effects of anti-epileptic drugs might also include anxiety.

Selective serotonin reuptake inhibitors (SSRIs)[15] should be the first-line drugs in the treatment of depression and anxiety in children with epilepsy due to their favourable side-effect profile, once a day administration, limited risk of drug overdose, and safe drug-drug interactions with anti-epileptic drugs. Tricyclic antidepressants are not recommended for use in children with epilepsy due to potential increased seizure risks. Psychotherapy such as cognitive-behaviour therapy (CBT) is also useful if expertise is available.

Autistic Spectrum Disorder (ASD)

ASD and epilepsy co-occur in approximately 30% of individuals with either ASD or epilepsy. There seems to be a bimodal age distribution of seizures in autism. One peak occurs in infancy before age 5 years and the other in adolescence after age 10 years.

It was found that complex partial and generalised seizures were the most common types of seizures. The researchers also found that in electroencephalogram (EEG) records, generalised seizures and abnormal activity appeared mostly in temporal and parietal areas of the brain. Intellectual disability was a risk factor for epilepsy in those with ASD, where the prevalence of epilepsy was 21.5% in those with intellectual disability, and 8% in those without intellectual disability[16]. Epilepsy in ASD was also associated with poorer verbal abilities[17]. Children with seizure disorders scored significantly lower in personal-social, communication scores, social maturity and adaptive scores than children without seizure disorders[18, 19, 20].

The clinical diagnosis of epilepsy in autism is complicated by the fact that subclinical complex absences may be mistaken for other childhood behaviours such as failing to respond to one's name or to participate in an activity introduced by someone else. The unusual stereotypic behaviours, common in children with autism can be difficult to distinguish clinically from seizures. It is recommended that structured follow-up and routine investigations of ASD in children with epilepsy, and of epilepsy in children with ASD[21].

There is no single treatment or treatment protocol for ASD with epilepsy. Comprehensive treatment should be based on a combination of therapeutic psychosocial interventions in combination with pharmacological agents[22]. Meta-analysis on anti-epileptic medications in ASD did not show differences in efficacy of anti-epileptic medications in ASD[23].

Summary

Psychiatric co-morbidities are common in children with epilepsy, but they are usually under-diagnosed and left untreated. The treating physician should have the awareness of the symptoms and perform screening in these cases. The general principle of treatment is to optimise the control of epilepsy first with the balance of side-effects of anti-epileptic drugs. The choice of medications is similar as those without epilepsy, i.e. first-line treatment of ADHD and mood/anxiety disorders is stimulant medication (such as methylphenidate) and selective serotonin reuptake inhibitors (SSRI) respectively. Psycho-education to patients and the caregivers, as well as other behavioural and cognitive therapies are also important parts of the holistic management.

