www.fmshk.org

THE HONG KONG MEDICAL DIARY

香 港 醫 訊

VOL.17 NO.9 SEPTEMBER 2012

Paediatric Neuroscience

OFFICIAL PUBLICATION FOR THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG ISSN 1812 - 1691

BOTOX®
Botulinum Toxin Type A
Purified Neurotoxin Complex

Deliver the Difference

Right muscle, Right dose.

20 years experience

Helping hands *around the world*

Turning heads *with a wealth of publications*

BOTOX®: one of the world's most widely researched medicines[1]

BOTOX®: a wealth of experience

- Treating serious and/or debilitating conditions for 20 years worldwide[2*]
- Over 4000 clinical publications[3]
- More licensed indications than any other botulinum toxin[4-6]
  - Strabismus and blepharospasm
  - Hemifacial spasm
  - Cervical dystonia
  - Dynamic equinus foot deformity due to spasticity in juvenile cerebral palsy
  - Wrist and hand disability due to upper limb spasticity associated with stroke
  - Severe axillary hyperhidrosis
  - Upper facial rhytides

References:

1. Allergan, data on file.
2. Mejia N et al. Long-term botulinum toxin efficacy, safety, and immunogenicity. Mov Disord 2005;20(5):592–597.
3. Search strategies are identical across all products. Searches are conducted on STN International® in the following databases: Medline®, Embase®, Embal®, Hcaplus®, Pascal®, Biosis®, Scisearch®. Data are reported separately from either peer-reviewed articles, letters, reports, or from congress abstracts, meeting posters. Results include clinical studies, case reports, reviews, and exclude trade magazines, news, book chapters.
4. BOTOX® Product Insert, Allergan HK, September 2009.
5. Dysport® Product Insert, Ipsen, June 2007.
6. Xeomin® Product Insert, Merz Pharma, January 2008.

ALLERGAN **Allergan Hong Kong Limited**
Suites 705-06, Cityplaza Three, 14 Taikoo Wan Road, Taikoo Shing, Island East, Hong Kong Tel: 852-2610 2525

HK-1041

Contents

Disclaimer

The Cover Shot

Double Helix

To many photographers, this spiral stairs at the exit of the Vatican Museums is no less photogenic than those invaluable masterpieces incarcerated inside. It might not be obvious to everyone though, like the DNA, it is a double spiral, one for ascending and the other for descending traffic and no path is crossed.

The original shot was taken on the already extinct Kodachrome 64 with a handheld Nikon F2 fisheye-Nikkor 16 mm f4 for 1 sec. Shutter speed was deliberately prolonged to add colours and life to the rigidity and stillness of the marbles abound. It is scanned here with Nikon Supercool Scan 9000 for the Medical Diary.

Dr. Dawson FONG
MBBS(HK), FRCS(Edin), FCSHK, FHKAM(Surgery)
Chief of Service and Consultant Neurosurgeon, Department of Neurosurgery, Tuen Mun Hospital, NTW Cluster

Published by
The Federation of Medical Societies of Hong Kong

Design and Production
A-PRO MULTIMEDIA LTD www.apro.com.hk

Editorial

Dr. Mario WK CHAK
MBBS, MRCP(UK), FHKCPaed, FHKAM(Paed)
Specialist in Paediatrics
Associate Consultant, Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital

Editor

Dr. Mario WK CHAK

The Developmental Brain is still full of myths and we lack its full understanding. With tremendous advances in Paediatric Neuroscience and related translational researches, we now have a better understanding of the underlying pathophysiology of various common Paediatric Neuro-developmental disorders and hence more effective treatments. In this volume, we have invited experts from different fields including Child Neurologist, Clinical Psychologist, Chemical Pathologist, Physiotherapist, Child Psychiatrist, Dietitian and Social Worker to share with us the update knowledge in Neuroscience applicable to our clinical practice. The focus would be on common Paediatric Neuro-developmental disorders, such as: Epilepsy, ADHD, Autism, Tourette's syndrome, Developmental Co-ordination Disorder, and Cerebral Palsy.

In order to provide holistic care in children with Neuro-developmental disorders, we need an interdisplinary team collaboration from different medical allied health and other professionals. It requires comprehensive medical and cognitive assessment of each individual and, in selective conditions, laboratory support from chemical pathology and genetic testing, to make an accurate and specific diagnosis. This will then greatly facilitate appropriate treatment and community rehabilitation afterwards.

In this issue of the Medial Diary, you will find nine articles contributed by various experts giving you insights to recent advances in Epilepsy, Cerebral Palsy, Autism, ADHD, DCD, Tourette's syndrome. Dr. WC Lee and I will discuss the evolution of concepts in the Classification of Seizures and Epilepsies. Dr. Lucia TSANG will talk about Neuropsychological assessment in Paediatric Epilepsy. Ms. Carmen YEUNG will discuss the Dietary Management of Intractable Epilepsy by Ketogenic Diet in Paediatric Patients. Ms. Anchor HUNG will discuss Enhancing Epilepsy care in Hong Kong. Dr. Carol SIU, Prof. CW LAM, Dr. Chloe MAK and Dr. Albert CHAN will discuss Genetics in Autism. Dr. Becky CHAN, Dr. Lorinda LAM, Ms. Vanessa LAU and Ms. Jasmine CHEUNG will discuss Diagnostic issues of assessment of ADHD and ASD. Dr. Tony LAI will discuss the Gilles de la Tourette syndrome: Diagnosis and Medical Treatment. Dr. CH KO will discuss Management of Spasticity in Cerebral Palsy: A Child Neurologist's Perspective. Ms. Rachel CHAN will discuss Physiotherapy management of children with Developmental Co-ordination Disorders. I am sure that you will enjoy reading these academic articles and I also thank Dr. Dawson FONG for the fascinating cover photo.

GlaxoSmithKline

In the Modern World Aim for Speed

For a newly diagnosed patient, speed is essential to ease their worries over the next seizure.

Keppra is as effective as carbamazepine at achieving seizure freedom in older patients,[1] but offers significantly better 12-month retention rates[1] with a good tolerability profile.[2]

But most important of all, Keppra gets to work FAST[3] – only 2 weeks to reach a therapeutic dose.[4]

Keppra™ levetiracetam

AIM for speed

KEPPRA abridged prescribing information

INDICATIONS KEPPRA is indicated 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. as adjunctive therapy: 1. in the treatment of partial onset seizures with or without secondary generalisation in adults and children from 4 years of age with epilepsy.2. in the treatment of myoclonic seizures in adults and adolescents from 12 years of age with Juvenile Myoclonic Epilepsy.3. in the treatment of primary generalised tonic-clonic seizures in adults and adolescents from 12 years of age with Idiopathic Generalised Epilepsy. **DOSAGE AND ADMINISTRATION** Monotherapy:- Adults and adolescents > 16 yrs: The recommended starting dose is 250 mg twice daily which should be increased to an initial therapeutic dose of 500 mg twice daily after two weeks. The dose can be further increased by 250 mg twice daily every two weeks depending upon the clinical response. The maximum dose is 1500 mg twice daily. Add on therapy:- Adults (≥ 18 yrs) & adolescents (12-17 yrs) ≥ 50kg: initial therapeutic dose is 500 mg twice daily. This dose can be started on the first day of treatment.Depending upon the clinical response and tolerance, the daily dose can be increased up to 1,500 mg twice daily. Dose changes can be made in 500 mg twice daily increases or decreases every two to four weeks. Elderly ≥ 65 yrs: Adjust dose in patients with compromised renal function. Children 4-11 yrs & adolescents (12-17 yrs) < 50 kg: Initial therapeutic dose 10mg/kg twice daily. The dose can be increased up to 30mg/kg twice daily. Dose changes should not exceed increases or decreases of 10mg/kg twice daily every two weeks. The lowest effective dose should be used. Infants & children < 4 yrs: Not recommended due to insufficient data. Patients with renal impairment: The daily dose must be individualised according to renal function. Patients with hepatic impairment: No dose adjustment is needed in patients with mild to moderate hepatic impairment. In patients with severe hepatic impairment, the creatinine clearance may underestimate the renal insufficiency. Therefore a 50% reduction of the daily maintenance dose is recommended when the creatinine clearance is < 70 ml/min. **CONTRAINDICATIONS** Hypersensitivity to levetiracetam or other pyrrolidone derivatives or any of the excipients. **WARNINGS AND PRECAUTIONS** It is recommended to withdraw it gradually (e.g. in adults: 500 mg decreases twice daily decrements every two to four weeks; in children: dose decrease should not exceed decrements of 10 mg/kg twice daily every two weeks).The administration of KEPPRA to patients with renal impairment may require dose adjustment.In patients with severely impaired hepatic function, assessment of renal function is recommended before dose selection Suicide, suicide attempt and suicidal ideation have been reported in patients treated with levetiracetam. Patients should be advised to immediately report any symptoms of depression and/or suicidal ideation to their prescribing physician. **INTERACTIONS** Data indicate that KEPPRA did not influence the serum concentrations of existing antiepileptic medicinal products (phenytoin, carbamazepine, valproic acid, phenobarbital, lamotrigine, gabapentin and primidone) and that these antiepileptic medicinal products did not influence the pharmacokinetics of KEPPRA. Dosage adjustment is not recommended. The clearance of KEPPRA was 22% higher in children taking enzyme-inducing antiepileptic medicinal products (AEDs) compared to children who did not take enzyme-inducing AEDs. Dosage adjustment is not recommended. KEPPRA had no effect on plasma concentrations of carbamazepine, valproate, topiramate, or lamotrigine. Probenecid (500 mg four times daily), a renal tubular secretion blocking agent, has been shown to inhibit the renal clearance of the primary metabolite but not of levetiracetam. The effect of levetiracetam on probenecid was not studied and the effect of levetiracetam on other actively secreted drugs, e.g. NSAIDs, sulphonamides and methotrexate is unknown. KEPPRA 1,000 mg daily did not influence the pharmacokinetics of oral contraceptives (ethinyl-estradiol and levonorgestrel); endocrine parameters (luteinizing hormone and progesterone) were not modified. KEPPRA 2,000 mg daily did not influence the pharmacokinetics of digoxin and warfarin; prothrombin times were not modified. Co-administration with digoxin, oral contraceptives and warfarin did not influence the pharmacokinetics of levetiracetam. No data on the interaction of KEPPRA with alcohol are available. **PREGNANCY AND LACTATION** There are no adequate data from the use of KEPPRA in pregnant women. Studies in animals have shown reproductive toxicity. The potential risk for human is unknown. KEPPRA should not be used during pregnancy unless clearly necessary. KEPPRA is excreted in human breast milk. Therefore, breast-feeding is not recommended. However, if KEPPRA treatment is needed during breastfeeding, the benefit/ risk of the treatment of the treatment should be weighed considering the importance of breastfeeding. **ADVERSE REACTIONS** Asthenia; somnolence/fatigue; thrombocytopenia, abdominal pain, diarrhoea, dyspepsia, nausea, vomiting; amnesia, ataxia, convulsion, dizziness, headache, hyperkinesia, tremor, balance disorder, disturbance in attention, memory impairment; aggression, agitation, depression, emotional lability/mood swings, hostility, insomnia, irritability, nervousness, personality disorders, thinking abnormal; anorexia, weight increase; The risk of anorexia is higher when topiramate is co administered with levetiracetam; vertigo; diplopia, vision blurred; myalgia; accidental injury; infection, nasopharyngitis; cough increased; eczema, pruritus, rash **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. (Version 03; Version date: 29 September, 2009)

Please refer to the full prescribing information before prescribing. Full prescribing information is available upon request.

For adverse events reporting, please call GlaxoSmithKline Limited at 9046 2498.

References

1. Arif H et al., Arch Neurol. 2010;67(4): 408-414. **2.** Brodie MJ et al. Neurology 2007; 68: 402-408. **3.** Panayiotopoulos CP. Principles of Therapy in Epilepsy; NCBI bookshelf http://www.ncbi.nlm.nih.gov/bookshelf/br.fcgi?book=epi&part=ch4 Accessed 03/09. **4.** Keppra Hong Kong prescribing information 2009.

GlaxoSmithKline Limited 23 / F, Tower 6, The Gateway, 9 Canton Road, Tsimshatsui, Kowloon, Hong Kong.
Tel: (852) 3189 8989 Fax: (852) 3189 8931 www.gsk.com.hk

HKRX/LTM/0001/12(08/2013)

Gilles de la Tourette syndrome: Diagnosis and medical treatment

Dr. Tony TS LAI

M.B.B.S (HK), FHKCPsych, FHKAM (Psychiatry)

Associate Consultant, Department of Child & Adolescent Psychiatry, Castle Peak Hospital

Dr. Tony TS LAI

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 September 2012.

Background

Gilles de la Tourette syndrome was first reported in 1825 by Dr Itard. He described a noblewoman, Marquise de Dampierre who presented with involuntary tics in different parts of her body and vocalisations including echolalia and coprolalia. This case was described again in 1883 by a French neurologist, Georges Albert Edouard Gilles de la Tourette. He described another 9 patients with the syndrome of multiple motor and vocal tics in 1885 and named after this publication.

Diagnostic criteria

Tourette's syndrome is a neuropsychiatric condition characterised by motor and vocal tics[1] that begins in childhood[2] and adolescence and persists over time. The diagnostic criteria as defined in the Diagnostic and Statistical Manual of Mental disorders IV-TR[3] are showed in Table 1.

Table 1. DSM IV TR Diagnostic criteria for Tourette's Disorder

Diagnostic criteria for 307.23 Tourette's Disorder
A. Both multiple motor and one or more vocal tics have been present at some time during the illness, although not necessarily concurrently. (A *tic* is a sudden, rapid, recurrent, nonrhythmic, stereotyped motor movement or vocalisation.)
B. The tics occur many times a day (usually in bouts) nearly every day or intermittently throughout a period of more than 1 year, and during this period there was never a tic-free period of more than 3 consecutive months.
C. The onset is before age 18 years.
D. The disturbance is not due to the direct physiological effects of a substance (e.g. Stimulants) general medical condition (e.g., Huntington's disease or postviral encephalitis).

Tics are commonly described in children. The prevalence rate in school aged children could be up to 20%[4]. The prevalence of Tourette's syndrome causing impairment is 1 to 10 per thousand[5]. The male to female ratio is around four to one[6]. The mean age of onset is from 6 to 8 years of age, peak in severity in the early to mid-teenage years[7]. Patients with Tourette's syndrome may have comorbid with other psychiatric disorders including attention deficit/ hyperactivity disorder, learning problem, obsessive compulsive disorder and sleep problem[8].

Clinical features

Patients with Tourette's syndrome commonly present with eye symptoms in the form of blinking. The common manifestations of tics could either be vocal or motor[1]. It could be in a simple form or a more complex form. Vocal tics usually develop later than motor tics. The common presentation is described in Table 2. Coprolalia could be presented in up to 33% of patients. It is a repetitive, inappropriate, obscene, aggressive or otherwise socially unacceptable words or phrases compulsive use during speech even when the child is not angry or upset. Most occur at the beginning of speech or during a transitional phrase. It is not a true reflection of the patient's thought or feelings. Copropraxia is an action form of coprolalia. It is an inappropriate display of obscene gesturing when the individual is not angry. It could manifest as sexually touching or exposing oneself or touching others. It could be found in about one fifth of Tourette's patients.

Table 2. Common presentations of motor or vocal tics

Simple vocal tics	Simple motor tics
1. Throat clearing	9. Eye blinking
2. Sniffing	10. Sticking tongue out
3. Barking	11. Head turning
4. Coughing	12. Shoulder jerking
5. Yelling	13. Muscle tensing
6. Hiccuping	14. Flexing finger
7. Belching	15. Kicking
8. Animal sounds	16. Facial grimacing
	17. Lip-licking
Complex vocal tics	**Complex motor tics**
1.Unusual change in pitch or volume	1. Flapping arms
2.Coprolilia	2. Picking clothing
3.Echo phenomena	3. Complex touching movement
	4. Smelling
	5. Jumping
	6. Pinching
	7. Shaking feet
	8. Poking
	9. Spitting
	10. Kissing self or others
	11. Copropraxia
	12. Echo phenomena

Tics are commonly exacerbated by psycho-social stress, fatigue, substances such as caffeine, nicotine or stimulants, hormonal changes during menstruation and environmental factors like hot weather. It could be reduced if the patient is calm or undergoing focused activities. Tic symptoms run a fluctuated course. Studies showed one half of patients will improve in adulthood.

Aetiology

The causes of Tourette's syndrome are multi-factorial. Genetic factors may have a role. Twin studies showed

there is a high concordance rate (86% vs. 20%) for chronic tics disorder in monozygotic than dizygotic twins suggesting a genetic contribution in aetiology. However, there is no clear susceptibility genes having been identified.

Biochemical evidence showed that the dopamine system was involved in symptoms development[9,10]. It was related to dopamine excess or supersensitivity of the post-synaptic dopamine receptor. Anti-dopaminergic agents could lead to the reduction of symptoms but stimulants exacerbated the symptom. Magnetic resonance spectroscopy (MRS) showed there was a reduction in N-acetylasparate in the putamen, and frontal cortex. N-acetylasparate is a marker for neuronal integrity. The disinhibition of excitatory thalamic output to the cerebral cortex will lead to hyper excitability of the cortical motor area resulting in tics.

Imaging studies have provided evidence of abnormalities in the basal ganglia. Magnetic Resonance Imaging (MRI) studies showed there is volume reduction in the putamen, caudate nucleus and globus pallidus in Tourette patients[11]. Abnormalities in basal ganglia, thalamus and frontal lobe were described in different studies[12]. Positron emission tomography (PET) study showed there was positive association between metabolism in the basal ganglia and cerebral cortex in patients with Tourette's syndrome. Single-photon emission computed tomography (SPECT) studies showed hypoperfusion in the basal ganglia, thalamus, frontal and temporal cortical area in patients with Tourette's syndrome[19]. Table 3 listed out the primary neurologic and neuropsychiatric disorder manifesting tics.

Table 3. Primary causes of tics

Primary neurologic disorders manifesting tics	Primary neuropsychiatric disorders manifesting tics
Acquired	1. Schizophrenia
1. Head trauma	2. Asperger's syndrome/ autism
2. Encephalitis	3. Mental retardation
3. Stroke	
4. Sydenham's chorea	**Drug reported to induce tics or worsening preexisting tics**
5. Carbon monoxide poisoning	1. Cocaine
6. Creutfeldt-Jacob disease	2. Methylphenidate
7. Neurosyphilis	3. Amphetamines
8. Hypoglycaemia	4. Anticholinergics
9. PANDAS	5. Lithium
	6. Levodopa
Genetic	
1. Huntington's disease	
2. Neuroacanthocytosis	
3. Hallervorden-Spatz disease	
4. Idiopathic dystonia	
5. Duchenne's disease	
6. Chromosomal disorders	
7. Down's syndrome	
8. XYY karyotype	
9. Fragile X syndrome	

Treatment

The treatment of Tourette's syndrome depends on the severity of the symptoms, the impact of symptoms on the patient's social, occupational or educational life, and the presence of comorbidities. The aim of treatment is for symptom control; to improve functioning and to treat co-morbidity. It is important to discuss with the patient and his family on the risks and benefits of using medications. The use of medications should be started in a low dose and titrated in a slow manner – Start Slow, Go Slow. The clinical response and possible adverse effects should be closely monitored. The occurrence of co-morbidities should be managed accordingly[14].

Pharmacological treatments have been the mainstay of treatment for patients with Tourette's syndrome. Dopamine antagonists are the most effective medication for reducing tic severity. First generation antipsychotics mainly act on the dopamine D_2 receptor system with high blocking potency. They are very effective in reducing symptoms related to their dopamine receptor blocking effect on substantia nigra and basal ganglia. However, their D_2 blockade also carries a high rate of extra-pyramidal adverse effects including akathisia, acute dystonia, parkinsonism, and tardive dyskinesia[14]. The commonly used first generation antipsychotics include haloperidol and pimozide. Haloperidol is the first antipsychotics approved by the Food and Drug Administration (FDA) for the treatment of Tourette's syndrome[15]. A randomised, double-blind and placebo-controlled study showed both haloperidol and pimozide significant reduced tics[16]. Another double-blind placebo-controlled crossover study showed significant improvement in symptoms in patients taking pimozide[17]. Pimozide carries a higher risk of cardiac adverse effects and should be used with caution[18].