References

1. Rutter M, Graham P, Yule W. (1970) A Neuropsychiatric Study in Childhood. Clinics in Developmental Medicine Nos. 35/36. London: S.I.M.P/ William Heineman Medical Books.
2. Davies S, Heyman I, Goodman R. (2003) A population survey of mental health problems in children with epilepsy. Dev Med Child Neurol 45: 292-295.
3. Nair J, Ehimare U, Beitman BD, Nair SS. Lavin A. (2006) Clinical review: evidence-based diagnosis treatment of ADHD in children. Mo Med 2006; 103, 6: 617-621.
4. Rader R. McCauley I., Callen E.C. (2009) Current strategies in the diagnosis and treatment of children attention-deficit/ hyperactivity disorder. Am Fam Physician 2009: 79, 8: 657-665.
5. Dunn. D. W., Autstin JK, Harezlak J, Ambrosius WT. (2003) ADHD and epilepsy in childhood. Dev Med Child Neurol 2003; 45, 1: 50-54.
6. Socanski D, Aurlien D, Herigstad A, Thomsen PH, Larsen TK, (2013) Epilepsy in a large cohort of children diagnosed with attention deficit/ hyperactivity disorder (ADHD). Seizure 2013; 22: 651-655.
7. Bourgeois BF. Determining the effects of anti-epileptic drugs on cognitive function in paediatric patients with epilepsy. J Child Neural 2004; 19 (Suppl. 1): S 15-24
8. Torres AR, Whitney J. Gonzalez-Heydrich J. (2008) Attention-deficit hyperactivity disorder in paediatric patients with epilepsy: review of pharmacological treatment. Epilepsy Behav 2008; 12: 217-233.
9. Gucuyener K, Erdemoglu AK, Senol S. Serdaroglu A. Soysal S, Kockar AI. (2003) Use of methylphenidate in attention-deficit hyperactivity disorder in patients with epilepsy or electroencephalograph abnormalities. J Child Neural 2003; 18: 109-112.
10. Dobrinko S, Dag A, Anita H, Per H. T., Tor K.L. (2013) Epilepsy in a large cohort of children diagnosed with attention deficit hyperactivity disorders (ADHD). Seizure 2013; 22: 651-655
11. Kaufmann R, Goldberg-Stern H, Shuper A. (2009) Attention-deficit disorders and epilepsy in childhood: incidence, causative relations and treatment possibilities. J Child Neurol 2009; 24: 727-733.
12. Jana E. J., (2014) Treating anxiety disorders in children and adolescents with epilepsy: what do we know? Epilepsy & Behaviour 2014; 39: 137-142.
13. Seyfhashemi, M., Bahadoran, P., (2013) Depression in children and Adolescents with epilepsy: a 15 year research review of prevalence, and demographic and seizure related correlates. Iran J Pediatric 2013; 23: 1-7
14. Kessler RC, Avenevoli S, McLaughlin KA, Green JG, Lakoma, Petukhova et al., (2012) Lifetime co-morbidity of DSM-IV disorders in the US National Comorbidity Survey Replication Adolescent Supplement (NCS-A) Psychol Med 2012; 42: 1997-2010.

15. Colin R, Robert A, Brian G.R. N., (2011) Depression and anxiety in childhood epilepsy: A review Seizure 2011; 20: 589-597
16. Amiet, C., Gourfinkel-An, I., Bouzamondo, A., Tordjman, S., Baulac, M., Lechat, P., et al. (2008). Epilepsy in autism is associated with intellectual disability and gender: Evidence from a meta-analysis. Biological Psychiatry. 64. 577-582
17. Bolton, P. F., Carcani-Rathwell, I., Hutton, J., Goode, S., Howlin, P., & Rutter. M. (2011) Epilepsy in autism: Features and correlates. British Journal of Psychiatry, 198. 289-294.
18. Matson, J. L., Neal, D., Hess, J. A., Mahan, S., & Fodstad, J.C. (2010) The effect of seizure disorder on symptom presentation in atypically developing children and children with autism spectrum disorders based on the BDI-2. Developmental Neurorehabilitation, 13(5), 310-314.
19. Hara, H. (2007). Autism and epilepsy: A retrospective follow-up study. Brain & Development, 29, 486-490.
20. Matsuo, M., Maeda, T., Sasaki, K., Ishii, K., & Hamasaki, Y. (2010) Frequent association of autism spectrum disorder in patients with childhood onset epilepsy. Brain & Development, 32. 759-763.
21. Robinson, S. J. (2012). Childhood epilepsy and autism spectrum disorders: Psychiatric problems, phenotypic expression and anticonvulsants. Neuropsychology Review, 22, 271-279.
22. Tuchman, R., Alessandri, M., & Cuccaro. M. M. (2010). Autism spectrum disorders and epilepsy: Moving towards a comprehensive approach to treatment. Brain & Development, 32, 719-730.
23. Hirota, T., Veenstra-VanderWeele, J., Hollander, E., & Kishi, T. (2013). Antiepileptic medications in autism spectrum disorder: A systematic review and meta-analysis. Journal of Autism and Developmental Disorders.