Second generation antipsychotics are selective D_2 receptor antagonists with fewer extra-pyramidal adverse effects when compared with the first generation[19]. Risperidone acts on both the dopamine and serotonin receptor systems and has a lower risk of having extra-pyramidal adverse effects. Action on the serotonin receptor system may also improve the co-morbid behavioural system[20]. Randomised, double-blind, placebo-controlled studies showed favourable response in symptom control[21]. Another single-blind placebo run-in study showed a reduction in aggression severity in Tourette's patients treated with olanzepine[22]. Patients taking ziprasidone[23] and aripiprazole[24] also showed improvements in tics symptoms.

Other pharmacological agents that can be used in managing Tourette's syndrome include clonidine[25], topiramate[26], and baclofen[27].

Deep brain stimulation also reported to have positive effects in treating Tourette's syndrome in recent years. It should be the last resort for those medically resistant Tourette's patients[28].

Conclusion

The Gilles de la Tourette syndrome is a neuropsychiatric condition with a high rate of comorbidity. It has a high impact on the patient's social, educational and occupational life. It is closely associated with the dopamine system and could be effectively treated by the use of medications particularly the anti-dopaminergic agents. The use of pharmacological treatment should take balance on the risk and benefit and with thorough discussions with the patients and their families before use.

References

1. Mink JW, Basal ganglia dysfunction in Tourette's Syndrome: a new hypothesis. Pediatr Neurol. 2001;25(3):190-198.

2. Leckman JF, Bloch MH, Schill, King RA. Tourette syndrome: the self under siege. J Child Neurol. 2006;21(8):642-649.
3. Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision. Copyright 2000 American Psychiatric Association.
4. Scahill L, Sukhodolsky DG, Williams SK, Leckman JF. Public health significance of tic disorders in children and adolescents. Adv Neurol. 2005;96:240-248.
5. Burd L, Kerbeshian J, Wikenheiser M, Fisher W. A prevalence study of Gilles de la Tourette syndrome in North Dakota schoolage children. J Am Acad Child Psychiatry. 1986;25:552-553.
6. Kenney, C., Kuo, S., & Jimenez-Shahed, J. (2008). Tourette's syndrome. Am Fam Physician, 77, 651-658.
7. Leckman JF, Zhang H, Vitale A, et al. Course of tic severity in Tourette syndrome: the first two decades. Pediatrics. 1998;102:14-19.
8. Khalifa N, von Knorring AL. Psychopathology in a Swedish population of school children with tic disorders. J Am Acad Child Adolesc Psychiatry. 2006;45:1346-1353.
9. Ernst, M., Zametkin, A. J., Jons, P. H., Matochik, J. A., Pascualvaca, D., & Cohen, R. (1999). High presynaptic dopaminergic activity in children with Tourette's disorder. J Am Acad Child Adolesc Psychiatry, 38, 86–94.
10. Singer, H. S., Szymanski, S., Giuliano, J., Yokoi, F., Dogan, A. S., Brasic, J. R., et al. (2002). Elevated intrasynaptic dopamine release in Tourette's syndrome measured by PET. Am J Psychiatry, 159, 1329–1336.
11. Gerard, E., & Peterson, B. (2003). Developmental processes and brain imaging studies in Tourette Syndrome. J Psychosomatic Res, 55, 13-22.
12. Peterson BS, Thomas P, Kane MJ, Scahill L, Zhang H, Bronen R, King RA, Leckman JF, Staib L: Basal Ganglia volumes in patients with Gilles de la Tourette syndrome. Arch Gen Psychiatry 2003, 60(4):415-424.
13. Albin RL, Mink JW: Recent advances in Tourette syndrome research. Trends Neurosci 2006, 29(3):175-182.
14. Scahill L, Erenberg G, Berlin C, et al. Contemporary assessment and Pharmacotherapy of Tourette syndrome (2006). NeuroRx. 2006;3(2):192-206.
15. Parraga HC, Harris KM, Parraga KL, Balen GM, Cruz C. An overview of the treatment of Tourette's disorder and tics. J Child Adolesc Psychopharmacol. 2010;20(4):249–262.
16. Ross MS, Moldofsky H. A comparison of pimozide and haloperidol in the treatment of Gilles de la Tourette's syndrome. Am J Psychiatry. 1978;135(5):585–587.
17. Sallee FR, Nesbitt L, Jackson C, et al. Relative efficacy of haloperidol and pimozide in children and adolescents with Tourette's disorder. Am J Psychiatry. 1997;154(8):1057–1062.
18. Gulisano M, Cali PV, Cavanna AE, Eddy C, Rickards H, Rizzo R. Cardiovascular safety of aripiprazole and pimozide in young patients with Tourette syndrome. Neurol Sci. 2011;32(6):1213–1217.
19. Singer HS. Treatment of tics and tourette syndrome. Curr Treat Options Neurol. 2010;12(6):539–561.
20. Sandor P, Stephens RJ. Risperidone treatment of aggressive behavior in children with Tourette syndrome. J Clin Psychopharmacol. 2000; 20(6):710–712.
21. Dion Y, Annable L, Sandor P, Chouinard G. Risperidone in the treatment of tourette syndrome: a double-blind, placebo-controlled trial. J Clin Psychopharmacol. 2002;22(1):31–39.
22. Stephens RJ, Bassel C, Sandor P. Olanzapine in the treatment of aggression and tics in children with Tourette's syndrome – a pilot study. J Child Adolescent Psychopharmacol. 2004;14(2):255–266.
23. Sallee FR, Kurlan R, Goetz CG, et al. Ziprasidone treatment of children and adolescents with Tourette's syndrome: a pilot study. J Am Acad Child Adolesc Psychiatry. 2000;39(3):292–299.
24. Budman C, Coffey BJ, Shechter R, et al. Aripiprazole in children and adolescents with Tourette disorder with and without explosive outbursts. J Child Adolesc Psychopharmacol. 2008;18(5):509–515.
25. Bloch MH, Panza KE, Landeros-Weisenberger A, Leckman JF: Meta-analysis: treatment of attentiondeficit/hyperactivity disorder in children with comorbid tic disorders. J Am Acad Child Adolesc Psychiatry 2009, 48:884–893.
26. Jankovic J, Jimenez-Shahed J, Brown LW: A randomised, double-blind, placebo-controlled study of topiramate in the treatment of Tourette syndrome. J Neurol Neurosurg Psychiatry 2009, 81:70–73
27. Singer HS, Wendlandt J, Krieger M, Giuliano J: Baclofen treatment in Tourette syndrome: a double-blind, placebo-controlled, crossover trial. Neurology 2001, 56:599–604.
28. Savica R, Stead M, Mack KJ et al. Deep brain stimulation in Tourette syndrome: a description of 3 patients with excellent outcome. Mayo clin Proc 2012;87(1):59-62.

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Gilles de la Tourette Syndrome: Diagnosis and Medical Treatment" by Dr. Tony TS LAI 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 September 2012. 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. Gilles de la Tourette syndrome was first reported in 1925 by Dr Itard.
2. Georges Albert Eouard Gilles de La Tourette described another 9 patients with the syndrome in 1885 and named after this publication.
3. Tourette syndrome should have onset before 18 year of age.
4. According to the DSM IV TR diagnostic criteria, the tics occur throughout a period of more than 1 year, and during this period there should be a tic-free period of more than 4 months.
5. Patient's with Tourette's syndrome commonly presented with copralalia.
6. Tics are commonly exacerbated by coffee drinking.
7. Biochemical evidence showed the serotonin system was involved in symptom development in Tourette's syndrome.
8. Magnetic Resonance Imaging (MRI) studies showed there is volume reduction in the basal ganglia.
9. Dopamine agonist is the most effective medication for the treatment of tics in Tourette's syndrome.
10. Secondary generation antipsychotics showed favourable response in symptoms reduction with fewer extra-pyramidal adverse effects when compared with the first generation antipsychotics.

ANSWER SHEET FOR SEPTEMBER 2012

Please return the completed answer sheet to the Federation Secretariat on or before 30 September 2012 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Gilles de la Tourette Syndrome: Diagnosis and Medical Treatment

Dr. Tony TS LAI

M.B.B.S (HK), FHKCPsych, FHKAM (Psychiatry)

Associate Consultant, Department of Child & Adolescent Psychiatry, Castle Peak Hospital

1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐

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

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

Contact Tel No.:_____

Answers to August 2012 Issue

Update on Pharmacological Management of Generalised Anxiety Disorder

1. F **2.** F **3.** T **4.** T **5.** T **6.** T **7.** T **8.** F **9.** F **10.** F

Classification of Seizures and Epileptic Syndromes: The Evolution of Concepts and Terminologies

Dr. Wing-cheong LEE
MBBS, MRCP(Ireland)
Resident, Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital

Dr. Mario WK CHAK
MBBS, MRCP(UK), FHKCPaed, FHKAM(Paed)
Specialist in Paediatrics
Associate Consultant, Department of Paediatrics and Adolescent Medicine, Tuen Mun Hospital


Dr. Wing-cheong LEE Dr. Mario WK CHAK

Currently the most widely used classification of seizures and epilepsies is that proposed by the International League Against Epilepsy (ILAE), which were published in 1968[2]and 1970[3], revised in 1981[4], 2006[5] and recently updated in 2010. [1]

Two classifications are often used in the diagnosis, management and study of epilepsy. The most elementary is according to the type of the epileptic seizure. The more comprehensive system of descriptive diagnosis categorises the types of epilepsy or epileptic syndromes. [1]

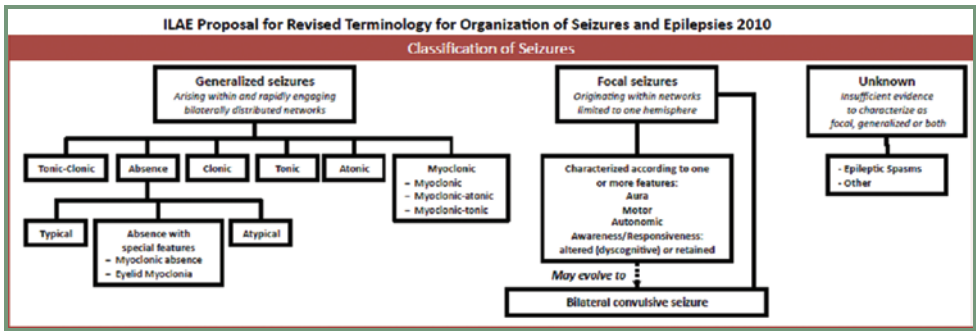
The Prototype:1981 Classification of seizures

Focal /Partial seizures: the seizures arise in localised regions of the cerebral cortex of one hemisphere

Generalised seizures: the seizures arise simultaneously from both cerebral hemispheres

For many years, impairment of consciousness has been considered as an important feature to classify focal seizures. In ILAE Classification of Seizures (1981), non-convulsive focal seizures were classified into Simple Partial Seizures (with no impairment of consciousness); Complex Partial Seizures (with impairment of consciousness) and Secondarily Generalised Seizures with partial onset. [4]

The latest 2010 proposal (Figure 1)[6,7,8,9]



The terms "simple" and "complex" are often misused or misunderstood. Moreover, the distinction based on impairment of consciousness, is impossible to define precisely.[10] The term "secondarily" generalised is poorly understood and inconsistently used. The terminology of simple partial seizure, complex partial seizure, secondarily generalised seizure is no longer recommended. [7]

Focal seizures are defined as seizures originating from networks limited to one hemisphere and are characterised by: 1) Seizure Semiology described according to specific subjective features: Aura, Motor, Autonomic; 2) retained or altered (dyscognitive) awareness/responsiveness. Focal seizures may evolve into a bilateral convulsive seizure. [9]

Generalised seizures are seizures arising from within and rapidly engaging bilateral distributed networks, which are divided into Tonic, Clonic, Tonic-clonic, Atonic, Myoclonic and Absence seizures. Absence seizures are further subdivided into Typical Absence, Atypical Absence and Absence with special features: Myolconic absence and Eyelid Myoclonia. The latter two are now newly recognised. Myoclonic seizures are further subdivided into Myoclonic, Myoclonic-tonic and Myoclonic-atonic. Myoclonic-atonic (previously called "myoclonic astatic") seizures are now recognised. [9]

Unknown seizures include seizures with insufficient evidence to be characterised as focal, generalised seizure, or both, for example, spasm. [9]

Epileptic syndromes

The epilepsies, also known as epileptic syndromes, are characterised by other features in addition to seizure types. An epileptic syndrome can present in several seizure types, while a particular seizure type can be seen in several epileptic syndromes. [1]

ILAE Classification of Epilepsies and Epileptic Syndromes (1989), categorised epilepsies according to 1) Localisation related epilepsies and syndromes: idiopathic/Cryptogenic/ Symptomatic; 2) Generalised epilepsies and syndromes: Idiopathic/ Cryptogenic/ Symptomatic; 3) Epilepsies and syndromes undetermined whether focal or generalised; 4) Special syndromes. [11]

Does aetiology matter ?

Idiopathic Epilepsies: Epilepsy can occur without any evidence of brain damage. It appears that some families or individuals can have a particularly low threshold to suffer from epileptic seizures without any underlying disease. The cause of idiopathic epilepsies is supposed to be genetic. [11]

Idiopathic Epilepsies tend to have good prognosis, with no developmental delay, often responding well to medical treatments, and seizures in some syndromes may disappear with age.

Symptomatic Epilepsies: Any type of brain damage or brain lesion can cause epilepsy and includes: brain tumours, scarring after head injury, metabolic disorders, brain infections etc. Symptomatic epilepsies have bad outcomes in terms of seizure and cognitive development. It is further divided into focal and generalised epilepsies. [12]

Symptomatic Generalised Epilepsies have poor prognosis: seizures tend to continue throughout life, with poor response to treatment, and resective surgery is not indicated since most of the brain might be structurally abnormal. [11]

Symptomatic Focal Epilepsies may or may not respond to medical treatment. If not, they may benefit from respective surgery. [11]

Cryptogenic Epilepsies
For those epilepsy patients who have no evidence of structural brain abnormalities, but have diffusely abnormal EEG background, delayed developmental milestones with normal neuroimaging and no clear history of any brain injury: ILAE recommends the term "Cryptogenic" (meaning "Presumed Symptomatic"). This presumed our present diagnostic methods are not sensitive enough to find a specific cause. [12]

Pitfalls of classification

Dichotomy that hinders appropriate treatment

The ILAE commission decided to discard the terms generalised and focal for modifying the epilepsies themselves. "Generalised" spasms arising from a focal lesion as occur in the West syndrome and focal seizures arising from diffuse genetic disorders occur in the Dravet syndrome were some of the examples of why and how these terms do not adequately reflect the processes underlying the epilepsies. The abundance of the dichotomy of focal versus generalised epilepsies is intended to separate the manifestations from the underlying pathology that produces them. [7]

Focal Epilepsies imply potentially surgical accessability. However not all focal epilepsies are surgically remediable, such as Autosomal Dominant Frontal Lobe Epilepsy; while Generalised Epilepsies imply no potentially surgical cure and thus may result in failure to refer, such as the West syndrome and Lennox Gastaut Syndrome.

"Cause" of epilepsy not specific enough

The old "idiopathic" meaning "presumed genetic", sounds silly in the post-genomic world. Why not use the word "Genetic" directly to replace the word "Idiopathic"? "Symptomatic" itself isn't such a bad word, but aren't all epilepsies always due to some underlying causes? What does the saying that epilepsy is "symptomatic" add? "Cryptogenic" meaning presumed symptomatic, but to what? [13] Why not use the word "Unknown cause" directly and show the need to investigate for underlying causes.

Cause does not equate to prognosis

Causes should not be confused with natural history or outcome. There is an assumption that cause equates to prognosis, for example idiopathic epilepsy must be of benign and good prognosis, which is subsequently found to be not always true. In reality, many types of genetic epilepsy could be lethal. The aligning of the term "idiopathic" with "benign" and "easily treated" is especially problematic in genetic epilepsies such as the Dravet syndrome, epilepsies secondary to SLC2A1 mutations, the gene that codes for the GLUT-1 transporter.[13]

The ILAE Commission has revised concepts, terminology, and approaches for classifying seizures and forms of epilepsy based on some guided principles: 1) not to accept assumptions and ascertains as the basis for classification and to acknowledge areas for which we do not have good information for making decisions. [7] 2) to bring epilepsy out of the shadows of expert opinion and ascertain-dominated arguments so that the classification of the epilepsies fully reflects and profits from all of the other advances being made in basic and clinical neurosciences and so that those advances can be incorporated into clinical practice. 3) to strive for clarify and simplicity so that terms refer to single qualities and are not a mixture of different concepts and dimensions. The new terminology and concepts require the concept of cause contains only one dimension and is not to be used to imply others. Cause is no longer equated with prognosis, and the implication that "idiopathic" confers the quality of "benign" is intentionally discarded.

Say what you mean directly

Instead of the terms idiopathic, symptomatic and cryptogenic, the following three terms and their associated concepts are recommended:

1) **Genetic:** The epilepsy is, as best as understood, the direct result of a known or presumed genetic defect(s) in which seizures are the core symptom of disorder. The knowledge regarding the genetic contributions may be derived from specific molecular genetic studies that have been well replicated and even become the basis of diagnostic tests (e.g., SCNIA and Dravet syndrome) or the evidence for a central role of a genetic component may come from appropriately designed family studies. (e.g. in the case of the genetic generalised epilepsies) [7]
2) **"Structural/Metabolic":** There is a distinct other structural or metabolic condition or disease that has been demonstrated to be associated with a substantially increased risk of developing epilepsy in appropriately designed studies. Structural lesions include acquired disorders such as stroke, trauma, and infection. [7]
3) **"Unknown cause":** Unknown is meant to be viewed neutrally and to designate that the nature of the underlying cause is as yet unknown. Further investigation is needed to identify the cause of the epilepsy. Unlike cryptogenic (presumed symptomatic), it makes no presumptions and requires no explanation or reinterpretation. [7]

Better Terminologies

The argument against the term, "Benign": One of new research Benchmarks of the National Institutes of Health for epilepsy research is to understand the various comorbidities of epilepsy including cognitive, behavioural, psychiatric disorders as well as mortality.[13] Increasingly, basic science and clinical studies are illuminating the shared mechanisms between epilepsy and these various other disorders. [7]

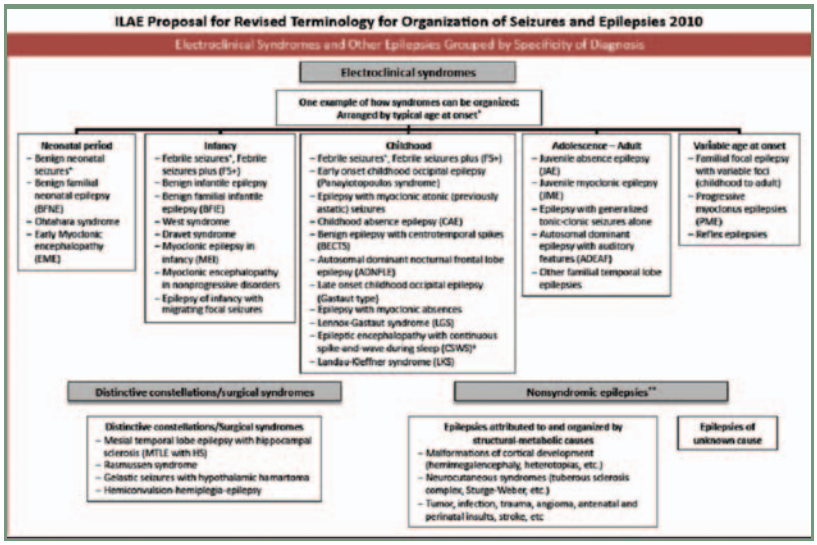
Self-limited:. Instead of designating a group of syndromes as "benign", one should recognise the different qualities that make up the concept of benign and apply them specifically and consistently. One of these features is predictive spontaneous remission. Instead of benign, we recommend the descriptive term "self-limited" to mean having a high likelihood of spontaneously remitting at a predictable age.[7]

Pharmacoresponsive: In syndromes designated as idiopathic, most cases tend to be pharmacoresponsive. Diagnosis of one of these syndromes allows, within a reasonable certainty, the prediction that the seizures will rapidly come under control with appropriate medication. Labeling these syndromes as pharmacoresponsive may be more meaningful to clinicians and provide anticipatory guidance to families better than the term "idiopathic", which requires explanation.[7]

For example, instead of saying idiopathic epilepsy, say what you mean: 1) self limited epilepsy;2) pharmacoresponsive.

Instead of saying symptomatic, say what you mean: for example, 1) pharmacoresistant; 2) surgically remediable and risk of developmental impairment. [9]

Electroclinical Syndromes and other epilepsies grouped by specificity of diagnosis (Figure 2)[9]



Organisation of forms of epilepsy is first by specificity: Electroclinical syndromes, Distinctive constellations and Surgical syndrome; Nonsyndromic epilepsies with structural-metabolic causes, and Epilepsies of unknown cause.[7]

Electroclinical Syndromes is a complex of clinical features, signs and symptoms that together define a distinctive recognisable clinical disorder, identifiable on the basis of a typical age of onset, specific EEG characteristics, seizure types, and often other clinical features, which when taken together, permits a specific diagnosis. The diagnosis is turn often has implications for treatment, management and prognosis. [7]

Electroclinical Syndromes (2010) arranged by age at onset, is classified into 1) Neonatal period; 2)Infancy; 3)Childhood; 4) Adolescence – Adult; 5) Variable Age of Onset.

Constellations: There are a number of entities that are not exactly electroclinical syndromes in the same sense but which represent clinical distinctive constellations on the basis of specific lesions or other causes. These are diagnostically meaningful forms of epilepsy and may have implications for clinical treatment, particularly surgery. Patients with surgically remedial syndromes should be referred for surgical treatment.[7]

Structural/metabolic Epilepsies: The next group includes epilepsies secondary to specific structural or metabolic lesions or conditions but which do notfit a specific electroclinical pattern, although that may change in future. Therefore, these entities represent a lower level of specificity than the two previous groups. [7]

Epilepsies of unknown cause: Those epilepsies, which in the past were term "cryptogenic" will now be referred to as being of "unknown" cause. These epilepsies account for one-third or more of all epilepsies, are most poorly understood, and represent perhaps the most fertile area for future research in imaging and genetics. [7]

Conclusion:

The old classification is commented to be too complicated: classification must be kept simple for physicians. Use of specific terms according to aetiologies, e.g. channelopathy or focal cortical dysplasia instead of idiopathic and symptomatic illustrates the notion to keep it as simple as possible but no simpler. Idiopathic and symptomatic are inadequate simplication. Classifying epilepsies along specific yet arbitrary lines such as categorisation of idiopathic versus symptomatic; dichotomy of focal versus generalised epilepsies; implicating cause equates to prognosis, renders the knowledge may not exist, or be misleading. On the contrary, epilepsy is found to be a very heterogeneous disease while a specific diagnosis should be as specific as possible. Given the extraordinary advances in knowledge and understanding, is it now time to start calling a spade a spade, and a channelopathy a channelopathy?[13] Revised classification has encouraged the new concepts and clearer terminology e.g. self-limited, pharmacoresponsive.

Each syndrome and each patient can be characterised according to a large number of other features, which are often routinely part of any patient's evaluation and which are essential features in distinguishing among established syndromes. These include the age of onset, cognitive and developmental antecedents and consequences, motor and sensory examinations, EEG features, provoking or triggering factors, the patterns of seizure occurrence with respect to sleep.[7]

In the future, the Classification of the Epilepsies will essentially be a database. The features discussed earlier and other essential pieces of information will form the basis for a diagnostic manual.[7] Classification has to be viewed as a work in progress, to be improved as we gain greater understanding of the underlying nature of different types of seizures. There is no perfect classification of seizure and epilepsy, but from time to time, we will have a better classification of seizure and epilepsy. Therefore, any classification put forth by this Commission should be viewed as a guide to summarise our current understanding about seizures and epilepsies in a useful manner, one that is responsive to the needs to which it is put and flexible enough to incorporate new information as it develops.[7]

References

1. S Sharvon, P Emilio, Engel J Jr. The Treatment of Epilepsy. 3rd edition. P3-4.
2. Gastaut H. Clinical and electroencephalographical classification of epileptic seizures. Epilepsia 1969; 10(Suppl.): 2-13.
3. Gastaut H. Clinical and electroencephalographical classification of epileptic seizures. Epilepsia 1970;11:102-113.
4. Anonymous. Proposal for revised clinical and electroencephalographic classification of epileptic seizures. From the Commission on Classification and Terminology of the International League Against Epilepsy. Epilepsia 1981;22:489-510.
5. Engel J Jr. Report of the ILAE classification core group. Epilepsia 2006; 47:1558-1568.
6. Berg AT, Cross JH. Lancet 2010:9;459-61.
7. Berg AT, 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.
8. Blume WT et al. Glossary of descriptive terminology for ictal semiology: Report of the ILAE task force on classification and terminology. Epilepsia 2001:42;1212-1218.
9. Berg AT, Scheffer IE. New concepts in classification of the epilepsies: Entering the 21st century. Epilepsia 2011,52(6):1058-1062.
10. Gloor P. (1986) Consciousness as a neurological concept in epileptology: a critical review. Epilepsia 27(suppl2):S14-S26.
11. Commission on Classification and Terminology of the International League Against Epilepsy: proposal for revised classification of epilepsies and epileptic syndromes. Epilepsia 1989;30;389-399.
12. Gonzalo Alarcon, Nashef L, Cross JH. Oxford Specialist Handbooks in Epilepsy p.72-73.
13. Berg AT et al. Classification and Epilepsy: The Future Awaits. Epilepsy Currents, Vol. 11, No.5 (Sep/Oct) 2011 pp.138-140.
14. Kelly MS, Jacobs MP, Lowenstein DH. (2009) The NINDS epilepsy research benchmarks. Epilepsia 50:579-582.

Pfizer

LIPITOR®

atorvastatin calcium – crystalline form

Power to do more

More Evidence across More Patient Types

Moderate Risk

Hypertension

36% RRR

of nonfatal MI + fatal CHD in patients with hypertension (p=0.0005)[1]

Diabetes

37% RRR

time to first occurrence of major CV events in patients with diabetes (p=0.0005)[2]

High Risk

CHD

59% RRR

of nonfatal MI in patients with CHD (p=0.0001)[3]

CHD

22% additional RRR

of major CV events in patients with CHD (p<0.001)[4]

Highest Risk

ACS

16% RRR

of major CV events in patients with ACS (p=0.005)[5]

References: 1. Sever PS, Dahlöf B, Poulter nR, et al; for the ASCOT investigators. Prevention of coronary and stroke events with atorvastatin in hypertensive patients who have average or lower-than-average cholesterol concentrations, in the Anglo-Scandinavian Cardiac Outcomes Trial-lipid lowering Arm (ASCOT-lla): a multicentre randomised controlled trial. Lancet. 2003;361(9364):1149-1158. **2.** Colhoun hm, Betteridge DJ, Durrington Pn, et al; on behalf of the CARDS investigators. Primary prevention of cardiovascular disease with atorvastatin in type 2 diabetes in the Collaborative Atorvastatin Diabetes Study (CARDS): multicentre randomised placebo-controlled trial. Lancet. 2004;364(9435):685-696. **3.** Athyros VG, Papageorgiou AA, mercouris BR, et al. Treatment with atorvastatin to the national Cholesterol education Program goal versus 'usual' care in secondary coronary heart disease prevention: the GReek Atorvastatin and Coronary-heart-disease evaluation (GReACe) study. Curr Med Res Opin. 2002;18(4):220-228. **4.** laRosa JC, Grundy Sm, waters DD, et al; for the Treating to new Targets (TnT) investigators intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med. 2005;352(14):1425-1435. **5.** Cannon CP, Braunwald e, mcCabe Ch, et al; for the Prevastatin or Atorvastatin evaluation and infection Therapy-Thrombolysis in myocardial infarction 22 investigators intensive versus moderate lipid lowering with statins after acute coronary syndromes. N Engl J Med. 2004;350(15):1495-1504. **Detailed information is available upon request.**

Pfizer

Pfizer Corporation Hong Kong Limited

16/F., Stanhope House, 738 King's Road, North Point, Hong Kong

Tel: (852) 2811 9711 Fax: (852) 2579 0599

Website: www.pfizer.com.hk

LIP100121

Diagnostic Issues in Assessment of Children with ADHD and ASD



Dr. Becky CHAN Dr. Lorinda LAM



Ms. Vanessa LAU Ms. Jasmine CHEUNG

Dr. Becky CHAN
Senior Clinical Psychologist, Child Assessment Service, Department of Health, HKSAR

Dr. Lorinda LAM, Ms. Vanessa LAU, Ms. Jasmine CHEUNG
Clinical Psychologist, Child Assessment Service, Department of Health, HKSAR

Introduction

Attention Deficit Hyperactivity Disorder (ADHD) and Autistic Spectrum Disorder (ASD) are two neuro-developmental disorders commonly seen in paediatric settings. In Child Assessment Service (CAS), over 3000 referrals presenting with behaviour problems are received every year. In 2011, ADHD / problems ranked second and ASD fourth as diagnoses most frequently made by CAS clinical psychologists and paediatricians.[1] Assessment for both disorders includes behavioural observations, interviews with parents, and the administration of rating scales for parents and testing with children. All these are indeed the "bread and butter" work in child assessment settings. Nevertheless, despite our accumulated years of work experience with these children and families, diagnosing a child with behavioural disorders is not always easy and straightforward. This is especially the case when the behavioural symptoms are subtle and not easily detected by direct observation in the clinic, or when the parent's report is inconsistent with the presenting symptoms. The following is a brief review of the issues faced in making diagnosis of both disorders. It is hoped that by highlighting these issues, clinicians may be alerted to pitfalls and areas of special caution, to assist them in their future diagnostic work and formulations.

Diagnostic issues for ADHD

The diagnosis of ADHD requires the manifestation of a number of symptoms, i.e. six or more each in the inattention domain, and hyperactivity / impulsivity domains. At least some of the symptoms are present before age 7 and for at least 6 months. Impairments caused by the symptoms should be noted in two or more settings, e.g. school, home, clinic, extracurricular activities, public places etc., and the problems are evidently maladaptive or inconsistent with the developmental level.

Symptom presentation in clinic situation

Although the disorder is neurobiological in nature, no specific laboratory or imaging tests are available to clinch the diagnosis. Instead, clinicians base their conclusions on observable symptoms and by ruling out other disorders. Typically a clinician assesses a suspected case by gathering evidences from multiple sources: comprehensive interview with parent about the child's conditions and behaviours, collecting information from school teacher (such as through teacher questionnaires), and direct observation of the child's behaviours. Attention tests or measures are also commonly used in the assessment, with the test results reflecting the child's attention level on one hand, and the tool as a means to observe the child's behaviours on the other. However, the difficulty lies in the fact that the child may not always present his ADHD features in the clinic when he is engaged in a one-on-one structured situation with the clinician. This is especially the case when the clinician can only spend a limited amount of time of around 1-2 hours with the child, to be followed by parent interviews, even when a whole morning is assigned to one family. It is quite common to learn from the parents that their child could behave well when he is in a new and unfamiliar situation. Our question therefore, is whether the diagnosis of ADHD could be made based on the information from the parents and teachers which is not supported by the clinician's direct observation of behavioural symptoms at the visit?

Problem behaviour as a result of Dyslexia or co-morbidity

To diagnose ADHD, clinicians need to carefully rule out possibilities of other developmental problems with similar behavioural presentations. A child with dyslexia may try to avoid academic tasks and appear inattentive, or a child with mood problems may appear irritable and restless in new and unfamiliar situations. Both would not be diagnosed as having ADHD. Nevertheless, the high co-morbidity rate of ADHD with dyslexia of up to 18 – 45 % is well known.[2] The clinician therefore has the responsibility to differentiate between inattentiveness and restless behaviour resulting purely from the child's learning problems, and real ADHD in addition to his dyslexia. It is, of course, always desirable to make direct behavioural observations across different situations.

Biases of caregivers or teachers

During assessment, clinicians need to integrate information gathered from different sources. Information reported by major caregivers or teachers could be affected by their background, mental or emotional states, e.g. depressed mothers would have a more negative perception on children's behaviour leading to over-reporting of problematic behaviour.[3] To gather information from multiple sources is thus important for minimising these biases.

Clinicians' practice and biases

Clinicians' practice and biases is another possible factor affecting the diagnostic process. A recent study

suggested that in clinical settings, some clinicians made diagnosis without careful adherence to DSM-IV or ICD-10 criteria,[4] while another study suggested that clinicians did not weigh all diagnostic criteria equally but focused only on the more typical symptoms leading to inaccurate diagnosis.[5]

Moreover, in the Bruchmuller, Margraf, and Schneider's (2011) study, boys were more likely to be diagnosed with ADHD than girls with similar behavioural presentations. It suggested that client factors, e.g. gender, also affected the making of diagnosis.

Scientific debate regarding the question of whether ADHD is over-diagnosed in children is on-going.[6] ADHD, however, is a concrete developmental disorder, and can be accurately diagnosed by qualified clinicians. An accurate diagnosis is crucial and has great implication on case management, as it helps the child to receive clinically proven treatment promptly and to avoid unnecessary medications. It is important for clinicians to professionally adhere to diagnostic criteria, and to be aware of the possible biases affecting the diagnostic process.

Diagnostic issues for ASD

Autism spectrum disorders (ASD) are a group of clinical behavioural syndromes characterised by impairment in reciprocal social interaction and communication, and the presence of stereotyped behaviours, interests, and activities. Although the two classification systems, DSM-IV and ICD-10, provide clear structures for categorising symptom clusters, it is believed that problems often arise when clinicians apply the criteria in clinical practice.

Challenges in assessing very young children with ASD

Controversy regarding the precise definition of the ASD is largely due to its undetermined aetiology (e.g. without biological or psychological markers). Moreover, this is a heterogeneous group of individuals, each with a unique developmental profile, posing great challenge to clinicians in sorting out the features and making diagnoses. Given the changing developmental trajectories of children's behaviours, autistic-like behaviours may occur transiently in typically developing children.[7,8] For example, egocentric and ritualistic play behaviours are commonly found among children before the age of two or three. Some very young children "obsessively" cling to sameness and are resistant to change. In language development, echolalia is common when a child is at emerging single-word level or around two years old when it is part of imitation. Echolalic speech and immature play behaviour are also commonly found in children with speech and language delay. In the very young or very profoundly delayed child, differentiating autism with developmental delay from developmental delay alone may be difficult.[9] While the rigid behaviours of an autistic child may wane, social and communication interactions may become progressively more strange and awkward by middle childhood, when social demands increase and becomes more complex.

Based on previous research,8 features highly indicative of ASD include a lack of the following: eye-contact, gaze-monitoring, proto-declarative pointing, joint-attention, sharing of emotion, ability to demonstrate pretend and cooperative play, and imitation. These early indicators should be particularly watched out for during the first two years of life.

Challenges of assessing children with subtle features

Identification and diagnosis of high-functioning children with Autism, Asperger's Syndrome or boarder phenotype of ASD (e.g., PDD-NOS) are indeed another great challenge to clinicians. The presentation of their social and communication impairments are usually more subtle and might be masked by compensatory skills resulting from higher cognitive abilities. In fact, many children with ASD are not aloof and show solid interest in other people. Sometimes they are good at social initiation, but lack adequate and appropriate social cognitive ability for navigating the complex social world. When they seek assessment in late childhood for behavioural problems, it may not be easy for clinicians to identify autistic features if parents do not report related strange behaviours, or if retrospective accounts by the informants are unreliable. Furthermore, children with ASD and higher cognitive functions are often able to do well on standardised assessments in a one-to-one 'laboratory' setting, while their problems in real life situations persist.

Possibility of co-morbidity

It is notable that the current diagnostic criteria for ASD in ICD-10 and DSM-IV do not allow for the dual-diagnosis of ASD with other psychiatric disorders, such as ADHD and Anxiety Disorders. However, clinical experience and recent research indicate that co-morbidity of psychiatric disorders in children with ASD children is actually common. These additional behavioural or emotional symptoms sometimes reach clinical levels and affect the child and family's functioning to a great extent. Cases of ASD earlier concluded as non-clinical, or previously misdiagnosed as ADHD, oppositional defiant disorder, social anxiety, etc., are often diagnosed with co-morbid ASD in subsequent review assessments. Simonoff's study[10] using a population-derived cohort of 112 children with ASD aged 10 to 14 years old, reported high rates of co-morbid oppositional defiant disorders (25%) and anxiety disorders (41.9%). Brereton et al.[11] found that depressive symptoms also increased with age. Identifying and delineating associated psychiatric problems and co-morbidities will lead to earlier and specific intervention that could reduce overall impairment of affected children and families.

Conclusion and learning points

From the above discussions, some points to note are suggested for clinicians when evaluating children with suspected ADHD or ASD. First and foremost, clinicians need to be aware of their own potential biases and exercise appropriate caution. A conservative approach should be taken for those presenting with ambiguous features, and differential diagnoses may be warranted. Providing a diagnostic label at too early a stage before confirmation may lead to adverse effects on the children as well as inducing unnecessary fear and anxiety for the parents. Making a conclusion with observations of single "autistic-like" or "ADHD-like" behaviours must be avoided. Detailed medical and developmental history is part and parcel of the diagnostic process. Follow-ups and

reviews by the clinician at critical points are recommended, especially for marginal and ambiguous cases.

Making a diagnosis for ADHD and ASD is indeed a collaborative effort between parents, other caregivers, teachers and multidisciplinary team clinicians. It is understandable that retrospective accounts and reports by parents might not be always reliable, since these depend highly on the sensitivity of parents and their understanding of relevant early signs. A multidisciplinary approach with multiple sources of information is essential for information gathering.

Evaluation of a child's social and communication abilities should include both structured testing (e.g. IQ and language assessments) and unstructured observations (e.g., interactive play assessments). Children's social interaction and quality of social reciprocity in natural setting should preferably be observed and assessed in both the child's familiar and unfamiliar social situations.

Diagnostic formulation could then be made from evidence thus gathered, and measured against established diagnostic criteria and in a multi-axial format. The sole reliance on standardised assessment tools or the simple application of the ICD and DSM diagnostic criteria alone is not recommended. Clinicians should also be vigilant for potential co-morbid learning problems and psychiatric conditions that will compound the child and family's challenges.

Finally, it must be mentioned that clinical experience and its sharing can only lead to raising awareness in daily professional work. With the rapid advances in bio-behavioural sciences and reports from rigorous epidemiological and longitudinal clinical studies, it remains for all clinicians to keep abreast of new knowledge and methods, to enable the best services for children with developmental disorders and their families.

References

1. Child Assessment Service, Department of Health, HKSAR. Internal statistics, unpublished; 2012.
2. Germanò E, Gagliano A, Curatolo P. Comorbidity of ADHD and dyslexia. Dev Neuropsychol. 2010;35(5):475-93.
3. Najman JM, Williams GM, Nikles J, Spence S, Bor W, O'Callaghan M, Le Brocque R, Andersen MJ. Mothers' mental illness and child behavior problems: cause-effect association or observation bias? J Am Acad Child Adolesc Psychiatry. 2000 May;39(5):592-602.
4. Bruchmüller K, Margraf J, Schneider S. Is ADHD diagnosed in accord with diagnostic criteria? Overdiagnosis and influence of client gender on diagnosis. J Consult Clin Psychol. 2012 Feb;80(1):128-38. Epub 2011 Dec 26.
5. Meyer F, Meyer TD. The misdiagnosis of bipolar disorder as a psychotic disorder: some of its causes and their influence on therapy. J Affect Disord. 2009 Jan;112(1-3):174-83. Epub 2008 Jun 13.
6. Sciutto MJ, Eisenberg M. Evaluating the evidence for and against the overdiagnosis of ADHD. J Atten Disord. 2007 Sep;11(2):106-13.
7. Stone WL, Lee EB, Ashford L, Brissie J, Hepburn SL, Coonrod EE, Weiss BH. Can autism be diagnosed accurately in children under 3 years? J Child Psychol Psychiatry. 1999 Feb;40(2):219-26.
8. Charman T, Swettenham J, Baron-Cohen S, Cox A, Baird G. and Drew, A. An experimental investigation of social-cognitive abilities in infants with autism: Clinical implications. Infant Ment. Health J. 1998;19:260-75.
9. Sigman M, Ruskin E, Arbeile S, Corona R, Dissanayake C, Espinosa M, Kim N, López A, Zierhut C. Continuity and change in the social competence of children with autism, Down syndrome, and developmental delays. Monogr Soc Res Child Dev. 1999;64(1):1-114.
10. Simonoff E, Pickles A, Charman T, Chandler S, Loucas T, Baird G. Psychiatric disorders in children with autism spectrum disorders: prevalence, comorbidity, and associated factors in a population-derived sample. J Am Acad Child Adolesc Psychiatry. 2008 Aug;47(8):921-9.
11. Brereton AV, Tonge BJ, Einfeld SL. Psychopathology in children and adolescents with autism compared to young people with intellectual disability. J Autism Dev Disord. 2006 Oct;36(7):863-70.