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5	6	7	8	★HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2015 – What does a General Surgeon Do Nowadays? ★HKMA Council Meeting 9	10	★HKMA Singing Competition ★Refresher Course for Health Care Providers 2014/2015 – Musculoskeletal assessments and rehabilitation 11
★HKMA Snooker Tournament 2015 12	13	★HKMA Yau Tsim Mong Community Network – Treating Patient Present with Joint Pain ★1)Updated on interstitial lung disease in rheumatic disease 2) Case presentation ★FMSHK Officers' Meeting 14	★HKMA Shatin Doctors Network – Update in Management of Acne Vulgaris ★HKMA Central, Western & Southern Community Network – Management of Erectile Dysfunction in Primary Practice – An Urologist's Perspective ★MPS Workshop – Mastering Difficult Interactions with Patients 15	★Soroanatomy Workshop (Shoulder) 16	17	★KECN & HKCEP & UCH – CME Course for Health Personnel 2015 (Session 1) – Update on Macular Degeneration ★MPS Workshop – Mastering Difficult Interactions with Patients 18
★HKMA Snooker Tournament 2015 19	20	21	22	★HKMA New Territories West Community Network – Management of Ketamine Abusers with Various Medical and Psychiatric Complications ★MPS Workshop – Mastering Shared Decision Making ★FMSHK Executive Committee Meeting 23	★HKMA Yau Tsim Mong Community Network – A Comprehensive Review of Diabetes Mellitus Affecting Erectile Dysfunction 24	★HKMA Community Service Committee – Visit to St. James' Settlement Wan Chai Day Care Centre for the Elderly ★MPS Workshop – Matering Your Risk 25
★Clinical Pharmacology 26	27	★HKMA Kowloon West Community Network – Uterine Fibroid – An Update 28	★HKMA Shatin Doctors Network – Nutrition Intervention for Prevention of Eczema ★HKMA Central, Western & Southern Community Network –Malnutrient Management for Oncology Patients 29	★Integrative Manager of Skin Hyperpigmentation 中西醫皮膚抗病法之色素增多 ★FMSHK Foundation Meeting 30		