Neuropsychological Assessment in Paediatric Epilepsy

Dr. Lucia TSANG

Clinical Psychologist, Child Assessment Service, Department of Health, HKSAR

Dr. Lucia TSANG

Neuropsychological assessment in evaluating children with epilepsy is essentially the same as it is with other neurological conditions except that the coverage of assessment may be more extensive and in-depth given the nature and severity of sequelae that epilepsy might bring along. In neurobehavioural disorders such as ADHD, one would not expect deterioration in higher cognitive functions such as memory though children with ADHD may present with such symptoms as inattention, hyperactivity and impulsivity which might affect them during the encoding and/or retrieval processes. In children with Autism Spectrum Disorder, some children might present with amazing "savant" skills in memorising all the minute details in their circumscribed interests.

Studies reported that children with uncomplicated epilepsy and even with an optimal seizure control might not fare as well as their controls in levels of achievement, vocational training, employment, socioeconomic status[1]. Therefore, the importance of timely neuropsychological assessments is receiving increasing attention.

As in most assessments, medical records are reviewed, collateral information and interviews from parents, caretakers and children themselves, questionnaires and rating forms as well as standardised psychometric tests are administered.

Behavioural observation is an integral part of the assessment to gauge whether or not the results are reliable in reflecting the children's current functioning. Children with epilepsy, who may be put through a cocktail of anticonvulsants, get fatigue more easily. On a one-to-one test situation, their attentional control and tolerance can be better contained and regulated through scheduled breaks and pacing according to their physical tolerance. Their test motivation can be fostered through social and sometimes light food as reinforcers.

Standardised Psychometric Tests Employed in Paediatric Epilepsy

No exact battery of tests is being used uniformly which very much depends on the presenting problems and

questions to be addressed. The choice and the selection of the standardised psychometric tests are essential so as to obtain valid and interpretable neurocognitive results. Those measures which are locally validated and normed, or relatively culturally-free tests are preferred.

Neuropsychological domains and tests commonly used in children with epilepsy

- Intelligence
  - Wechsler Intelligence Scale for Children-4th Edition (Hong Kong)
  - Raven's Standard Progressive Matrices[2]
  - Test of Nonverbal Intelligence 3rd Edition
- Learning and Memory
  - Hong Kong List Learning Test 2nd Edition
  - Rey Complex Figure Test and Recognition Trial
  - Continuous Visual Memory Test
- Working Memory
  - Working Memory Index- Wechsler Intelligence Scale for Children-4th Edition (Hong Kong)
- Attention
  - Conners' Continuous Performance Test-II
  - Test of Everyday Attention for Children[3,4]
  - Letter Cancellation Task
- Executive/Frontal
  - Wisconsin Card Sorting Test
  - Category Fluency Test[5]
  - Contingency Naming Test[3]
  - Stroop Colour & Word Test[3]
  - Tower of London Test[3]
  - Children's Color Trails Test
  - Behavior Rating Inventory of Executive Function
- Visual-spatial/Visual Perceptual
  - Perceptual Reasoning Index in Wechsler Intelligence Scale for Children-4th Edition (Hong Kong)
  - Rey Complex Figure Test and Recognition Trial-Copy
  - Judgment of Line Orientation
  - Hooper Visual Organization Test
- Reading and Writing
  - The Hong Kong Test of Specific Learning Difficulties in Reading and Writing for Primary School Students - Second Edition
  - The Hong Kong Test of Specific Learning Difficulties in Reading and Writing for Junior Secondary School Students - Second Edition
- Lateral Dominance
  - Edinburgh Handedness Inventory[6]
- Psychological-Emotional
  - Child Depression Inventory[7]
  - Child Behaviour Checklist[8]
  - Teacher's Report Form[8]
  - Youth Self-Report Form[8]
- Health-Related Quality of Life
  - The Chinese version of the Parent-Proxy Health-Related Quality of Life Measure for children with Epilepsy[9]
  - The Chinese version of the self-report health-related quality of life measure for Children and adolescents with epilepsy[10]

Impact of Epilepsy on Neurocognitive Functions

Early age of seizure onset, higher seizure frequency, incomplete seizure control, more EEG abnormalities, polypharmacy, and generalised symptomatic epilepsy subtypes have been considered risk factors for neuropsychological impairment in children[11]. Given the large number of distinctly different epilepsy syndromes, children might present with varying and unique neurocognitive profiles across the different domains: from normal functions, subtle to minimal impact, to catastrophic impairments.

General Intelligence

Studies on Intelligence in children with epilepsy have obtained mixed results. Some studies found that intelligence in most children with epilepsy was normal, with an average IQ (99.7) that did not differ significantly from their sibling controls[12]. Other researchers have identified age at seizure onset as one of the most important factors determining cognitive outcome[13]. Based on our clinical experience, a single Full Scale Intelligent Quotient (FSIQ) score may not be too informative since children with epilepsy mostly present with erratic profiles. We often see statistically significant discrepancies among the four composite indices (Verbal Comprehension Index, Perceptual Reasoning Index, Working Memory Index and Processing Speed Index). These scores together provide further essential information about a child's cognitive strengths and weaknesses, to which the unique discrepancy may be related to the underlying pathology, duration and severity, focal versus diffused pattern of the epilepsy as well as comorbidities and iatrogenic factors that contribute to the cognitive disturbance.

Children with epilepsy and normal IQ scores still have a higher prevalence of academic difficulties, increased utilisation of educational support services and lower academic achievement[14]. Therefore, a comprehensive assessment on other important neurocognitive domains such as memory, attention, executive functions, processing speed, etc. is warranted.

Memory and Learning

The specialised function of the hippocampal system for the acquisition of material-specific information into memory storage is well-established. Consistent with brain-behaviour relationship observed in adults, impairment in new learning and memory are frequently associated with temporal lobe epilepsy though lateralisation of memory deficits in children is still equivocal and conflicting results have been reported which warranted cautious interpretations.

Children with epilepsy were found to have significantly lower achievement scores than expected for their general intellectual ability[14]. Studies reported higher rates of learning problems in children with partial seizure disorders compared to generalised epilepsy and in children with symptomatic (lesional) syndromes compared with idiopathic syndromes[15,16]. Children with left temporal discharges show lower reading performances than children with right temporal lobe epilepsy[15]. The worst performance was found on measures of mathematical achievement while poor performance was also reported in spelling, reading comprehension and word reading[17]. Depending on

their premorbid learning history, children with epilepsy presented with sub-optimal literacy scores might not be further diagnosed as dyslexia, though remediation and accommodation should be provided on a timely and similar manner.

Executive Functions and Attention

Studies suggested that 30-40% of children with all types of epilepsy have difficulties with attention, and that the predominantly inattentive type of ADHD is more common than the hyperactive-impulsive or combined type, while the combined subtype was associated with earlier age of onset, a higher degree of intractability, and lower quality of life[18,19,20]. Children with idiopathic seizures are reported to have more frequent behaviour problems than those with symptomatic epilepsy[21].

Studies reported an association between impaired executive function and frontal lobe epilepsy. The frontal lobe dysfunction includes impairment in planning, problem solving, lower performance on attention measures, working memory, slower processing speed, greater susceptibility to interference and intrusion errors in memory testing, and poorer ratings on behaviour rating forms[22,23]. We also see impulsive, explosive temper outbursts and inappropriate social behaviours in children with prefrontal lesions and their behaviours can become a challenge particularly in classroom and group settings.

Psychological-Emotional

Epidemiological studies have identified higher rates of psychological disturbance and worse quality of life in children with epilepsy than in the general population[24]. Mood disturbance such as depression and anxiety and internalising behaviours are among the most commonly reported, yet externalising behaviours also occur with greater frequency among children with epilepsy than among children with other disorders[25]. Psychosocial factors such as family burden, low family mastery increase the risk of behaviour problems in children with new-onset epilepsy[26,27], while other factors such as laterality of seizure onset have proved inconsistent in the onset of depression[28,29] .

Conclusion

Given the large number of distinctly different epilepsy syndromes and the vast number of potential underlying neuropathological causes of epilepsy, one would not expect to have a single or a few neurocognitive phenotypes of epilepsy. Comprehensive neuropsychological assessments conducted at critical junctures can help establish profiles of the children's cognitive strengths and weaknesses across multiple cognitive and behavioural domains, so as to arrive at a neurobehavioural diagnosis and likely explanation to their presenting problems and current functions. The results can assist in monitoring the efficacy of medical treatment, signal the need for alternative or supplemental treatments, pre-post epilepsy surgery, monitoring the iatrogenic factors such as prior and after the initiation of AED treatment, track progress and deterioration over time, and to ensure necessary remediation and accommodation in education and vocational planning be implemented. Concerted efforts from different professionals in linking medical treatment, assessments by multi-disciplines to rehabilitation based on evidence-based practice is essential to enhance optimal functioning in these children as well as to their family at large.

References

1. Sillanpää, M. (2004). Learning disability: Occurrence and long-term consequences in childhood-onset epilepsy. Epilepsy & Behavior, 5, 937-944.
2. Education Bureau (1986). Hong Kong Supplement to the Standard Progressive Matrices.
3. Normative Data of Neuropsychological Measures for School-Aged Children in Hong Kong (2007). Taskforce for Research on Child Neuropsychological Profile in Hong Kong, Division of Clinical Psychology, Hong Kong Psychological Society.
4. Cantonese Instructions and Norms of TEA-Ch (Hong Kong Version) (2008). Taskforce for Research on Child Neuropsychological Profile in Hong Kong, Division of Clinical Psychology, Hong Kong Psychological Society.
5. Chan, A. S., & Poon, M.W. (1999). Performance of 7-to 95-year-old individuals in a Chinese version of the category fluency test. Journal of the International Neuropsychological Society, 5, 525-533.
6. Oldfield, R.C. (1971). The assessment and analysis of handedness: the Edinburgh Inventory. Neuropsychologia; 9, 97-113.
7. Normative Data of Children's Depression Scale for School-age Children in Hong Kong (2008). Taskforce for Research on Child Neuropsychological Profile in Hong Kong, Division of Clinical Psychology, Hong Kong Psychological Society.
8. Leung, Patrick W.L., Kwong, S.L., Tang, C.P., Ho, T.P., Hung, S.F., Lee, C.C., Hong, S.L., Chiu, C.M., & Liu, W.S. (2006) Test-retest reliability and criterion validity of the Chinese version of CBCL, TRF, and YSR. Journal of Child Psychology and Psychiatry, 47, 9, 970-973.
9. Yam, W. K.L., Chow, S.M.K., Ronen, G. M. (2005). Chinese version of the Parent-Proxy Health-Related Quality of Life Measure for Children with Epilepsy: Translation, cross-cultural adaptation, and reliability studies. Epilepsy and Behavior, 7, 697-707.
10. Ma, K.H., Yan, K.L., Tsui, K.W., Yau, F. T. (2006). Internal consistency and test-retest reliability of the Chinese version of the self-report health-related quality of life measure for children and adolescents with epilepsy. Epilepsy & Behavior, 9, 51-57.
11. Mandelbaum, D. E., & Burack, G.D. (1997). The effect of seizure type and medication on cognitive and behavioral functioning in children with idiopathic epilepsy. Developmental Medicine & Child Neurology, 39, 731-735.
12. Bourgeois, B., Prensky, A.L., Palkes, H.S., Talent, B.K., Busch, & S.G. (1983). Intelligence in epilepsy: A prospective study in children, Annals of Neurology, 14(4), 438-444.
13. Berg A.T., Langfitt, J.T., Testa, F.M., Levy, S.R., Dimario, F., Westerveld, M., et al. (2008). Global cognitive function in children with epilepsy: A community-based study. Epilepsia, 49(4), 608-614.
14. Bailet, L.L., & Turk, W.R. (2000). The impact of childhood epilepsy on neurocognitive and behavioral performance: A prospective longitudinal study. Epilepsia,41(4), 248-255.
15. Stores, G., Hart, J. (1976). Reading skills of children with generalized or focal epilepsy attending ordinary school. Developmental Medicine & Child Neurology, 18, 705-716.
16. Zelnik, N., Sa'adi, L., Silman-Stolar, Z., Goikhman, I. (2001). Seziaure control and educational outcome in childhood-onset epilepsy. Journal of Child Neurology, 16, 820-824.
17. Seidenberg, M., Beck, N., Geisser, M., Giordani, B., Sackellares, J.C., Berent, S., et al. (1986). Academic achievement of children with epilepsy. Epilepsia, 27(6), 753-759.
18. Dunn, D.W., & Kronenberger, W.G. (2005). Childhood epilepsy, attention problems, and ADHD: Review and practical considerations. Seminars in Pediatric Neurology, 12(4), 222-228.
19. Hermann, B., Jones, J., Dabbs, K., Allen, C.A., Sheth, R., Fine, J., et al. (2007). The frequency, complications and aetiology of ADHD in new onset paediatric epilepsy. Brain, 130(12), 3135-3148.
20. Sherman, E.M., Slick, D.J., Connolly, M.B., & Eyrl, K.L. (2007). ADHD, neurological correlates and health-related quality of life in severe pediatric epilepsy. Epilepsia, 48(6), 1083-1091.
21. Berg, A.T., Vickrey, B.G., Testa, F.M., Levy, S.R., Shinnar, S., & DiMario, F. (2007). Behavior and social competency in idiopathic and cryptogenic childhood epilepsy. Neurology, 49(7), 487-492.
22. Culhane-Shelburne, K., Chapieski, L., Hiscock, M., & Glaze, D. (2002). Executive functions in children with frontal and temporal lobe epilepsy. Journal of International Neuropsychological Society, 8(5), 623-632.
23. Hernandez, M.T., Sauerwein, H.C., Jambaque, Il, deGuise, E., Lussier, F., Lortie, A., et al. (2003). Attention, memory, and behavioral adjustment in children with frontal lobe epilepsy. Epilepsy and Behavior, 4(5), 522-536.
24. Davies, S., Heyman, I., & Goodman, R. (2003). A population survey of mental health problems in children with epilepsy. Developmental Medicine and Child Neurology, 45, 292-295.
25. Plioplys, S., Dunn, D.W. & Caplan, R. (2007). 10-year research update review: Psychiatric problems in children with epilepsy. Journal of the American Academy of Child and Adolescent Psychiatry, 46(11), 1389-1402.
26. Rodenburg, R., Stams, G.J., Meijer, A.M., Aldenkamp, A.P., & Dekovic, M. (2005). Psychopathology in children with epilepsy: A meta-analysis. Journal of Pediatric Psychology, 30(6), 453-468.
27. Baum, K.T., Byars, A.W., deGrauw, T.J., Johnson, C.S., Perkins, S.M., Dunn, D.W., et al. (2007). Temperament, family environment, and behavior problems in children with new-onset seizures. Epilepsy and Behavior, 10(2), 319-327.
28. Quigg, M., Broshek, D.K., Heidal-Schiltz, S., Maedgen, J.W. & Bertram, E.H. (2003). Depression in intractable partial epilepsy varies by laterality of focus and surgery. Epilepsia, 44(3), 419-424.
29. Altshuler, L.L., Devinsky,O., Post, R.M., & Theodore, W. (1990). Depression, anxiety, and temporal lobe epilepsy. Laterality of focus and symptoms. Archives of Neurology, 47(3), 284-288.

Dietary Management of Intractable Epilepsy with Ketogenic Diet in Paediatric Patients

Ms. Carmen YEUNG

Accredited Practising Dietitian (Australia)
Dietitian in Tuen Mun Hospital, NTWC, Hospital Authority

Ms. Carmen YEUNG

Introduction

Ketogenic diet (KD) is a high fat, restricted carbohydrate regimen that was first introduced to treat epilepsy in the 1920s. After the resurgence of the KD since mid-1990s in the United State, it has been used extensively and recognised as a safe and effective alternative therapy for intractable childhood epilepsy.[1] Although the exact mechanism of action is still unclear, the high fat and restricted carbohydrate content of the diet is thought to mimic the biochemical response to starvation, when ketone bodies become the main fuel for the brain's energy demands.

Dietitians work closely with neurologist, nurses, pharmacists and social workers, each one plays an important role in both initiating and maintaining the diet. Dietitians are not only there to teach the diet while the family is in the hospital for diet initiation, but also to help the family with questions and dietary changes when they are discharged home.

Types of Ketogenic Diets

There are two main types of KD, Classical and MCT (medium train triglyceride) type, both are effective for treating seizure.[2] The classical diet is based on a diet ratio of fat to carbohydrate and protein. The long chain fat is mainly provided from foods, protein is based on minimum requirements for growth and carbohydrate is very restricted. The ratio is based on the grams of fat to grams of protein plus carbohydrate. For example, the most common ratio is 4g fat to 1g protein plus carbohydrate. This means that 90% of the energy comes from fat and 10% from protein plus carbohydrate, which is usually expressed as a 4:1 ratio. For lower ratios, there is 3:1, giving 87% of diet energy as fat. Sometimes, a classical ketogenic diet may start from 2:1 ratio, which contains 82% energy from fat, and gradually builds to a higher ratio as tolerated.

The MCT type has no diet ratio for fat to protein plus carbohydrate. Usually, children achieve optimum ketone levels with 60% energy from MCT.[2] However, some children may experience abdominal cramps, diarrhoea and vomiting. Therefore, MCT oil needs to be introduced slowly, and can be increased as tolerated to achieve the desired ketosis. MCT oil needed to be purchased as medical food. This can be given in the diet as oil, or as an emulsion which can be easily mixed with food or drink. MCT oil should be included in all meals when used, less quantity of MCT with each meal, while more meals per day could improve the tolerance of this diet.

MCT oils yield more ketones per kilocalories of energy than the long chain fat; because they are absorbed more efficiently and carried directly to the liver. This increased ketogenic potential means less total fat is needed in the MCT diet, which allows considerably more carbohydrate and protein, therefore a more normal diet, which may be better suited to some children, especially those with limited food choices.

In the past few years, a Modified Atkins Diet has been developed for the treatment of epilepsy. It is similar to the classical KD in the composition and is approximately a 1:1 ketogenic ratio. The initial daily carbohydrate consumption on the modified Atkins diet is approximately 10g, then with gradual increases to 15-20 gram per day after 1-3 months.[3] However, there are no limitations on protein, fluids and calories; therefore it makes meal planning easier. So far, there is too little study on the efficacy between the modified Atkins and classical ketogenic diet.

Meal arrangement

It was common to do fasting before commencement of KD, however this has been shown to be unnecessary and adequate ketosis can be achieved by commencing directly onto the full dietary prescription.[4]

For Classical KD, each meal and snack must be calculated in the correct ketogenic ratio. For MCT diet, the MCT source should be included with each meal and snack and evenly divided up over the day. It is important to give the last meal or snack as possible to maintain the best possible overnight ketosis. In the past, fluid restriction to 90% of usual maintenance was applied. However, many centres worldwide are no longer having fluid restriction for children on KD.

A well-balanced diet will have sufficient vitamins and minerals intake, however, KD usually requires full vitamin and mineral supplementation due to the limited food variety of fruits, vegetables, enriched grains, etc. and with high fat intake. Dietitians require regular dietary assessments, in order to closely monitor the adequacy on all micronutrients based on dietary reference intake guidelines. A recommendation on supplement may be required, and more importantly

the multivitamins and mineral products should be carbohydrate free or minimal carbohydrate containing.

Dietary education plays an important role in increasing the efficacy of KD, it helps the family members develop a positive attitude toward the diet. Usually, patients and their families require for a 3-month commitment. After starting the diet, it takes time to fine-tune it, involves finding the correct amounts of calories, macro- and micronutrients, getting both the child and the family accustomed to this new eating style. There are very limited free foods on KD, only sugar free drinks or food with use of carbohydrate free sweetener is allowed. KD is never been an easy diet for Asians, since carbohydrates are considered to be a main dietary composition, our diet contains substantially less fat than traditional Western diet; therefore it becomes a limitation on adapting KD. Parents would also have the concern about complications caused by an imbalanced diet; it turns out to be the major holdback of KD.

Monitoring and discontinuation of ketogenic diet

The majority of the ketogenic centres worldwide advise routine urine ketosis check by parents daily initially, and may reduce to several times per week. Long term follow-up assessments for children on KD including accurate growth parameters, such as weight and height, laboratory studies on micronutrients are recommended for routine checkups. Special attention is given to vitamin D and calcium due to little intake of this nutrients from KD.[5] On the other hand, serum albumin may reveal if KD is providing adequate calories and protein for growth. Typically, children on KD may experience rise of cholesterol and triglyceride, these markers should be monitored.

Discontinuation of the ketogenic diet is often based on patient response to the diet. Most parents are advised to continue the KD for at least 3 months for trial before considering discontinuation. In general, children who found success on the KD were generally weaned slower, however, there is no association existed between the specific rate of discontinuation and likelihood of seizures worsening.[6] Overall, weaning the KD over several months is not necessary, and a 4-6 week discontinuation is feasible and well-tolerated. KD tapering over days perhaps could be done in some children without obvious KD success.

Conclusion

A sincere communication with patient and caregivers is very important for KD, it allows dietitians to provide more accurate and supported counsel, allowing patients to have a greater personal preference without deprived seizure control. Work with a neurologist as a team is very important to patients on KD, the efficacy of the diet whether it meets parents' expectations, the possibility of reducing anticonvulsant and how long the KD should be continued need to be well discussed between parents and the team.

References

1. Kossoff EH, McGrogan JR. (2005) Worldwide use of the ketogenic diet. Epilepsia 46(2): 280-289
2. Kossoff EH, Zupec-Kania BA, Amark PE, Ballaban-Gil KR, Christina Bergqvist AG, Blackford R, et al (2009) Optimal clinical management of children receiving the ketogenic diet: Recommendations of the international ketogenic diet study group. Epilepsia 50(2): 304-317
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. Vining EP. Clinical efficacy of the ketogenic diet. Epilepsy Res 1999; 37: 181-90
5. Bergqvist AG, Schall JI, Stallings VA. (2007) Vitamin D status in children with intractable epilepsy, and impact of ketogenic diet. Epilepsia 48:66-71
6. 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.

KetoCal

Epilepsy Controlled. Childhood Regained.

A New Future for Epilepsy Care

Ketogenic Diet (KD) therapy induces a state of ketosis to control epileptic seizures. It is a diet high in fat, with adequate protein and low carbohydrate, deriving ketone bodies used as fuel by the brain and body. KD therapy offers proven, effective seizure control without cognitive antiepileptic medication side effects.[1,2,3]

KetoCal The only convenient, nutritionally complete formula for KD therapy

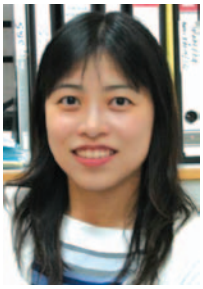
- For the dietary management of intractable or drug-resistant epilepsy
- Nutritionally complete formula to ensure children on KD therapy receive sufficient nutrients for growth and development
- Can be used as drink, added to food, as meal replacement and sole source of nutrition. Also can be used as tube feed
- Quick and easy to prepare
- Palatable texture, "melted ice-cream"

Reference:
1. Henderson C et al. J Child Neurol 2006; 21:193-198 2. Neal E et al. Abstract presented at the 27th International Epilepsy Congress. 8-12 July, 2007; Singapore
3. Rubenstein J et al. Child Neurol 2005; 20(1):31-34

Ranges of supplement also available for the support of specific treatment regimes. Please contact our hotline at **8103 3329** for more information.

NUTRICIA
Advanced Medical Nutrition

Enhancing Epilepsy Care in Hong Kong



Ms. Anchor TF HUNG

Ms. Anchor TF HUNG

BSW(HK), MA in Disability Studies(Leeds), Master of Public Health (HK); RSW

Manager, Centre on Research and Advocacy, The Hong Kong Society for Rehabilitation

Summary

Epilepsy is a very common neurological disorder across the lifespan affecting children, adults as well as the elderly. It is not only a medical condition, but also a public health issue with great health and social repercussions on the patients and the society[1]. This article is aimed at highlighting some current situation of patients with epilepsy and facilitating discussion on enhancing epilepsy care in Hong Kong with reference to some local and overseas experience.

Introduction

The Hong Kong Society for Rehabilitation, The Hong Kong Epilepsy Society, The Hong Kong Neurological Society and The Hong Kong Epilepsy Association have jointly conducted 'A study on self-management behaviour of people with epilepsy in Hong Kong[2]' and published the Seizure Diary[3] in a press conference held on 10th June 2012 in InfoWorld, Hospital Authority.

Seizure Diary

The study reflected some typical conditions of epilepsy patients in Hong Kong. Among the 226 subjects with epilepsy recruited in the community settings, some findings are highlighted as follows:

- **The score of self efficacy in coping with epilepsy is 5.97. It is relatively lower than the standard score of 7 .**
- **About 65.2% of respondents reported to have at least one or more seizures in the preceding year. Only 34.8% are seizure free.**
- **About 87.7% are on anti-epileptic drugs. 30% are on one medication, 26% on two types of drugs and 31.7% are on three and more.**
- **During their medical consultations, 20% of respondents reflected that their consultation time is less than five minutes. Among those patients with refractory epilepsy, 80% of them are similarly having less than five minutes in communicating with their physicians.**
- **As for the socio-economic aspects, 60% respondents have secondary school education and only 18.9% achieve university or higher education.**
- **Regarding the employment rate, about 28.1% have full-time jobs and 30% are unemployed. Even worse, 15% are now receiving Comprehensive Social Security Assistance from the government.**

Common difficulties encountered by patients with epilepsy

- **A teenage girl idled at home and suffered from depression after her completion of secondary school education.(Depression)**
- **An adolescent passed away quietly when his mom was reading newspaper in the living room at night. When she came to his bedroom, he had already gone.(Sudden Death in Epilepsy)**
- **A manual worker, with frequent seizures, could not have his contract renewed in his workplace. (Unemployment)**
- **A middle-aged male patient went to work in the morning as usual. He suddenly fell onto the ground due to a seizure. He passed away leaving her wife widowed. (Death from injury)**

All these are only the tip of an iceberg among patients with epilepsy who are confronted with multi-faceted difficulties. Their health and social outcomes are far from satisfactory.

Epilepsy as both local and worldwide public health issues

Epilepsy is a very common neurological disorder, affecting 50 million people in the world[4]. In Hong Kong, a study showed a prevalence of active epilepsy

of 3.94/1000[5]. Epilepsy has much disabling effects on the patients including impairment of their cognition, injuries during seizures, education opportunities as well as social network especially for those who are with refractory epilepsy. The burden of disease to both the individuals and the society is enormous.

Various studies have examined the economic impact of epilepsy[6, 7]. It is found that the indirect cost to society (productivity-related costs) generally exceed direct costs (treatment-related cost). Overall, lifetime productivity is estimated to decline by 34% for men and 25% for women. Estimation of indirect costs is significantly higher for people with refractory epilepsy.

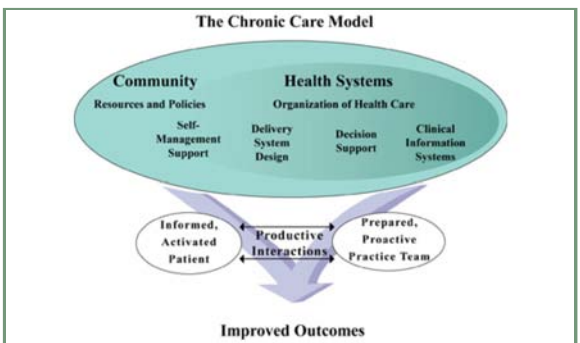
Delayed recognition of seizures and inadequate treatment will result in increasing a person's risk of subsequent seizures, brain damage, disability and death from injuries incurred during a seizure. Hence, access to quality health and social care would be vital to the patients.

The World Health Organization, World Bank, and together with many international organisations and countries have made very proactive and tremendous efforts to enhance better epilepsy care at different levels.

Rising trend of using the Chronic Disease Management Model

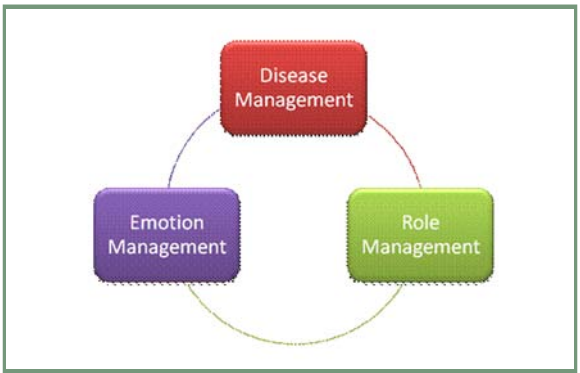
There is an international move to transform the way chronic diseases are managed[8]. The transformation aims to move from the episodic reactive model of health care delivery to one that prevents the occurrence of disease, averts or delays further deterioration, and improves the health and quality of life of those already suffering from the condition. To achieve the transformation, the recommendations of chronic disease management (CDM) models and strategies include:

1. Self Management - Promotion of patients' active participation in managing their health
2. Development of shared care that is integrated across organisational boundaries
3. Implementation of guidelines that support clinical management decisions
4. Use of clinical information systems, such as electronic health records to provide timely access to comprehensive patients' information to those who deliver and receive care.



Chronic Care Model

As for **Self Management support**, it is important to develop 'knowledgeable patients', who actively participate in communicating with medical professionals in partnership, as well as to comply with and adopt healthy lifestyles for better health outcomes. Patients are empowered to manage their disease, emotion and role well.



Three Tasks of Self Management

In the chronic care model, it is important to enhance the self management support of patients. Self management is to increase the knowledge, skills and sense of efficacy of patients to cope with their illness. Promoting self management support for patients with epilepsy, it is important for clinicians or health care professionals to impart knowledge and train skills to the patients and their family members like pathology and first aid management.

Direct communication is also very important among patients with epilepsy and their doctors. Seizure activities of patients are seldom witnessed by the doctors. It is of paramount importance that the patients can report a clear description of seizure activities during the consultation. It will help the doctor to have a more accurate diagnosis and prescribe suitable medications so that the patients' epilepsy can be well-controlled.

To have quality epilepsy care, expert physicians should be able to make accurate diagnosis, access to sufficient resources to undergo necessary investigations like neuroimaging for patients, as well as to communicate sufficiently with patients during their consultation time.

Chronic Disease Self Management in Hong Kong

In Hong Kong, the Hospital Authority has started a three-year pilot Patient Empowerment Programme (PEP) to enhance patient self management. Current targets are those disease types with greater burdens like Diabetes mellitus (DM) and hypertension. This concept and practice should also be extended to other diseases like epilepsy so that patients can get more support and minimise the burden of the disease.

In past years, CRN has adopted a self management approach to provide services to different disease groups

[1] *A study of the cost burden of epilepsy in the United States estimated a total amount cost of $12.5 billion per year, $10.8 billion in indirect costs (86.5%) and $1.7 billion in direct costs (13.5%).*

including DM, rheumatology, stroke and epilepsy. The effectiveness of enhancing self management behaviour has been very positive. For epilepsy services as an example, the six-session Breakthrough from Epilepsy Self Help course has demonstrated its effectiveness in enhancing participants' knowledge and skills in coping with epilepsy.

For children with epilepsy, they need to acquire knowledge and skills in coping with the disease (disease management). With the frustration of seizure activities, they have to learn to deal with their emotion (emotion management). As a student or family member, they need to perform their role despite their illness (role management). The ability to communicate with parents and physicians shall also be enhanced to have a better control of their seizures.

Looking ahead - some more strategies for epilepsy care especially for Paediatrics

Apart from self management support, there are many other strategies to enhance epilepsy care. The following are some key strategies adopted by different countries to improve their service[7-9]:

- **Setting up of Advanced Practice Nurse or Epilepsy Specialist Nurse**
- **Managing epilepsy in Primary care**
- **Strengthening the interfacing between primary care and secondary care**
- **Multi-disciplinary team approach for the multi-needs of the patients**
- **Specialised tertiary care for those with refractory epilepsy**

It may take time for experts to explore further strategies to enhance epilepsy care in Hong Kong with our local considerations. With the setting up of a Children's Hospital in Hong Kong and other initiatives, it is hoped that more quality epilepsy care will be provided to help our children with epilepsy, enhancing their health, happiness and productivity in our society.

Conclusion

Having a good control of epilepsy is critical to patients with epilepsy especially during their childhood. Otherwise, it will exert great impact to their physical development, education opportunities and social network. It will also bring great costs of burden to the society as a whole. To bring change, it will be important our stakeholders like the Food and Health Bureau, Hospital Authority and other parties to have a strong determination on the issue. We need enhancing the existing epilepsy care with self management support, building an integrated care pathways encompassing tertiary, secondary, primary care and social care, as well as promoting an inclusive society.

References

1. Hung ATF. Psycho-social Impact of Epilepsy and Issues of Stigma. Hong Kong Medical Diary, 2009; 14(5), 15-17.
2. 熊德鳳、陳樂耀、劉國光、李應儀 .《香港腦癇症患者的自我管理及治療情況研究報告》, 2012.
3. 香港復康會、香港協癇會、香港抗癲癇學會、香港腦科學會 . 《腦癇日記》, 2012.
4. World Health Organization. Epilepsy The Public Health Aspects. Epilepsy Atlas, 2005.
5. Fong GC, Kwan P, Hui AC, Lui CH, Fong JK, Wong V. An epidemiological study of epilepsy in Hong Kong SAR, China. Seizure, 2008; 17, 457-64
6. Begley et al. The Cost of Epilepsy in the United States: An Estimate from Population-Based Clinical and Survey Data. Epilepsia, 2000; 41(3), 342–351
7. The Institute of Medicine (IOM). Epilepsy Across the Spectrum: Promoting Health and Understanding, 2012. www.iom.edu/Reports/2012/Epilepsy-Across-the-Spectrum.aspx. (Accessed 9 August 2012).
8. Fitzsimons M, et al., Evidence-based models of care for people with epilepsy. Epilepsy Behav, 2012; 23(1), 1-6.
9. Centers for Disease Control and Prevention. Targeting Epilepsy: Improving the Lives of People with One of the Nation's Most Common Neurological Conditions at A Glance 2011. www.cdc.gov/chronicdisease/resources/publications/AAG/epilepsy.htm. (Accessed 9 August 2012).

Press conference on 'A study on self-management behaviour of people with epilepsy in Hong Kong' on 10th June 2012.

HealthBaby
生寶臍帶血庫

Most Professional Accreditations
Most Recommended by O&G Doctors[1]
Over 70% Market Share[2]

The First & Only

HK Cord Blood Laboratory Accredited By CAP

Introduction of CAP

- Most Credible International Accreditation Authority
- The World's Largest Pathology Association
- >18,000 Board-Certified Pathologists

Significance of CAP Accreditation

- Technology, Quality And Operation Met Up With The Stringent Standard
- Worldwide Recognized Laboratory Testing Report
- Accurate Data Ensuring Cord Blood Transplant Safety

cap ACCREDITED™

Medical Grade Cord Blood Laboratory

Source: 1. IMS 2010 Cord Blood Bank Market Research in Hong Kong (with Private O&G physicians) 2. Synovate Healthcare 2009-2011 Cord Blood Bank Survey

HK 3188 8899 MACAU 2878 6717 CHINA 147 1492 8842 | www.healthbaby.hk

Genetic Diagnosis of Autism Spectrum Disorders

Dr. Carol WK SIU
MBBS, MSc, FHKCPath
Resident, Department of Clinical Pathology, Tuen Mun Hospital & Department of Pathology, Princess Margaret Hospital

Prof. Ching-wan LAM
MBChB, PhD, MAACB, FAACB, FRCPA, FHKCPath, FHKAM(Pathology), FRCP (G)
Clinical Professor, Department of Pathology, Li Ka Shing Faculty of Medicine, The University of Hong Kong

Dr. Chloe M MAK
MBBS, PhD, FRCPA, FHKCPath, FHKAM(Pathology)
Consultant Chemical Pathologist, Department of Pathology, Princess Margaret Hospital

Dr. Albert YW CHAN
MBChB, MD, FRCP (G), FHKCP, FRCPath, FRCPA, FHKCPath, FHKAM (Pathology)
Consultant Chemical Pathologist, Department of Pathology, Princess Margaret Hospital



Dr. Carol WK SIU Prof. Ching-wan LAM



Dr. Chloe M MAK Dr. Albert YW CHAN

Introduction

Autistic spectrum disorders (ASDs) are a group of neurodevelopment diseases in childhood, which are characterised by the impairment of social interactions, deficit in verbal communication, restricted interest and stereotyped behaviour. The symptoms and severity are extremely variable between the subtypes of ASDs. The onset of symptoms usually occurs by the age of three. The diagnostic criteria are based on the fourth edition of the American Psychiatric Association Diagnostic and Statistical Manual of Mental Disorders (DSM–IV). Currently, three subgroups (autistic disorders, Asperger syndrome and pervasive developmental disorder–not otherwise specified) are recognised. Using a list of diagnostic criteria, at least six criteria must be demonstrated with onset of conditions prior to age three, including at least two concerning social abnormalities and one each regarding impaired communication and range of interests and activities.[1]

There are a dramatic growing number of children being diagnosed with autism. The prevalence of autism in the general population was considered steady at 4–5/10,000 (1/2,000 – 1/2,500) before 1990.[2] In 1990s, the prevalence rates in school children had increased to 21–31/10,000 (1/476 – 1/323). By 2005, the reported prevalence was 22/10,000 (1/455) for classic autism and 59/10,000 (1/169) for all pervasive developmental disorders in children.[3] The latest data in 2008 from the United States showed that the prevalence of ASDs was 1/88.[4] The prevalence of autism in Hong Kong was about 16 /10,000 (1/621) using the data till 2005.[5] This group of neurodevelopmental disorders among children now seems to occur at an epidemic rate. It has been suggested that the apparent "autism epidemics" is attributable to the increased awareness by both the public and professionals, leading to more complete case finding together with broadening of diagnostic criteria. However, there is also evidence showing the continued rise in autism might represent a genuine increase rather than a result of reclassification. ASDs are aetiologically and clinically heterogeneous. Genetics has a significant role in the aetiology of autism. The advances in the genetics of autism have also been translated into clinical practice.

Genetic elements of ASDs

Autism is a highly genetic disorder with heritability of 80%.[6] Twin family studies have demonstrated concordance rates of 70% – 90% in monozygotic twins vs. about 10% in dizygotic twins.[7] The recurrence rate among latter sibs was 8.6% and for families with two or more affected children, the recurrence risk approached 35%.[8] The disorder best fits into the model of "multifactorial inheritance" and the genetic mechanism is heterogeneous and complex.[6] Understanding the genetics of autism has proven to be difficult.

Different approaches have been used to study the genetic basis of ASDs including karyotyping, linkage analysis, candidate gene analysis and genome–wide association study. Linkage analysis identified autism loci on multiple regions such as 2q, 7q, 15q, 16p, 17q, 19p and Xq and about 7% of ASD patients was identified to have chromosomal structural aberrations.[9] Furthermore, it is significant to note that Lam et al. provided the first evidence linking *MECP2* gene mutations with autism.[10] Mutations in other single genes were subsequently identified including *CNTNAP2, SHANK3, NLGN3* and *NLGN4* genes.[11-13] It was also associated with single gene disorders including Rett syndrome[14], fragile X syndrome[15] and tuberous sclerosis.[16] Autism or mental retardation and progressive macrocephaly were reported in patients with genetic syndrome due to germline mutations in a tumour suppressor gene *PTEN*.[17] With genome-wide association studies, six single nucleotide polymorphisms between cadherin 10 and cadherin 9, which encode neuronal cell adhesion molecules, revealed strong association with autism.[18] In addition, autism has been associated with a number of inherited metabolic diseases including creatine deficiency, adenylosuccinate lyase deficiency, mitochondrial disorders, phenylketonuria and Smith–Lemli–Opitz syndrome.[19] Traditional approaches had considerable limitation to reveal the complex and heterogeneous genetic basis of autism. For example, conventional karyotyping had limited resolution in detection of chromosomal deletion and duplication.