Date / Time	Function	Enquiry / Remarks
9 THU 2:00 PM	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2015 – What does a General Surgeon Do Nowadays?** Organisers: The Hong Kong Medical Association & Hong Kong Sanatorium & Hospital; Speaker: Dr. SIU Wing Tai; Venue: Function Room A, HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 1 CME Point
8:00 PM	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association; Chairman: Dr. SHIH Tai Cho, Louis; Venue: HKMA Head Office, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong	Ms. Christine WONG Tel: 2527 8285
11 SAT 1:00 PM	**HKMA Singing Competition** Organiser: The Hong Kong Medical Association; Chairpersons: Dr. PONG Chiu Fai, Jeffrey & Dr. SIN Pui Yee, Helena; Venue: Neway CEO, 2-8 Sugar Street, Causeway Bay	Miss Kayin LEE Tel: 2527 8285
2:15 PM	**Refresher Course for Health Care Providers 2014/2015 – Musculoskeletal assessments and rehabilitation** Organisers: Hong Kong Medical Association & HK College of Family Physicians & HA - Our Lady of Maryknoll Hospital; Speaker: Ms. Jane MAN; Venue: Training Room II, 1/F, OPD Block, Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon	Ms. Clara TSANG Tel: 2354 2440 2 CME Points
12 SUN 2:00 PM	**HKMA Snooker Tournament 2015** Organiser: The Hong Kong Medical Association; Chairman: Dr. CHEUNG Wan Kit, Raymond; Venue: Youth Billiard Club, Houston Centre, 63 Mody Road, Tsim ShaTsui East, Kowloon	Mr. Andie HO Tel: 2527 8285
14 TUE 1:00 PM	**HKMA Yau Tsim Mong Community Network – Treating Patient Present with Joint Pain** Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. HO Hok Ming; Speaker: Dr. SUNG Chi Keung; Venue: Pearl Ballroom, Level 2, Eaton, Hong Kong, 380 Nathan Road, Kowloon	Ms. Candice TONG Tel: 2527 8285 1 CME Point
6:00 PM	**1) Updated on interstitial lung disease in rheumatic disease 2) Case presentation** Organiser: The Hong Kong Society of Rheumatology; Chairman: Dr. MC WAN; Speaker: Dr HO Yan Sze; Venue: Hospital Autority Headquarters, Room 205S	Dr. LEE Ka Lai Tel: 9229 4616 Fax: 2505 1652 1 CME Point
8:00 PM	**FMSHK Officers' Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Gallop, 2/F, Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
15 WED 1:00 PM	**HKMA Shatin Doctors Network – Update in Management of Acne Vulgaris** Organiser: HKMA Shatin Doctors Network; Chairman: Dr. MAK Wing Kin; Speaker: Dr. HO Ka Keung; Venue: Jasmine Room, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Ms. Wendy CHENG Tel: 2824 0333
1:00 PM	**HKMA Central, Western & Southern Community Network – Management of Erectile Dysfunction in Primary Practice – An Urologist's Perspective** Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. YIK Ping Yin; Speaker: Dr. HO Kwan Lun; Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
6:30 PM	**MPS Workshop – Mastering Difficult Interactions with Patients** Organisers: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. CHENG Ngai Shing, Justin; Venue: Jordon Room, 2/F, Eaton Hong Kong, 380 Nathan Road, Kowloon	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
16 THU 1:00 PM	**Soroanatomy Workshop (Shoulder)** Organisers: The Hong Kong Society of Rheumatology and Department of Anatomy, University of Hong Kong; Speakers: Dr. Ingril MOLLER, Dr. LK CHAN and Dr. Carina LI; Venue: University of Hong Kong, Sassoon Road, Pukfulam	Dr. LEE Ka Lai Tel: 9229 4616 Fax: 2505 1652 4 CME Points
18 SAT 1:30 PM	**KECN & HKCEP & UCH – CME Course for Health Personnel 2015 (Session I) – Update on Macular Degeneration** Organisers: HKMA Kowloon East Community Network & HK College of Family Physicians & United Christian Hospital; Chairman: Dr. LEUNG Man Fuk; Speaker: Dr. TANG Hoi Yau, Heather; Venue: Lecture Theatre, G/F, Block P, United Christian Hospital, 130 Hip Wo Street, Kwun Tong, Kowloon	Ms. Polly TAI / Ms. Cordy WONG Tel: 3949 3430 (Polly) / 3949 3087 (Cordy) Fax: 3949 5505 1.5 CME Points
2:30 PM	**MPS Workshop – Mastering Difficult Interactions with Patients** Organiser: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. CHENG Ngai Shing, Justin; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
19 SUN 2:00 PM	**HKMA Snooker Tournament 2015** Organiser: The Hong Kong Medical Association; Chairman: Dr. CHEUNG Wan Kit, Raymond; Venue: Youth Billiard Club, Houston Centre, 63 Mody Road, Tsim ShaTsui East, Kowloon.	Mr. Andie HO Tel: 2527 8285
23 THU 1:00 PM	**HKMA New Territories West Community Network – Management of Ketamine Abusers with Various Medical and Psychiatric Complications** Organiser: HKMA New Territories West Community Network; Chairman: Dr. TSANG Yat Fai; Speaker: Dr. CHAN Hoi Chung, Samuel; Venue: Xin Dau Ji (新斗記), Shop 2190A, 2/F, Tuen Mun Town Plaza, 3 Tuen Lung Street, Tuen Mun	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
6:30 PM	**MPS Workshop – Mastering Shared Decision Making** Organisers: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. FUNG Shu Yan, Anthony; Venue: Jordon Room, 2/F, Eaton Hong Kong, 380 Nathan Road, Kowloon	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points
8:00 PM	**FMSHK Executive Committee Meeting** Organiser: The Federation of Medical Societies of Hong Kong; Venue: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898
24 FRI 1:00 PM	**HKMA Yau Tsim Mong Community Network – A Comprehensive Review of Diabetes Mellitus Affecting Erectile Dysfunction** Organiser: HKMA Yau Tsim Mong Community Network; Chairman: Dr. HO Fung; Speaker: Dr. CHAN Wing Bun; Venue: Pearl Ballroom, Level 2, Eaton, Hong Kong, 380 Nathan Road, Kowloon	Ms. Candice TONG Tel: 2527 8285
25 SAT 2:00 PM	**HKMA Community Service Committee – Visit to St. James' Settlement Wan Chai Day Care Centre for the Elderly** Organiser: The Hong Kong Medical Association; Chairman: Dr. SHIH Tai Cho, Louis; Venue: St. James' Settlement Wan Chai Day Care Centre for the Elderly	Miss Hana YEUNG Tel: 2527 8285
2:30 PM	**MPS Workshop – Matering Your Risk** Organisers: The Hong Kong Medical Association & Medical Protection Society; Speaker: Dr. LEE Wai Hung, Danny; Venue: HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road, Central, Hong Kong	HKMA CME Dept. Tel: 2527 8452 2.5 CME Points