With the advance in diagnostic technology, array comparative genomic hybridisation (CGH) has emerged

as a powerful new tool for the detection of genome-wide submicroscopic deletion and duplications, collectively known as copy number variations (CNVs). Jacquemont et al. identified deletions and duplications in 27.5% of ASD patients using array-based CGH. Their results suggested that array CGH should be an essential part of genetic analysis for ASD patients. The array CGH findings not only can provide important information for diagnosis and genetic counselling but also may allow delineation of new genes involved in ASDs.[20] In another study by Marshall et al., unbalanced CNVs were identified in 44% of ASD families and de novo CNVs were found in ~7% of idiopathic families. The study identified 13 loci with recurrent CNVs in unrelated ASD families where deletions or duplications of the same genes were detected in different individuals. Their findings further revealed the role of *SHANK3-NLGN4-NRXN1* post-synaptic density genes and novel loci at *DPP6-DPP10-PCDH9* (synapse complex) in ASD susceptibility.[21] Analyses of CNVs contribute significantly to the discovery of new candidate ASD pathways. Genome-wide CNV analyses identified susceptibility genes involved in neuronal cell adhesion (*NLGN1, ASTN2* genes) and ubiquitin pathway (*UBE3A, PARK2, RFWD2, FBXO40* genes) associated with ASDs.[22] A significant increase in the number of genes intersected by rare CNVs was identified in ASD patients. The rare CNVs enrichments in gene sets in ASDs denoted new candidate pathways including gene sets involving in cell and neuronal development and function, GTPase/Ras signalling, microtubule cytoskeleton, glycosylation and CNS development/adhesion.[23]

Exome sequencing has been used to explore the genetic basis of sporadic ASDs. A study examined 20 trios with idiopathic ASDs had identified four disruptive mutations in *GRIN2B, SCN1A, LAMC3* and *FOXP1* genes.[24]

The gene discovery for autism has rapidly progressed in the last two decades. The genes reported to be associated with ASDs have considerable overlaps with other disorders like intellectual disability, epilepsy, schizophrenia, and attention deficit hyperactivity disorder.[25] The evidence suggested that ASDs are complex disorders resulting from simultaneous genetic variations in multiple genes as well as complex interactions between genetic, epigenetic and environmental factors. Furthermore, some of the sequence variants associated with ASDs could be common in the general population. ASD phenotype could be the result of involvement of single genes in combination with non-genetic factors, or multiple genes through locus heterogeneity, or, multiple genes through allelic heterogeneity. It has also been suggested that ASDs may well be a collection of rare disorders resulting from a number of different genetic diseases leading to a shared phenotype.[6]

Translation of genetic research into clinical management of ASDs

Advancement on the knowledge and technology in the genetics of autism facilitates the development of guidelines to identify the underlying aetiology. Testing of *MECP2* gene has been included in the American College of Clinical Geneticists guideline on clinical genetic evaluation for ASD patients in 2008.[26] Tiered evaluation has been suggested. Pre–evaluation included confirmation of diagnosis of autism by objective criteria and tools, sensory testing, electroencephalogram, cognitive testing and verifying newborn screening results. The first tier evaluation was to identify known syndromes and associated conditions by examining for dysmorphic features. High–resolution chromosomal analysis, testing for Fragile X syndrome, metabolic screening including urine mucopolysaccharides, urine organic acids, serum lactate, amino acids, ammonia, acylcarnitine profile were included in the first tier. Second tier tests included chromosomal microarray, genetic testing for *MECP2* and *PTEN* genes. Third tier tests included brain magnetic resonance imaging, serum and urine uric acid. The diagnostic yield of a thorough clinical genetic evaluation for ASD patients was up to 40%.[26]

CNVs were found in sufficiently high frequency influencing ASDs to suggest that cytogenetic and chromosomal microarray be considered in routine clinical workup.[21] A consensus statement has been published in 2010 to advocate chromosomal microarray to be the first tier clinical diagnostic test for individuals with developmental delay/intellectual disability, ASDs or multiple congenital anomalies.[27] Chromosomal array offered a much higher diagnostic yield (15 – 20%) than G-banding karyotype because of its higher sensitivity for submicroscopic deletions and duplications. Performing chromosomal array and karyotyping on every patient substantially increased the total cost of genetic testing. Although truly unbalanced rearrangements and low-level mosaicism were generally not detectable by chromosomal array, these were relatively infrequent causes of abnormal phenotype in this population (<1%).[27]

The increased understanding on the pathophysiology of autism also enhances the development on novel treatment for ASDs. In animal models, treatment by Rapamycin could improve the neurological dysfunction of tuberous sclerosis, which was associated with autism in 20 – 60% of cases.[28] Risperidone ameliorated the targeted repetitive behaviours in the *CNTNAP2* knock-out mice with autistic features.[29] A recent study showed bone marrow transplant can treat the mouse model of Rett syndrome, a X-linked ASD.[30]

Conclusion

The knowledge on the genetics of autism has advanced rapidly in the last two decades. The discovery of genetics in autism greatly enhances our understanding on the disease aetiology. This facilitates the development of appropriate clinical evaluation guidelines and the exploration of novel treatments for ASDs. However, the current understanding on the genetics of autism is incomplete and it is likely that we are just at the beginning to recognise what controls human behaviour. The ongoing research in the genetics of ASDs will continue to provide new insights on the management for ASD patients.

References

1. Diagnostic and Statistical Manual of Mental Disorders IV-TR. Washington, DC: American Psychiatric Association; 2000.
2. Fombonne E. Is there an epidemic of autism? Pediatrics 2001;107:411-412.

3. Chakrabarti S, Fombonne E. Pervasive developmental disorders in preschool children: confirmation of high prevalence. Am J Psychiatry 2005;162:1133-1141.
4. Prevalence of autism spectrum disorders - autism and developmental disabilities monitoring network, 14 sites, United States, 2008. MMWR Surveill Summ 2012;61:1-19.
5. Wong VC, Hui SL. Epidemiological study of autism spectrum disorder in China. J Child Neurol 2008;23:67-72.
6. Eapen V. Genetic basis of autism: is there a way forward? Curr Opin Psychiatry 2011;24:226-236.
7. Bailey A, Le Couteur A, Gottesman I, et al. Autism as a strongly genetic disorder: evidence from a British twin study. Psychol Med 1995;25:63-77.
8. Ritvo ER, Jorde LB, Mason-Brothers A, et al. The UCLA-University of Utah epidemiologic survey of autism: recurrence risk estimates and genetic counseling. Am J Psychiatry 1989;146:1032-1036.
9. Vorstman JA, Staal WG, van Daalen E, van Engeland H, Hochstenbach PF, Franke L. Identification of novel autism candidate regions through analysis of reported cytogenetic abnormalities associated with autism. Mol Psychiatry 2006;11:1, 18-28.
10. Lam CW, Yeung WL, Ko CH, et al. Spectrum of mutations in the MECP2 gene in patients with infantile autism and Rett syndrome. J Med Genet 2000;37:E41.
11. Durand CM, Betancur C, Boeckers TM, et al. Mutations in the gene encoding the synaptic scaffolding protein SHANK3 are associated with autism spectrum disorders. Nat Genet 2007;39:25-27.
12. Jamain S, Quach H, Betancur C, et al. Mutations of the X-linked genes encoding neuroligins NLGN3 and NLGN4 are associated with autism. Nat Genet 2003;34:27-29.
13. Bakkaloglu B, O'Roak BJ, Louvi A, et al. Molecular cytogenetic analysis and resequencing of contactin associated protein-like 2 in autism spectrum disorders. Am J Hum Genet 2008;82:165-173.
14. Carney RM, Wolpert CM, Ravan SA, et al. Identification of MeCP2 mutations in a series of females with autistic disorder. Pediatr Neurol 2003;28:205-211.
15. Harris SW, Hessl D, Goodlin-Jones B, et al. Autism profiles of males with fragile X syndrome. Am J Ment Retard 2008;113:427-438.
16. Identification and characterization of the tuberous sclerosis gene on chromosome 16. Cell 1993;75:1305-1315.
17. Goffin A, Hoefsloot LH, Bosgoed E, Swillen A, Fryns JP. PTEN mutation in a family with Cowden syndrome and autism. Am J Med Genet 2001;105:521-524.
18. Wang K, Zhang H, Ma D, et al. Common genetic variants on 5p14.1 associate with autism spectrum disorders. Nature 2009;459:528-533.
19. Miles JH. Autism spectrum disorders--a genetics review. Genet Med 2011;13:278-294.
20. Jacquemont ML, Sanlaville D, Redon R, et al. Array-based comparative genomic hybridisation identifies high frequency of cryptic chromosomal rearrangements in patients with syndromic autism spectrum disorders. J Med Genet 2006;43:843-849.
21. Marshall CR, Noor A, Vincent JB, et al. Structural variation of chromosomes in autism spectrum disorder. Am J Hum Genet 2008;82:477-488.
22. Glessner JT, Wang K, Cai G, et al. Autism genome-wide copy number variation reveals ubiquitin and neuronal genes. Nature 2009;459:569-573.
23. Pinto D, Pagnamenta AT, Klei L, et al. Functional impact of global rare copy number variation in autism spectrum disorders. Nature 2010;466:368-372.
24. O'Roak BJ, Deriziotis P, Lee C, et al. Exome sequencing in sporadic autism spectrum disorders identifies severe de novo mutations. Nat Genet 2011;43:585-589.
25. Betancur C. Etiological heterogeneity in autism spectrum disorders: more than 100 genetic and genomic disorders and still counting. Brain Res 2011;1380:42-77.
26. Schaefer GB, Mendelsohn NJ. Clinical genetics evaluation in identifying the etiology of autism spectrum disorders. Genet Med 2008;10:301-305.
27. Miller DT, Adam MP, Aradhya S, et al. Consensus statement: chromosomal microarray is a first-tier clinical diagnostic test for individuals with developmental disabilities or congenital anomalies. Am J Hum Genet 2010;86:749-764.
28. Ehninger D, Silva AJ. Rapamycin for treating Tuberous sclerosis and Autism spectrum disorders. Trends Mol Med 2011;17:78-87.
29. Penagarikano O, Abrahams BS, Herman EI, et al. Absence of CNTNAP2 leads to epilepsy, neuronal migration abnormalities, and core autism-related deficits. Cell 2011;147:235-246.
30. Derecki NC, Cronk JC, Lu Z, et al. Wild-type microglia arrest pathology in a mouse model of Rett syndrome. Nature 2012;484:105-109.

5th Certificate Course in Recent Medical Advances for General Practitioners 2012-2013

Jointly organized by
Department of Family Medicine and Primary Care, the University of Hong Kong and
the Family Medicine Division, Hong Kong Sanatorium and Hospital

2012

18/11

Cardiology

Updates on Management of Acute Coronary Syndrome
Dr. KWOK On Hing, Vincent
Director, Cardiac Catheterization and Intervention Centre
Director, Cardiology Centre
Hong Kong Sanatorium & Hospital

Diagnosis and Management of Common Cardiovascular Diseases in General Practice
Dr. HO Hung Kwong, Duncan
Honorary Consultant in Cardiology, Hong Kong Sanatorium & Hospital

Orthopaedics

Latest Development in the Treatment of Osteoarthritis of the Knee
Dr. WU Wing Cheung, Stephen
Head, Department of Orthopaedics & Traumatology
Director, Orthopaedic & Sports Medicine Centre
Hong Kong Sanatorium & Hospital

16/12

Urology

Updates on Management of Urolithiasis
Dr. WONG Wai Sang
Director, Urology Centre
Hong Kong Sanatorium & Hospital

Nephrology

Diagnosis and Management of Common Kidney Diseases
Dr. LAI Kar Neng
Director, Department of Health Assessment
Director, Nephrology Centre
Hong Kong Sanatorium & Hospital

2013

20/1

Endocrinology

Updates on Management of Type 2 Diabetes Mellitus and starting Insulin in Primary Care
Dr. TSUI Yee Ling, Elaine
Assistant Director, Department of Health Assessment
Co-Director, Endocrine & Diabetes Centre
Hong Kong Sanatorium & Hospital

Gastroenterology

Updates on Management of Irritable Bowel Syndrome
Dr. CHAN On On, Annie
Director, Gastroenterology & Hepatology Centre
Hong Kong Sanatorium & Hospital

17/2

Hematology

Updates on Management of Anemia
Dr. LIANG Hin Suen, Raymond
Head, Department of Medicine
Director, Comprehensive Oncology Centre
Director, Haematology Centre
Hong Kong Sanatorium & Hospital

Oncology

Updates on Management of Common Oncology Emergency
Dr. LEUNG Wai Tong, Thomas
Associate Director, Comprehensive Oncology Centre
Hong Kong Sanatorium & Hospital

17/3

Infectious Disease

Updates on Management of Tuberculosis
Dr. TANG Siu Fai, Bone
Honorary Consultant in Microbiology, Hong Kong Sanatorium & Hospital

Paediatrics

Updates on Management of Recurrent Urinary Tract Infections

Updates on Management of Febrile Convulsion
Dr. LOW Chung Kai, Louis
Honorary Consultant in Paediatrics, Hong Kong Sanatorium & Hospital

2013

21/4

Surgery

Updates on Management of Colonic Polyps
Dr. CHAN Chi Wai, Angus
Director, Endoscopy Centre
Associate Director, Surgery Centre
Hong Kong Sanatorium & Hospital

Plastic Surgery

Updates on Management of Burns, Wounds, Facial Lacerations and Scars
Dr. KING Wing Keung, Walter
Director, Plastic & Reconstructive Surgery Centre
Hong Kong Sanatorium & Hospital

19/5

Radiology

Recent Advances in Imaging for Ischemic Heart Diseases
Dr. CHAN Ka Fat, John
Honorary Consultant in Radiology, Hong Kong Sanatorium & Hospital

Recent Advances in Interventional Radiology
Dr. AI Ho Gong, Victor
Honorary Consultant in Radiology, Hong Kong Sanatorium & Hospital

Recent Advances in Imaging applicable to General Practice
Dr. LO GOH, Gladys
Radiologist-in-Charge, Department of Diagnostic & Interventional Radiology
Hong Kong Sanatorium & Hospital

Nuclear Medicine

Application of PET scan in Dementia
Dr. LEUNG Yim Lung, Eric
Deputy Director, Department of Nuclear Medicine & Positron Emission Tomography
Hong Kong Sanatorium & Hospital

Recent Advances in Nuclear Medicine Applicable to General Practice
Dr. WONG Ka Nin
Honorary Consultant in Nuclear Medicine, Hong Kong Sanatorium & Hospital

23/6

Allergy

A selection of Allergy cases
Dr. LEE Tak Hong
Director, Allergy Centre
Hong Kong Sanatorium & Hospital

Food Allergies and Applications of Skin Testing
Ms. June CHAN
Senior Dietitian, Allergy Centre
Hong Kong Sanatorium & Hospital

Dermatology

Dermatology Pictures Quiz
Dr. FUNG Ho Chuen, Alec
Honorary Consultant in Dermatology, Hong Kong Sanatorium & Hospital

Skin Manifestation of Systemic Diseases
Dr. WONG Hok Wai, Wendy
Honorary Consultant in Dermatology, Hong Kong Sanatorium & Hospital

21/7

Ophthalmology

Dry eyes & Eye Emergencies
Dr. LEUNG Yu Lung, Dexter
Honorary Consultant in Ophthalmology, Hong Kong Sanatorium & Hospital

ENT

Neck Mass - Look, Feel & then What?
Dr. WEI, William Ignace
Head, Department of Surgery
Director, Li Shu Pui ENT Head & Neck Surgery Centre
Hong Kong Sanatorium & Hospital

18/8

Respiratory

Updates on Management of Obstructive Lung Disease
Dr. LAM Bing
Director, Respiratory Medicine Centre
Hong Kong Sanatorium & Hospital

O&G

What alerts you that your Patient is Suffering from a Gynaecological Cancer?
Dr. TAM Kar Fai
Honorary Consultant in Obstetrics & Gynaecology, Hong Kong Sanatorium & Hospital

Venue : Auditorium, 4/F, 2 Village Road, Happy Valley, HK, Hong Kong Sanatorium and Hospital
Time : 1:00 - 2:00pm (Lunch), 2:00 - 4:40pm(Lecture)
Fee : HK$300 for the whole course, HK$50 per lecture
Enquiries : 2835 8800 (Tel), 2835 8008 (Fax), hospadm@hksh.com (Email)
Registration Form : Download from HKSH website - http://www.hksh.com/CME.pdf

*Rev. 6/8/2012

Management of Spasticity in Cerebral Palsy: a Child Neurologist's Perspectives

Dr. Chun-hung KO

MMedSc, FHKAM (Paed), FRCP(Glasg)

Paediatric Rehabilitation Unit, Caritas Medical Centre

Dr. Chun-hung KO

Introduction

Spasticity is defined as an upper motor neuron syndrome characterised by velocity dependent increase in muscle tone resulting from hyperexcitability in the stretch reflex.[1] Together with associated weakness and poor motor control, spasticity contributes to significant functional disability to the child with cerebral palsy (CP). The goals for tone reduction treatment include functional improvement, ease of care, and prevention of secondary pain, contractures and orthopaedic problems. In setting treatment goals, the physician should go beyond ordinary clinical assessment and think in the context of the child's activities at home and in school, as well as interests and recreation.[1] For example, over enthusiastic treatment of lower limb spasticity may affect the child in maintaining an erect posture.[1,2]

Evaluation of the child with spasticity

The pattern of body part involvement in spastic CP can be broadly classified into spastic diplegia, hemiplegia, triplegia (one arm relatively spared), and quadriplegia.[1] The Gross Motor Function Classification System (GMFCS) is a useful five-level ordinal grading system, ranging from independent community walker (level 1) to non-ambulant subjects (level 5).[3]

Muscle tone is commonly classified with the modified Asthworth scale, a subjective clinical scale that rates tone from 1 (no hypertonia) to 4 (rigid in flexion and extension). The Tardieu scale is a clinically useful tool in assessing focal spasticity and predict clinical response. In essence, we compare the angle of catch at the most rapid velocity (R1) and the joint angle when the muscle length is maximal in slow passive movement (R2). The difference reflects the relative contribution of spasticity and contracture and the potential gain in range of motion from focal spasticity treatment.[1-3]

Evaluation of the CP child includes not only tone estimation with the above scales, but also measures of motor function and performance. Commonly utilised outcome measure tools include the Gross Motor Function Measure (GMFM), the Functional Independence Measure for Children (WeeFIM), and the Paediatric Evaluation of Disability Inventory (PEDI). Three-dimensional instrumental gait analysis is the gold standard for comprehensive assessment of gait in ambulant CP children. Its use is however largely limited by cost and availability, and limitations such as young age, limited ambulatory ability, and lack of cooperation.[3]

Oral medications for generalised spasticity

Oral antispasticity agents are commonly used for CP children with generalised spasticity. However, most oral medications have been inadequately studied in spastic children. Dose escalation is often limited by significant systemic side effects. Some oral antispasticity medications are summarised in Table 1.[1,2]

Table 1: Oral antispasticity medications

Medication	Mechanism of action	Common dosages	Adverse effects
Baclofen	GABA-B agonist	Starting at 2.5mg/d Titrate to 20-60mg/d	CNS suppression, GI upset, hypotension, weakness
Diazepam	Postsynaptic facilitation of GABA	0.12-0.8mg/kg/d in 3-4 divided doses	Fatigue, respiratory depression, weakness, ataxia, somnolence
Dantrolene sodium	Inibitation of calcium release from muscle sarcoplasmic reticulum	Starting at 0.5mg/kg daily. Maximum 100mg 4 times a day	Asthenia, somnolence, malaise, GI upset, diplopia Hepatoxicity in 1% of patients
Tizanidine	Centrally acting alpha-2 nonadrenergic agonist	Safety and efficacy not yet determined in children	CNS suppression, xerostomia, hypotension

Chemodenervation for focal spasticity

Chemodenervation refers to interruption of nerve-muscle transmission with an injectable agent. At Caritas Medical Centre, we employ two injection strategies, namely perineural injection of phenol and intramuscular injection of botulinum A toxin (BoNT-A). We utilise phenol at a concentration of 6% aqueous solution for perineural injection, resulting in axonal degeneration. The target nerve is identified with electrical stimulation. Sedation is often required in paediatric patients. In the functional limb, the volume of injection can be titrated to eliminate spasticity while retaining desirable function. In nonfunctional extremities, more extensive neurolysis may be employed to facilitate hygiene care and comfort. For example, we often target the musculoskeletal nerve and obturator nerve to alleviate severe elbow flexion and hip adductor spasms in quadriplegic patients. Unlike BoNT-A, in our experience the onset of denervation effect after phenol block is quite instant. The effect is not permanent; clinical benefit varies from a few weeks to nearly one year.[1] Caution should be made when targeting a mixed motor and sensory nerve, which carries a significant risk of pain and paraesthesia. Compared to BoNT-A injection, phenol nerve block is technically demanding, but does not have immunogenic problem and the agent is of much lower cost.[1]

Botulinum toxin is an exotoxin produced by Clostridium botulinum. Therapeutic injection into muscle inhibits synaptic release of acetylcholine, resulting in chemical denervation and focal paralysis.[1,3] Of the eight immunologically distinct serotypes, serotypes A and B are commercially available. BoNT-A is marketed under the trade names of Botox, Dysport and Xeomin. As the potency of a single unit varies greatly among different commercial types and there is no simple inter-brand dose exchange equivalence, it is important to specify the commercial brand in prescribing dosing units.[1,3]

BoNT-A has been used extensively for lower limb spasticity for nearly two decades. A recent international consensus statement reviews randomised controlled trials of BoNT-A therapy in CP children, and formulates appropriate treatment recommendations for the lower limbs. Areas without high levels of evidence, including assessment, outcome measures, adjunctive therapies, recommended doses, dilution, muscle localisation techniques and screening for adverse events are also reviewed. Recommendations are summarised in Table 2.[3]

Table 2: Treatment recommendations of BoNT-A for lower limb spasticity

Choice of assessment tools:

Need to reliably differentiate spasticity from fixed contractures and other causes of hypertonia (level U);

- Modified Tardieu Score and Australian Spasticity Assessment Scale to quantify spasticity

Document GMFCS and baseline functioning such as care needs and gait (level U);

For ambulant children: describe gait and function using appropriate scales ± video recording (level U);

- Instrumental gait analysis is the most objective measure of gait, but its use is largely limited to research context.
- Observational gait analysis and gait classifications are recommended for routine clinical use.