Date / Time	Function	Enquiry / Remarks
26 SUN 2:00 PM	**Clinical Pharmacology** Organiser: Hong Kong College of Paediatricians; Chairpersons: Prof. LAU Yu Lung and Dr NS TSOI; Speakers: Dr. Celeste EWIG, Ms Amanda WM LI and Dr Amelia PW HUI; Venue: M Block, Ground Floor, Lecture Theatre, QEH	Ms. Lily Lin Tel: 2871 8752 2 CME Points
28 TUE 1:00 PM	**HKMA Kowloon West Community Network – Uterine Fibroid – An Update** Organiser: HKMA Kowloon West Community Network; Chairman: Dr. TONG Kai Sing; Speaker: Dr. YAN Choi Man; Venue: Crystal Room I-III, 30/F, Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
29 WED 1:00 PM	**HKMA Shatin Doctors Network – Nutrition Intervention for Prevention of Eczema** Organiser: HKMA Shatin Doctors Network; Chairman: Dr. MAK Wing Kin; Speaker: Dr. CHOW Chung Mo; Venue: Jasmine Room, Level 2, Royal Park Hotel, 8 Pak Hok Ting Street, Shatin	Miss Cathy LAU Tel: 2859 6324
1:00 PM	**HKMA Central, Western & Southern Community Network – Malnutrient Management for Oncology Patients** Organiser: HKMA Central, Western & Southern Community Network; Chairman: Dr. TSANG Chun Au; Speaker: Dr. LUI Siu Fai, MH, JP; Venue: HKMA Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Hana YEUNG Tel: 2527 8285 1 CME Point
30 THU 7:00 PM	**Integrative Manager of Skin Hyperpigmentation** 中西醫皮膚抗病法之色素增多 Organiser: Association for Integrative Aesthetic Medicine, HK; Chairman: Dr. Lee Tin Chak, David; Speakers: Prof. HL CHAN, Henry, Prof/CMP FU Wen Shu and CMP LAU Hon Cheung; Venue: Ching Room, 4/F, Sheraton Hotel, Tsim Sha Tsui	Ms. Suen Tel: 3575 8600 CME Point (Pending)
8:00 PM	**FMSHK Foundation Meeting** Organiser: The Federation of Medical Societies of Hong Kong, Veune: Council Chamber, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Ms. Nancy CHAN Tel: 2527 8898

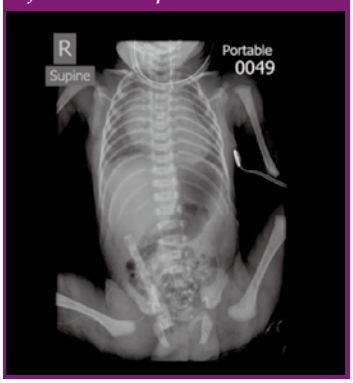
Radiology Quiz

Dr Charlotte KWONG

Department of Radiology, Queen Mary Hospital

Dr Charlotte KWONG

Reference: Radiopaedia



Questions:

1. Please look at the babygram of a newborn infant. What are your findings?
2. What is your diagnosis?
3. What is the classification system for oesophageal atresia?
4. What further investigation would you suggest?

(See P.32 for answers)

"Family Cohesion-Caring for the Younger Generation" Symposium

On 13 December 2014, a symposium on Family Cohesion-Caring for the Younger Generation was held at the Lecture Hall, FMSHK Office. The symposium was well attended by doctors, nurses, social workers and educational professionals. We were glad to have the Department of Health, and the Committee on Home-School Co-operation to be our supporting organisations.

The Federation is honoured to have Dr Constance Hon-yee CHAN, Director of Health to deliver the opening remarks and Ms Carol YIP, Director of Social Welfare as the distinguished guest. We are privileged to invite three speakers, Dr HUNG Se-fong, Clinical Professor (Honorary), Department of Psychiatry of CUHK to deliver a talk on "Emotional Problems of Children and Adolescents; Dr Amos CY CHEUNG, Clinical Psychologist of Kwai Chung Hospital (Psycho-geriatric) to deliver a talk on "Resolving Family Conflict"; Mr James LAM, Principal of Lions College cum Chairman of the Hong Kong Subsidised Schools Council to deliver a talk on "Students have any pressure; how they cope with pressure?". We are glad to have Dr Chun-bong CHOW and Dr Ephraem TSUI to be our moderators. The symposium ended fruitfully with active questioning from participants. The Federation looks forward to organise further educational activities on issues and concerns raised from the community in the near future.

Federation President Cup Soccer Five and Basketball Tournament 2014

The Federation President Cup Soccer Five & Basketball Tournament for 2014 was held at the Ying Wa College on 23 November and 7 December 2014. This year we are making the fourth attempt in organising the basketball matches, which have proved to make our fraternal activity an even bigger success. There are 19 participating teams for the Soccer Five and Basketball Tournament respectively, with a record number of participants.

For Soccer Five, teams include Federation Invitation Team, AstraZeneca, Bayer, Bupa, Baxter Healthcare Ltd., Hong Kong Dental Association, Johnson & Johnson (Hong Kong) Ltd., Merck Pharmaceutical (HK) Ltd., Pfizer Corporation HK Ltd., The Hong Kong Medical Association and The Hong Kong Ophthalmological Society. As for the Basketball Tournament : Baxter Healthcare Ltd., Hong Kong Urological Association, Hong Kong Dental Association, The Hong Kong Medical Association, Hong Kong Medical Supplies Ltd., Johnson & Johnson (Hong Kong) Ltd., Pfizer Corporation HK Ltd., and Sanofi-aventis Hong Kong Ltd.

This year we are honoured to have again the participation of Sun Hei All Stars Football team (晨曦明星足球隊) on the closing day. Our Federation United Team, comprising of members from various teams of the tournament, played a friendly exhibition match with the All Star Sun Hei Football team.

We were delighted to have our honourable guest Mr Man-leung CHOW, President of Sun Hei Sports Club Limited in joining us to present trophies to the winning teams.

We would like to congratulate all the winners in the tournaments and express our sincere gratitude to all the participants and guests for their active participation and support. We look forward to seeing you again at the Federation President Cup Soccer Five & Basketball Tournament in 2015!

The photos are nicely taken and they are already uploaded onto the Federation's website http://www.fmshk.org/fmshk.html?id=498.

The followings were the results of the tournaments:

Soccer Five Tournament

Champion	: AstraZeneca Hong Kong Ltd.
1st Runner Up	: The Federation Invitation Team
2nd Runner Up	: Pfizer Corporation Hong Kong Ltd.
Top Scorers	: Mr NG Tsz Kin - Pfizer Corporation Hong Kong Ltd. Mr LEE Tsun Ho, Anthony - Bayer

Basketball Tournament

Champion	: Pfizer Corporation Hong Kong Ltd.
1st Runner Up	: Hong Kong Urological Association
2nd Runner Up	: Hong Kong Medical Supplies Ltd.
Top Scorer	: Mr YUEN Ka Wai - Pfizer Corporation Hong Kong Ltd.

Exhibition Match

Champion	: Sun Hei All Stars Football Team
1st Runner Up	: Federation United Team

Federation President Cup Soccer Five and Basketball Tournament 2014

Certificate Course for Health Care Professionals | Course No. C265 | CME/CNE Course

Certificate Course on

Best Practices in Quality of Life Assessments

Jointly organised by

The Federation of Medical Societies of Hong Kong

World Association for Chinese Quality of Life

Date	Topics	Speakers
2 Jul	Quality of Life (QoL) Assessment: Principles and Concepts	Dr. Wendy WONG Assistant Professor Hong Kong Institute of Integrative Medicine and School of Chinese Medicine The Chinese University of Hong Kong
9 Jul	QoL Assessment: A Chinese Medicinal Approach	Dr. Zhao LI Chief of Chinese Medicine Service The Hong Kong Tuberculosis Association The University of Hong Kong Clinical Centre for Teaching and Research in Chinese Medicine (Aberdeen)
16 Jul	Psychometric Evaluation in SPSS	Dr. Daniel Yee-tak FONG Associate Professor, School of Nursing The University of Hong Kong / Chairman, World Association for Chinese Quality of Life
23 Jul	Interpreting QoL: Strategies and Challenges	
6 Aug	Best Practice in Selecting a QoL Measure: measurement of the quality of life in cancer patients	Dr. Winnie Kwok-wei SO Associate Professor The Nethersole School of Nursing The Chinese University of Hong Kong
13 Aug	Best Practice of using QoL in health economic evaluation	Dr. Carlos King-ho WONG Research Assistant Professor Department of Family Medicine and Primary Care The University of Hong Kong / Life Member, World Association for Chinese Quality of Life

Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

CME/CNE Course | Certificate Course for Healthcare Professionals | Course No. C266

Certificate Course on

Diagnosis and Management of Allergy

Jointly organised by

The Federation of Medical Societies of Hong Kong

Hong Kong Institute of Allergy

Date	Topics	Speakers
6 Oct	How to set up an allergy clinic and allergy diagnosis	Dr. Tak-hong LEE
13 Oct	Urticaria, angioedema and eczema	Dr. Helen Hei-ling CHAN
20 Oct	Difficult asthma	Dr. Fanny Wai-san KO
27 Oct	Food allergies and anaphylaxis	Prof. Ting-fan LEUNG
3 Nov	Diagnosis and management of drug allergies	Dr. Eric Yuk-tat CHAN
10 Nov	Immunotherapies	Dr. Adrian Young-yuen WU

Enquiry : The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

Answers to Radiology Quiz

1. The tip of the infant feeding tube is noted at the level of T3, above the diaphragm. The stomach bubble is present and the bowel loops are gas-filled. No aspiration is noted. Tip of the R femoral catheter is noted in-situ at L3 level.

2. Oesophageal atresia with distal TEF (tracheo-oesophageal fistula).

3. Oesophageal atresia is closely related to tracheo-oesophageal fistula and can be divided into:

   ype A: isolated oesophageal atresia: 8%
   type B: proximal fistula with distal atresia: 1%
   type C: proximal atresia with distal fistula: 85%
   type D: double fistulae with intervening atresia: 1%
   type E: isolated fistula (H-type): 4%

4. CT thorax for confirming the diagnosis and to delineate the distance between the two ends of the oesophagus for surgical planning.

   US urinary system, ECHO, US spine, and skeletal survey to look for associated anomalies as this condition could be related to VACTERL associations.

Dr Charlotte KWONG
Department of Radiology, Queen Mary Hospital

香港鐳射醫學會
HONG KONG SURGICAL LASER ASSOCIATION

HONG KONG SURGICAL LASER ASSOCAITION / HONG KONG MEDICAL ASSOCIATION CERTIFICATE COURSE ON COSMETIC-RELATED PROCEDURES

Program Directors: Dr. Walter King and Dr. Moniz Wong

Essential lecture:

Date: *19th April, 2015 (Sunday)*
Course Fee: *HK$10,000*
Venue: *Royal Garden Hotel*
69 Mondy Road, Tsimshatsui East, Kowloon, Hong Kong
** Lecture is essential for workshop registration*

Workshop for injectables:

Date: *26th April , 2015 (Sunday)*
Course Fee: *HK$20,000*
Venue: *18F Wellington Place (M88) 2-8 Wellington Street, Central, Hong Kong*

Workshop for Laser, IPL and energy-based devices:

Date: *17th May, 2015 (Sunday)*
Course Fee: *HK$20,000*
Venue: *18F Wellington Place (M88) 2-8 Wellington Street, Central, Hong Kong*

** 20% discount for HKSLA and HKMA members*

This course will cover basic knowledge for practitioners who wish to offer botulinum toxin and filler injections, light and laser therapy, energy-based treatments, chemical peels and cosmeceuticals in their clinics. Hands-on training/ demonstration will be provided in the two workshops.
**CME points pending*

To register for the course, please kindly email HKSLA.HKMA2015@gmail.com and include your name and contact number. Places are filled on a first come first served basis. Please contact Ms. Jacqueline Shum at 2632 2879 for further inquiries.

Supporting Organization:
- Hong Kong Medical Aesthetic Association (HKMAA)

http://www.fmshk.com.hk/hksla/

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KetoCal: quick and easy preparation helps reduce the burden of preparing 3 KD therapy meals a day

KetoCal: makes a real difference to lives on KD therapy

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We look forward to working with you.