For non-ambulant children: describe abnormal postures and care needs (level U).

Optimal treatment regimen:

BoNT-A is established as effective in the management of spastic equinus to improve gait (level A);

Serial casting is at least as strong as BoNT-A in the management of spastic equinus (level U);

Injections to the adductors is probably effective in some areas of goal attainment (level B);

Injections to the adductors are not effective to improve gross motor function in CP children, but may help to delay hip displacement in the short term (level A);

Injections to multiple lower limb muscles have inadequate and conflicting data in respect of gait, goal attainment and function (level U).

Injection protocols, dose and injection site:

Conversion factors between different preparations of BoNT-A is strongly discouraged (level A);

Dose determination relates to severity, treatment goals, muscle size, and previous treatment response;

Product	Recommended dose	Maximum Total Dose
BOTOX	GMFCS I-IV without risk factors: 16-20U/kg GMFCS V with risk factors: 12-16U/kg (level U)	<400-600U
Dysport	20U/kg (level B)	<900U

Cautious with GMFCS level V and any patient with breathing problems or dysphagia;

Injection interval for serial injections should generally be not less than six months;

Precise localisation of muscle injection sites helps to reduce unwanted toxin migration (level U).

Traditional identification by palpation and anatomical landmark is inaccurate except for the gastrocsoleus. Electrical stimulation is uncomfortable. Ultrasound emerges as the preferred method for localisation (figure 1), with the advantages of being pain-free, quick, and supports real-time visualisation of BoNT-A spread, as well as estimation of muscle size and fibrosis.

Adjunctive interventions:

Serial casting should follow BoNT-A for management of fixed calf contracture (level U);

AFOs help to improve gait and protect foot integrity (level U);

Prolonged stretching assists in management of muscle length (level U);

Strengthening and target motor training are essential adjunctives when goals to improve motor function are identified (level U).

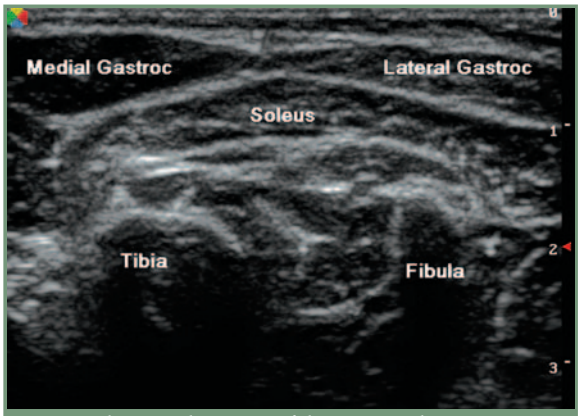


Figure 1: Ultrasound imaging of the gastrocsoleus in a 4 year old diplegic boy.

Selective Dorsal Rhizotomy

Selective Dorsal Rhizotomy (SDR) is a common neurosurgical treatment for moderate to severe lower limb spasticity. The best candidates are children aged between 4 to 8 years, with spasticity predominantly interfering with lower limb mobility, while strength and control are reasonably well preserved.[1] The nerve roots from L2 to S2 are exposed, identified and stimulated separately. Those afferent rootlets that elicit excessive EMG activity are cut. Typically 20 to 70% of rootlets are cut. Classic electrophysiological criteria for posterior rootlet spastic process include a low threshold for response to the single electrical stimulation, a sustained response to the 50-Hz stimulation, and spread of response beyond the segmental level being stimulated. However, the validity of the electrophysiological concept for a good outcome is questioned in recent studies, as there is no evidence supporting that axons with a particular distribution of central connections are segregated together.[4]

Potential complications include intraoperative bronchospasms, transient urinary retention or incontinence, transient dysesthesias, hip subluxations and spinal deformity, especially with multi-level laminectomies in non-ambulatory spastic quadriplegic patients.[4]

A recent systemic review explores the long-term outcomes of SDR as classified according to the International Classification of Functioning, Disability and Health (ICF). There is poor to moderate evidence that SDR has a positive long-term effect on the ICF body structure and function domains, but no evidence of influence on the ICF activity and participation domains.[5] A Cochrane review is underway to determine the effectiveness of SDR in reducing spasticity, improving motor function and reducing the need for subsequent orthopaedic intervention in ambulatory diplegic CP children.[6]

Intrathecal Baclofen

Intrathecal baclofen (ITB) is a treatment for severe focal and generalised spasticity. ITB is delivered to

the intrathecal space via a catheter attached to a pump surgically implanted to the abdomen subcutaneously or subfascially. The required dose is below 1% of the oral dose, minimising the side effect of lethargy. The rate of infusion can further be programmed via telemetry to titrate against observed spasticity and weakness. Transcutaneous refills of baclofen into the pump reservoir are required every 2 to 3 months. A screening trial with bolus injections via lumbar puncture is required to identify potential candidates who demonstrate significant reduction in tone. Complications can be serious, including infection, respiratory failure or coma from overdose, pump failure, kinking or breakage of catheter, and rebound spasticity on abrupt withdrawal.[1,2] In 1996, ITB received FDA approval to treat spasticity of cerebral origin. However, to date there is insufficient evidence to support or refute the use of continuous ITB for the treatment of spasticity in children with CP.[7]

Conclusion

Treatment of spasticity in CP children is challenging, and requires multi-disciplinary input for optimal outcome. While every case is unique, in general orthopaedic surgery should be delayed until the gait is mature.[1] Meanwhile, the range of motion should be maintained by physical therapy and proper splinting. Spasticity may be managed by oral medications, BoNT-A injections, casting, ITB and SDR as indicated. Towards gait maturation at ages 6 to 10 years, instrumental gait analysis can be used to aid decisions for orthopaedic interventions.[1]

References

1. Tilton A. Management of spasticity in children with cerebral palsy. Semin Pediatr Neurol 2009;16:82-89.
2. Flett PJ. Rehabilitation of spasticity and related problems in childhood cerebral palsy. J Paediatr Child Health 2003;39:6-14.
3. Love SC, Novak I, Kentish M et al. Botulinum toxin assessment, intervention and after-care for lower limb spasticity in children with cerebral palsy: international consensus statement. Eur J Neurol 2010;17(Suppl. 2):9-37.
4. Steinbok P. Selective dorsal rhizotomy for spastic cerebral palsy: a review. Child's Nerv Syst 2007;23:981-90.
5. Grunt S, Becher JG, Vermeulen RJ. Longterm outcome and adverse effects of selective dorsal rhizotomy in children with cerebral palsy: a systemic review. Dev Med Child Neurol 2011;53:490-8.
6. Narayanan UG, Howard AW. Selective dorsal rhizotomy in the management of children with spastic cerebral palsy (Protocol). The Cochrane Collaboration, John Wiley & Sons Ltd 2009, pp1-4.
7. Delgado MR, Hirtz D, Aisen M et al. Practice parameter: pharmacologic treatment of spasticity in children and adolescents with cerebral palsy (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology and the Practice Committee of the Child Neurology Society. Neurology 2010;74:336-43.

Physiotherapy Management for Children with Developmental Coordination Disorder

Ms. Rachel SH CHAN

MPhty (paed)
Physiotherapist

Background

Developmental Coordination Disorder (DCD) (Table 1) is a common childhood disorder affecting at least 6% of school age children[1]. It has significant impacts throughout the lifespan of a child if left untreated. Without intervention, the motor difficulties and psychosocial problems of children with DCD persist into adolescence and adulthood[2-7]. With growing awareness of DCD, physiotherapists play an important role in accurately assessing the function, planning a specific treatment and improving the motor coordination of this group of children, and thus improve their activities of daily living and promote active participation in recreational and leisure activities.

Table 1. DCD Diagnostic criteria DSM-IV-TR[1]

(a) "performance in daily activities that require *motor coordination* is substantially *below* that expected, given a person's chronological age and intelligence;

(b) the disturbance… significantly interferes with academic achievement or activities of daily living; and

(c) the disturbance is not due to a general medical condition…. does not meet criteria for a Pervasive Developmental Disorder;

(d) If mental retardation is present, motor difficulties are in excess of those usually associated with it." (DSM-IV-R, p. 56-58).

High levels of overlap of DCD with other developmental disorders, such as Attention Deficit and Hyperactive Disorder (ADHD), Dyslexia, Autism Spectrum Disorder (ASD), Specific Language Impairment and Reading Disorder are well recognised[8-15]. With growing awareness of issues of co-morbidity, complexity and diversity of function in children with DCD, a multidisciplinary team assessment and management for children with DCD is a current trend in both health and education settings[16].

However, parents in Hong Kong usually focus on the learning and communication areas and may not recognise the motor-coordination problems, and thus proper early motor-coordination training will be missed resulting in possible aggravation of physical or psychosocial problems. In fact the discrete DCD features also have big influence on daily activities and academic areas. Therefore, children with ADHD, Dyslexia and ASD, etc. would be benefited from detailed physiotherapy screening of motor coordination problems that may hinder their function, activities or participation, and psychological development.

Problems of children with DCD

With reference to the International classification of Functioning, Disabilities and Health (ICF) framework[17] (Table 2), the problems of children with DCD may be illustrated in these components – body structure and function, activities, participation levels; and personal and environmental factors (Table 3).

Table 2. ICF Framework

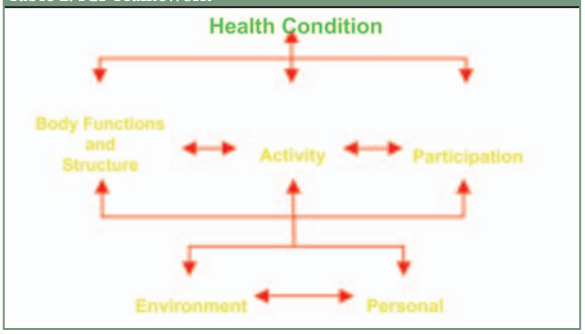


Table 3. Common problems of children with DCD

Body Structure and function:
Deficit in muscle length, visual-motor integration, strength and tone[18]

Function:
Poor fine motor, oral-motor, gross motor skills[19,20]

Participation:
Show withdrawal from physical activity[21]

Impact on the child:
low self-concept, low achievement, and emotional and behavioural difficulties[5, 22, 23]

Physiotherapy Assessment and Intervention

ICF framework can be used as the guideline for assessment. While there are many assessment tools for different components of ICF, only the common clinical assessment tools used by physiotherapists will be illustrated here. To plan the treatment for children with DCD, it requires an accurate full neurodevelopment assessment, so the physiotherapist could evaluate each child's specific and unique combination of functional difficulties.

Movement ABC (M-ABC) or Bruininks-Oseretsky Motor Proficiency Test is commonly used standardized test for diagnostic and evaluative purpose for children with DCD. For example, M-ABC consists of eight items grouped under manual dexterity, ball skills and balance. According to the norms of the M-ABC test, scoring

at or below the 5th percentile suggests definite motor impairment, scoring between 6th and 15th percentile indicates at risk of motor impairment. However, the standardized tests may not provide sufficient information to understand causes of the dysfunction in order to plan the intervention[24].

Neurodevelopmental Physiotherapy Assessment

Many physiotherapists in Hong Kong follow the Neurodevelopmental Physiotherapy Assessment (Table 4) developed by Watter[18]. It assesses sensory and neuromotor performance, which represents the body structure/functions and activities components of the ICF. For the participation component, an interview with the child and parents is essential to understand the child's limitation in this area.

Table 4. Neurodevelopmental Physiotherapy Assessment

Focal neurological signs
muscle tone, reflexes, clonus, associated reactions, tremor
Primitive Movements
extensor thrust, asymmetric tonic neck reflex, symmetric tonic neck reflex, tonic labyrinthine reflex
Sensorimotor Function
tactile, proprioception, vestibular, ocular-motor, motor planning, diadochokinesia, crossing midline, auditory sequence, fine and gross motor performance
Postural Control and Balance
weight shift, positive support, righting reactions, protective reactions, equilibrium reactions
Musculoskeletal Features
Range of Movement and muscle length, deformity, alignment

Common features of children with DCD

Focal neurological signs

Low muscle tone is the common problem for children with DCD which affects the strength, endurance and posture of the child. Also associated and synkinetic reactions may be increased due to inadequate suppression or inhibition of unwanted movements.

Primitive Movements

The immature movements commonly persist in the DCD population, such as, extensor thrust, asymmetric tonic neck reflex, symmetric tonic neck reflex, tonic labyrinthine reflex. These patterns could be elicited by more advanced test positions rather than the classical infant tests. The primitive patterns may appear in the sitting or standing position and thus affecting the posture, e.g. tip-toe walking and slump sitting.

Postural Control and Balance

Abnormal postural response is a common problem of children with DCD. They may trip or fall easily, or they act too fast or jerky, or they react too slowly with resultant clumsiness.

Sensorimotor Aspects

When a child has tactile problems, he may have difficulties in interpreting different levels of input; for example, if he may not be sensitive to pain, he may be clarified as aggressive when he does not feel how hard he is touching or hugging others. When proprioception is fair, the child may fall over easily and he shows difficulty in copying a position even with proprioceptive guidance. Again fair vestibular sense leads to balance and postural control problems; and with its close interaction with the visual system, reading speed is commonly slower. Another important system for balance is the ocular-motor system. Apart from influence on balance, fair visual tracking, visual fixation/release, fair dissociation of eye and head movement will affect the ball skill development and classroom activities. Motor planning is also a common difficulty for children with DCD in that they may not able to plan or organise movements shown to them, which will have an impact on classroom behaviour as well.

Musculoskeletal Features

Scoliosis and foot abnormalities are common deformities that many children with DCD present including hip flexors tightness, hamstring tightness, or other postural problems such as thoracic kyphosis. Overuse of some muscles for stability may increase the restlessness and fidgeting in sitting and thus affects their classroom concentration.

Intervention

The specific treatment plan is guided by the detailed assessment. Following the assessment, physiotherapists can understand how the various problems interact with each other, establishing the underlying factors and thus how to plan a specific tailored-made treatment programme. Also, the activities designed are continually tailored to the child to ensure he/she is optimally challenged. For instance, optimal writing performance should concur with stable sitting balance, shoulder stability and rapid repetitive and dissociated finger movements. Optimal postural reaction and balance should concur with good interaction between proprioception, vestibular and ocular-motor senses. Optimal reading speed should concur with good visual track, vestibulo-ocular reflex and stabilisation of head.

There are several treatment philosophies, such as bottom-up or top-down approaches. Examples of bottom-up approaches are the process-oriented treatment approach, and perceptual motor training; while two commonly used top-down approaches are task-specific intervention and cognitive approaches. Physiotherapists usually adopt an eclectic approach, for example, bottom up approach to improve the child's balance, strength or intersensory processing; and top-down approach to teach specific tasks such as skipping and riding a bicycle. However, it is quite common that after the improvement in body functions and structures, activity limitations and participation restrictions would be reduced.

Furthermore, parents' education and communication with teachers are also the important roles of physiotherapists, so that the right level of expectation would be given to the children with DCD. In turn, parents and teachers could accept the child's strengths and weaknesses and assist him/her to adjust according to different situations or contexts; or to overcome the obstacles so as to minimise the secondary psychological or behavioural problems.

Conclusion

Children with DCD often demonstrate motor coordination difficulties which significantly interfere

with their daily activities and academic achievement. With the overlapping pictures of developmental disorders, timely identification with a multidisciplinary team approach is the global trend in the management of children with DCD; and collaborations amongst parents, health professionals and teachers are imperative. Therefore, the role of physiotherapists is essential in accurately assessing and specifically treating the motor coordination of this group of children to yield a good outcome and to prevent the secondary emotional, behavioural and social problems.

References

1. American Psychiatric Association. (2000). Diagnostic and Statistical Manual of Mental Disorders: DSM-IV-R (Rev. 4th ed.). Washington, DC: Author.
2. Cantall M. H., Smyth M. M. & Ahonen T. P. (1994). Clumsiness in adolescence: Educational, motor, and social outcomes of motor delay detected at 5 years. Adapted Physical Activity Quarterly, 11, 115-129.
3. Geuze R. H., Borger H. (1993). Children who are clumsy: five years later. Adapted Physical Activity Quarterly, 10, 10-21.
4. Gillberg I. C. & Gillberg C. (1989). Children with preschool minor neurodevelopmental disorders. IV: Behaviour and school achievement at age 13. Developmental Medicine and Child Neurology, 31, 3-13.
5. Loose A., Henderson S. E., Elliman D., Hall D., Knight E. & Jongmans M. (1991). Clumsiness in Children – do they grow out of it? A 10-year follow-up study. Developmental Medicine and Child Neurology, 33, 55-68.
6. Gillberg I. C., Gillberg C. & Groth J. (1989). Children with preschool minor neurodevelopmental disorders. V. Neurodevelopmental profiles at age 13. Developmental Medicine and Child Neurology, 31, 14-24.
7. Hellgren L., Gillberg C., Gillberg I. C. & Enerskog I. (1993). Children with deficits in attention, motor control and perception (DAMP) almost grown up: general health at 16 years. Developmental Medicine and Child Neurology, 35, 881-892.
8. Pitcher, T. M., Piek, J. P. & Hay, D. A. (2003) Fine and gross motor ability in males with ADHD. Developmental Medicine and Child Neurology, 45, 525-35.
9. Rasta, S. P. & Eliot, J. (1999). Written expression in boys with attention deficit hyperactivity disorder. Developmental Medicine and Child Neurology, 41, 159-65.
10. Kaplan, B. J., Crawford, S. G., Wilson, B. N. & Dewey, D. (1997). Comorbidity of developmental coordination disorder and different types of reading disability. Journal of Internal Neuropsychological Society, 3, 54.
11. Hill, E. L. (1998). A dyspraxic deficit in specific language impairment and developmental coordination disorder? Evidence from hand and arm movements. Developmental Medicine and Child Neurology, 40, 388-95.
12. Dewey, D., Kalpan, B., et al. (2002). Developmental coordination disorder: associated problems in attention, learning and psychosocial adjustment. Human Movement Science, 21, 905-918.
13. Fox, A.M., & Lent, B. (1996). Clumsy children primer on developmental coordination disorder. Canadian Family Physician, 42, 1965-1971.
14. Henderson, S. E. & Sugden, D. (1982). Concomitants of clumsiness in young school children. Developmental Medicine and Child Neurology, 24, 448-460.
15. Kadejo, B., & Gillberg, C. (1999). Developmental coordination disorder in Swedish 7 year-old children. Journal of the American Academy of Child and Adolescent Psychiatry, 38, 820-828.
16. Watter P, Rodger S, Marinac J, Woodyatt G, Ziviani J, Ozanne A. (2008). Multidisciplinary assessment of children with developmental coordination disorder: using the ICF framework to inform assessment. Physiotherapy and Occupational Therapy in Pediatrics, 28(4), 331-52.
17. World Health Organization (2001). International classification of functioning, disability and health. Geneva: World Health Organization.
18. Watter P (1996). Physiotherapy management of children-minor coordination dysfunction. In YR Burns and J. MacDonald (Eds.), Physiotherapy and the Growing Child (pp, 415-436). London: W.B. Saunders Co Ltd.
19. Cermak, S.A., Gubbay, S.S., & Larkin, D. (2002). What is Developmental Coordination Disorder? In Cermak, S.A. & Larkin, D. (Eds). Developmental Coordination Disorder. Canada: Thomson Learning, 365p.
20. Hill, E.L. (2001). Non-specific nature of specific language impairment: A review of the literature with regard to concomitant motor impairments. International Journal of Language and Communication disorders, 36, 149-171.
21. Bouffard M., Watkinson E. J., Thompson L. P., Causgrove Dunn J. L. & Romanow S. (1996). A test of the activity deficit hypothesis with children with movement difficulties. Adapted Physical Activity Quarterly, 13, 61-73.
22. Henderson S. E. & Sugden D. A. (1992). Movement Assessment Battery for Children. London: Psychological Corporation.
23. Skinner R. A. & Piek J. P. (2001). Psychosocial implications of poor motor coordination in children and adolescents. Human Movement Science, 20(1-2), 73-94.
24. Johnston L. & Watter P (2006). Clinimetrics: Movement Assessment Battery for Children. Australian Journal of Physiotherapy, 52, 68.