Nutrition Information

	Per 100g Powder	Per 100 kcal*	Per 100 ml**
Energy kJ	3011	413	602
kcal	700	100	146
Protein g	18.25	2.1	3.1
Carbohydrate g	3	0.4	0.6
as sugars g	0.59	0.09	0.12
Fat g	73	10	14.6
of which saturates g	58.2	2.2	3.2
monounsaturates (as fatty acids) g	17.4	2.4	3.5
polyunsaturates (as fatty acids) g	10.9	1.5	2.2
total trans fatty acids g	25.3	3.5	5.1
% LCT	100		
Ratio n6: n3 fatty acids	11:1		
% energy from linoleic acid	13.8		
% energy from a linolenic acid	1.3		
Fat: protein + carbohydrate	4:1		
Fibre g	nil added		

* approximately 13.7g powder
** 20g made up to 100ml

Typical Amino Acid Profile	g / 100g Powder
L-Alanine	0.49
L-Arginine	0.62
L-Aspartic Acid	1.05
L-Cystine	0.35
L-Glutamic Acid	2.2
Glycine	0.28
L-Histidine	0.44
L-Isoleucine	0.8
L-Leucine	1.45
L-Lysine	1.2
L-Methionine	0.41
L-Phenylalanine	0.74
L-Proline	1.6
L-Serine	0.78
L-Threonine	0.65
L-Tryptophan	0.4
L-Tyrosine	0.78
L-Valine	0.96
L-Carnitine	0.04
Taurine	0.03

Carbohydrate Profile	g / 100g Carbohydrate	g / 100g Powder
Dextrose	1.7	3.06
Lactose	3.3	0.1
Sucrose	6.3	0.38
Maltose	5.3	0.16
Maltohkose	8	0.24
Raffinose	4.7	0.14
Higher Saccharides	67.7	2.03

Typical Fatty Acid Profile	g / 100g Fatty Acids
C12:0	0.1
C14:0	0.1
C16:0	12.1
C18:0	10.3
C18:1 cis	25.0
C18:1 trans	34.3
C18:2 cis	14.5
C18:2 trans	1.9
C18:3 cis	1.2
C18:3 trans	0.3
C20:0	0.3
C22:0	0.2

Vitamins	Per 100g Powder	Per 100 kcal*	Per 100 ml**
Vitamin A µg RE	380	52.1	76
IU	1269	179	253
Vitamin D µg	5.2	0.71	1
IU	208	28.5	41.6
Vitamin E mg a TE	7.4	1	1.5
IU	11	1.5	2.2
Vitamin C mg	45	6.2	9
Vitamin K µg	30	4.1	6
Thiamin mg	0.7	0.1	0.14
Riboflavin mg	0.75	0.1	0.15
Niacin mg	7.5	1	1.5
Niacin equivalent (mg NE)	14.2	1.9	2.8
Vitamin B6 mg	0.75	0.1	0.15
Folic Acid µg	110	15.1	22
Vitamin B12 µg	0.8	0.11	0.16
Biotin µg	20	2.7	4
Pantothenic Acid mg	3	0.41	0.6
Choline mg	250	34.3	50
Inositol mg	20	2.7	4

Minerals	Per 100g Powder	Per 100 kcal*	Per100 ml**
Sodium mg	300	88.5	100
mmol	21.7	3	4.3
Potassium mg	900	110	180
mmol	20.5	2.8	4.1
Chloride mg	750	103	150
mmol	21.4	3	4.3
Calcium mg	430	58.9	86
Phosphorus mg	430	58.9	86
Magnesium mg	110	15.1	22

Trace Elements	Per 100g Powder	Per 100 kcal*	Per100 ml**
Iron mg	7.4	1	1.5
Copper µg	600	82.2	120
Zinc mg	6	0.82	1.2
Manganese mg	0.66	0.09	0.13
Iodine µg	90	12.3	18
Molybdenum µg	30	4.1	6
Selenium µg	22	3	4.4
Chromium µg	15	2.1	3

References
1. Wirrell E et al Epilepsia 2007;42:760-763.
2. Loring D. Psychiatric Times. 2006;22(10)
3. Henderson C et al. J Child Neurol 2006;21:193-198.
4. Neal E et al. Abstract presented at the 27th International Epilepsy Congress; 9-12 July, 2007, Singapore
5. Rubenstein J et al. Child Neurol 2005;20(1):31-34.
6. Nordli D and De Vivo D. Epilepsia 1997;38:743-749.
7. Kossoff E et al. Epilepsia 2007;XX:1-5.

Further information available upon request. Please call our Hotline: 3460 5498

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