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
						* MPS Workshop – Mastering Your Risk **1**
* HKMA Dragon Boat Team – Summer Vigor 2012 Mini Dragon Boat Races * Joint Professional Badminton Tournament 2012 * Joint Professional Basketball Tournament 2012 (Semi-final) * MPS Workshop – Mastering Difficult Interactions with Patients **2**	* Adrenal Nodules – When is it significant? **3**	* HKMA CME – The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 4) * FMSHK Officers' Meeting * HKMA Council Meeting **4**	* HKMA Shatin Doctors Network – Update on Spine Examination and Investigation * MPS Workshop – Mastering Professional Interactions **5**	* HKMA NTW Community Network - Cause and Treatment of Allergic Rhinitis and Other Allergies * MPS Workshop – Mastering Shared Decision Making **6**	* Joint Surgical Symposium - Recent Advances in Vascular and Endovascular Surgery **7**	* Refresher Course for Health Care Providers 2012/2013 * MPS Workshop – Mastering Adverse Outcomes **8**
* HKMA Badminton Tornament 2012 * MPS Workshop – Mastering Shared Decision Making **9**	**10**	* HKMA Kowloon West Community Network - 3rd Annual Meeting cum CME Lecture on Updated Management on Airway Diseases **11**	* MEDICAL FAIR ASIA 2012 – 8th International Exhibition on Hospital, Diagnostic, Pharmaceutical, Medical & Rehabilitation Equipment & Supplies * Hong Kong Neurosurgical Society Monthly Academic Meeting –The Merits of Endoscopic-assisted Minimally Invasive Neurosurgery * HKMA Shatin Doctors Network – Practical Tips on Knee Examination and Case Sharing **12**	* MEDICAL FAIR ASIA 2012 – 8th International Exhibition on Hospital, Diagnostic, Pharmaceutical, Medical & Rehabilitation Equipment & Supplies * HKMA NTW Community Network- Cause and Treatment of Asthma and COPD * HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2012 – Update on female urinary incontinence * Clinical Meeting (1) Who digs the holes? (2) One in Four **13**	* MEDICAL FAIR ASIA 2012 – 8th International Exhibition on Hospital, Diagnostic, Pharmaceutical, Medical & Rehabilitation Equipment & Supplies * HKMA Yau Tsim Mong Community Network –Moving to HPV Gender Neutral Vaccination * Free Intro Talk - BodyTalk Fundamentals Seminar (Module 1&2) **14**	* MPS Workshop – Mastering Shared Decision Making **15**
* HKMAPS 3rd Seasonal Photo Competition * Joint Professional Basketball Tournament 2012 (Final) * MPS Workshop Mastering Your Risk **16**	**17**	* HKMA Kowloon City Community Network – BPH Management: Not only Focus on Prostate? * HKMA CME – The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 5) **18**	* HKMA Golf Tornament 2012 * HKMA Shatin Doctors Network – Shoulder Examination: Something Not to Miss * HKMA Yau Tsim Mong Community Network – Clinical Nephrology Update 2012 (Session 5) * MPS Workshop – Mastering Difficult Interactions with Patients **19**	* HKMA NTW Community Network - Paediatrics Asthma and AHR * HKMA CME – Certificate Course for GPs 2012 * FMSHK Executive Committee Meeting **20**	**21**	* MPS Workshop – Mastering Your Risk **22**
* 2012 Paediatric Update No. 2 – Recent Advances in Paediatric Surgery * HKMA Badminton Tornament 2012 * MPS Workshop – Mastering Difficult Interactions with Patients * HKMA Tennis Tornament 2012 **23**	**24**	* HKMA Kowloon West Community Network - Role of Combination Treatment in BPH * HKMA Tai Po CME – A New Insight in Anticoagulation Therapy in Non-valvular AF patient – Role of Direct Xa Inhibitor * HKMA CME – The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 1) **25**	* HKMA CW&S Community Network - The Benefits of Incretin -based Therapy * HKMA Shatin Doctors Network – Practical Minor Orthopaedic Operation in Clinic * MPS Workshop – Mastering Professional Interactions **26**	* HKMA Kowloon East Community Network- Right Treatment, Right Patient and Right Prostate **27**	**28**	* YTM Community Network – Certificate Course on Bringing Better Health to Our Community (Session 5) * MPS Workshop – Mastering Adverse Outcomes * BodyTalk Fundamantals Seminar (Module 1 & 2) -Certification for BodyTalk Practitioner (to Oct 2) **29**
* BodyTalk Fundamantals Seminar (Module 1 & 2) * HKMA Tennis Tornament 2012 **30**						

Date / Time	Function	Enquiry / Remarks
1 SAT 2:00 pm	**MPS Workshop – Mastering Your Risk** Organiser: The Hong Kong Medical Association, Speaker: Dr. HAU Ka Lam, Venue: Level B3, Holiday Inn Golden Mile Hong Kong	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
2 SUN 9:00 am	**HKMA Dragon Boat Team – Summer Vigor 2012 Mini Dragon Boat Races** Organiser: The Hong Kong Medical Association, Venue: Sai Kung	Miss Phoebe WONG Tel: 2527 8285
12:00 noon	**Joint Professional Badminton Tournament 2012** Organiser: The Hong Kong Medical Association, Venue: SYS Memorial Park Sports Centre	Miss Phoebe WONG Tel: 2527 8285
2:00 pm	**Joint Professional Basketball Tournament 2012 (Semi-final)** Organiser: The Hong Kong Medical Association	Miss Phoebe WONG Tel: 2527 8285
2:00 pm	**MPS Workshop – Mastering Difficult Interactions with Patients** Organiser: The Hong Kong Medical Association, Speaker: Dr. CHENG Ngai Sing, Justin, Venue: Level B3, Holiday Inn Golden Mile Hong Kong	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
3 MON 7:30 pm	**Adrenal Nodules – When is it significant?** Organiser: Hong Kong Urological Association, Chairman: Dr. SUN Wai Ho, Speakers: Dr. Bill WONG, Dr. CHAN Yu Leung & Dr. SIU Kam Wang, Venue: Multi-disciplinary Simulation and Skills Centre, 4/F Block F, QEH	Dr. HUNG Hing Hoi Ms. Tammy HUNG Tel:2958 6006 1 CME point
4 TUE 1:30 pm	**HKMA CME – The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 4)** Organiser: The Hong Kong Medical Association, Speaker: Mr. CHOW Jacky, Venue: Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, NT	Ms. Viviane LAM Tel: 2527 8452 2 CME points
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
8:00 pm	**HKMA Council Meeting** Organiser: The Hong Kong Medical Association, Chairman: Dr. TSE Hung Hing, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Ms. Christine WONG Tel: 2527 8285
5 WED 1:00 pm	**HKMA Shatin Doctors Network – Update on Spine Examination and Investigation** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. NG Wing Kit, Venue: Suite 709, The One Grand Tower, 639 Nathan Road, Mongkok, Kowloon	Miss Candice TONG Tel: 2527 8285 1 CME point
6:30 pm	**MPS Workshop – Mastering Professional Interactions** Organiser: The Hong Kong Medical Association, Speaker: Dr. LEE Wai Hung, Danny, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
6 THU 1:00 pm	**HKMA NTW Community Network - Cause and Treatment of Allergic Rhinitis and Other Allergies** Organiser: HKMA NTW Community Network, Chairman: Dr. WONG Yu Man, James, Speaker: Dr. HO Fung, Venue: Plentiful Delight Banquet, 1/F, Ho Shun Tai Building, 10 Sai Ching Street, Yuen Long	Mr. Alan LAW Tel: 2527 8285 1 CME point
6:30 pm	**MPS Workshop – Mastering Shared Decision Making** Organiser: The Hong Kong Medical Association, Speaker: Dr. CHENG Ngai Sing, Justin, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
7 FRI 8:00 am	**Joint Surgical Symposium - Recent Advances in Vascular and Endovascular Surgery** Organiser: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Chairman: Prof. Stephen CHENG, Speakers: Dr. Chan Yiu-Che & Dr. Wong Chiu-Cheuk, Venue: Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 1 CME point
8 SAT 2:30 pm	**Refresher Course for Health Care Providers 2012/2013** Organiser: The Hong Kong Medical Association, Speaker: Dr. TAM Cheuk Kwan, 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
2:30 pm	**MPS Workshop – Mastering Adverse Outcomes** Organiser: The Hong Kong Medical Association, Speaker: Dr. LEUNG Kwok Ling, Ares, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
9 SUN 1:00 pm	**HKMA Badminton Tornament 2012** Organiser: The Hong Kong Medical Association, Venue: MacLehose Medical Rehabilitation Centre, 7 Sha Wan Drive, Pokfulam	Miss Phoebe WONG Tel: 2527 8285
2:30 pm	**MPS Workshop – Mastering Shared Decision Making** Organiser: The Hong Kong Medical Association, Speaker: Dr. FUNG Shu Yan, Anthony, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
11 TUE 1:00 pm	**HKMA Kowloon West Community Network - 3rd Annual Meeting cum CME Lecture on Updated Management on Airway Diseases** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. TONG Kai Sing, Speaker: Dr. LAM Bing, Venue: Crystal Room I-III, 30/F, Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, NT	Miss Candice TONG Tel: 2527 8285 1 CME point
12 WED *(13-14)*	**MEDICAL FAIR ASIA 2012 – 8th International Exhibition on Hospital, Diagnostic, Pharmaceutical, Medical & Rehabilitation Equipment & Supplies** Organiser: Messe Düsseldorf Asia Pte Ltd, Venue: Suntec, Singapore	Miss Lucinda CHIU Miss Natalie TSANG Tel: 2838 3183
7:30 am	**Hong Kong Neurosurgical Society Monthly Academic Meeting –The Merits of Endoscopic-assisted Minimally Invasive Neurosurgery** Organiser: Hong Kong Neurosurgical Society, Chairman: Dr. TSE Yat Hang, Speaker: Dr. CHENG King Fai, Kevin, Venue: Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital	Dr. Gilberto LEUNG Tel: 2255 3368 1.5 CME points
1:00 pm	**HKMA Shatin Doctors Network – Practical Tips on Knee Examination and Case Sharing** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. CHAN Wai Fu, Venue: Suite 709-711, One Grand Tower, 639 Nathan Road, Mongkok	Miss Candice TONG Tel: 2527 8285 1 CME point

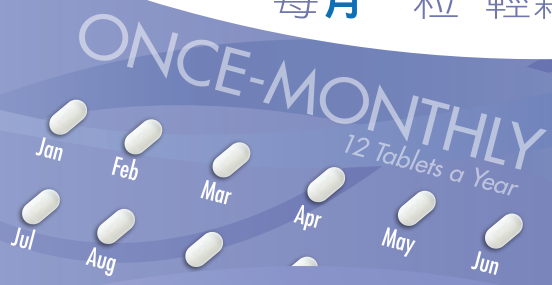
Date / Time	Function	Enquiry / Remarks
13 THU 1:00 pm	**HKMA NTW Community Network- Cause and Treatment of Asthma and COPD** Organiser: HKMA-New Territories West Community Network, Chairman: Dr. LEE Huen, Speaker: Dr. CHAN Chio Ho, Michael, Venue: Plentiful Delight Banquet, 1/F, Ho Shun Tai Building, 10 Sai Ching Street, Yuen Long	Mr. Alan LAW Tel: 2527 8285 1 CME point
2:00 pm	**HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2012 – Update on female urinary incontinence** Organiser: The Hong Kong Medical Association, Speaker: Dr. LAU Nga Ting, Winnie, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 1 CME point
6:30 pm	**Clinical Meeting (1) Who digs the holes? (2) One in Four** Organiser: Hong Kong Thoracic Society & American College of Chest Physicians (HK & Macau Chapter), Chairmen: Dr. LIU Wai To, Raymond & Dr. LO Ho Yin, Speakers: Dr. WAN Chi Kin, Raymond & Dr. CHIU Pui Hing, Venue: LG1, Lecture Room, Ruttonjee Hospital	Dr. Fanny Wai San KO Dr. Arthur Chun Wing LAU Tel: 2632 2785 1.5 CME points (HKCP) 2 CME points (HKCFP) 1.5 CME points (CSHK)
14 FRI 1:00 pm	**HKMA Yau Tsim Mong Community Network –Moving to HPV Gender Neutral Vaccination** Organiser: HKMA Yau Tsim Mong Community Network, Speaker: Dr. LI Chiu Fai, Ivy, Venue: Eaton Smart, Hong Kong, 380 Nathan Road, Kowloon	Miss Candice TONG Tel: 2527 8285
6:30 pm - 7:30 pm	**Free Intro Talk - BodyTalk Fundamentals Seminar (Module 1&2)** Venue: Holistic Central 13F1, Asia Standard Tower, 59-65 Queen's Rd, Central (BodyTalk Fundamentals Seminar on Sep 29,30, Oct 1&2) www.bodytalksystem.com.hk	Ms. Angie TOURANI Tel: 6683 2755
15 SAT 2:00 pm	**MPS Workshop – Mastering Shared Decision Making** Organiser: The Hong Kong Medical Association, Speaker: Dr. FUNG Shu Yan, Anthony, Venue: Level B3, Holiday Inn Goden Mile Hong Kong	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
16 SUN 2:00 pm	**HKMAPS 3rd Seasonal Photo Competition** Organiser: The Hong Kong Medical Association, Venue: HKMA Head Office (5/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong)	Miss Phoebe WONG Tel: 2527 8285
2:00 pm	**Joint Professional Basketball Tournament 2012 (Final)** Organiser: The Hong Kong Medical Association,	Miss Phoebe WONG Tel: 2527 8285
2:30 pm	**MPS Workshop Mastering Your Risk** Organiser: The Hong Kong Medical Association, Speaker: Dr. CHEUNG Kit Ying, Andy, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
18 TUE 1:00 pm	**HKMA Kowloon City Community Network – BPH Management: Not only Focus on Prostate?** Organiser: HKMA Kowloon City Community Network, Speaker: Dr. HO Shing Chee, Sammy, Venue: Spotlight Recreation Club, Hung Hom	Miss Candice TONG Tel: 2527 8285 1 CME point
1:30 pm	**HKMA CME – The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 5)** Organiser: The Hong Kong Medical Association, Speaker: Prof. Stanley HUI or Mr. Sam WONG, Venue: Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, NT	Ms. Viviane LAM Tel: 2527 8452 2 CME points
19 WED 11:33 am	**HKMA Golf Tornament 2012** Organiser: The Hong Kong Medical Association, Venue: Eden Course, Hong Kong Golf Club, Fanling	Miss Phoebe WONG Tel: 2527 8285
1:00 pm	**HKMA Shatin Doctors Network – Shoulder Examination: Something Not to Miss** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. TIO Man Kwun, Peter, Venue: Suite 709-711, One Grand Tower, 639 Nathan Road, Mongkok	Miss Candice TONG Tel: 2527 8285 1 CME point
1:00 pm	**HKMA Yau Tsim Mong Community Network – Clinical Nephrology Update 2012 (Session 5)** Organiser: HKMA Yau Tsim Mong Community Network, Queen Elizabeth Hospital and Hong Kong Nephrology Group, Chairman: Dr. YUNG Chee Unn, Jonathan, Speaker: Dr. CHEUNG Chi Yuen, Simon; Dr. CHAN Yiu Han, John, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital, 30 Gascoigne Road, Kowloon, Hong Kong	Miss Candice TONG Tel: 2527 8285 1 CME point
6:30 pm	**MPS Workshop – Mastering Difficult Interactions with Patients** Organiser: The Hong Kong Medical Association, Speaker: Dr. CHENG Ngai Sing, Justin, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
20 THU 1:00 pm	**HKMA NTW Community Network - Paediatrics Asthma and AHR** Organiser: HKMA NTW Community Network, Chairman: Dr. CHUNG Siu Kwan, Ivan, Speaker: Dr. CHENG Man Yung, Venue: Plentiful Delight Banquet, 1/F, Ho Shun Tai Building, 10 Sai Ching Street, Yuen Long	Mr. Alan LAW Tel: 25278285 1 CME point
1:00 pm	**HKMA CME – Certificate Course for GPs 2012** Organiser: The Hong Kong Medical Association, Chairman: Dr. David CHAO Vai Kiong, Speaker: Dr. David LUK Chi Kong, Venue: East Ocean Seafood Restaurant, Shop 137, 1/F, Metro City Plaza 3, Mau Yip Road, Tseung Kwan O, Kowloon	Ms. Gary WONG Tel: 3513 4821 1 CME point
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
22 SAT 2:30 pm	**MPS Workshop – Mastering Your Risk** Organiser: The Hong Kong Medical Association, Speaker: Dr. HAU Ka Lam, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
23 SUN	**2012 Paediatric Update No. 2 – Recent Advances in Paediatric Surgery** Organiser: Hong Kong College of Paediatricians, Chairmen: Dr. WONG Sik-nin & Dr. Kelvin LIU, Speakers: Dr. Patrick CHUNG, Dr. Jennifer SIHOE, Dr. Michael LEUNG & Dr. Kelvin LIU, Venue: Hospital Authority Head Office M Floor, Lecture Theatre	Hong Kong College of Paediatricians Tel: 2871 8773 3 CME points (Category A)
1:00 pm	**HKMA Badminton Tornament 2012** Organiser: The Hong Kong Medical Association, Venue: MacLehose Medical Rehabilitation Centre, 7 Sha Wan Drive, Pokfulam	Miss Phoebe WONG Tel: 2527 8285
2:00 pm	**MPS Workshop – Mastering Difficult Interactions with Patients** Organiser: The Hong Kong Medical Association, Speaker: Dr. CHENG Ngai Sing, Justin, Venue: Level B3, Holiday Inn Golden Mile Hong Kong	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
8:00 pm	**HKMA Tennis Tornament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club, 113A Waterloo Road, Kowloon	Miss Phoebe WONG Tel: 2527 8285

Date / Time	Function	Enquiry / Remarks
25 TUE 1:00 pm	**HKMA Kowloon West Community Network - Role of Combination Treatment in BPH** Organiser: HKMA Kowloon West Community Network, Chairman: Dr. CHAN Siu Man, Bernard, Speaker: Dr. CHAN Kwok Keung, Sammy, Venue: Crystal Room IV-VI, 3/F., Panda Hotel, 3 Tsuen Wah Street, Tsuen Wan, N.T.	Miss Candice TONG Tel: 2527 8285
1:30 pm	**HKMA Tai Po CME – A New Insight in Anticoagulation Therapy in Non-valvular AF patient – Role of Direct Xa Inhibitor** Organiser: HKMA Tai Po, Speaker: Dr. LAI Wai Keung, Steve, Venue: Chiu Chow Garden, Shops 001-003, 1/F, Uptown Plaza, Tai Po, NT	Ms. Sabrina CHANG Tel: 8200 2187 1.5 CME points
1:30 pm	**HKMA CME – The Hong Kong Medical Association Community Network Exercise Prescription Courses (Session 1)** Organiser: The Hong Kong Medical Association, Speaker: Prof. IP Wing Yuk, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2 CME points
26 WED 1:00 pm	**HKMA CW&S Community Network - The Benefits of Incretin-based Therapy** Organiser: HKMA CW&S Community Network, Chairman: Dr. LAW Yim Kwai, Speaker: Dr. CHOW Wing Sun, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Mr. Alan LAW Tel: 25278285 1 CME point
1:00 pm	**HKMA Shatin Doctors Network – Practical Minor Orthopaedic Operation in Clinic** Organiser: HKMA Shatin Doctors Network, Chairman: Dr. MAK Wing Kin, Speaker: Dr. CHAN Wai Fu; Dr. TIO Man Kwun, Peter; Dr. NG Wing Kit, Venue: Suite 709-711, One Grand Tower, 639 Nathan Road, Mongkok	Miss Candice TONG Tel: 2527 8285 1 CME point
6:30 pm	**MPS Workshop – Mastering Professional Interactions** Organiser: The Hong Kong Medical Association, Speaker: Dr. CHEUNG Kit Ying, Andy, Venue: HKMA Central Premises, 2/F. Chinese Club Building, 21-22 Connaught Road Central, HK	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
27 THU 1:00 pm	**HKMA Kowloon East Community Network- Right Treatment, Right Patient and Right Prostate** Organiser: HKMA Kln East Community Network, Chairman: Dr. MA Ping Kwan, Danny, Speaker: Dr.FUNG Tat Chow, Berry, Venue: East Ocean Seafood Restaurant, Tseung Kwan O	Mr. Alan LAW Tel: 2527 8285 1 CME point
29 SAT 1:00 pm	**YTM Community Network – Certificate Course on Bringing Better Health to Our Community (Session 5)** Organiser: YTM Community Network and Department of Family Medicine & General Outpatient Clinic and Department of Medicine, Kowloon Central Cluster, Speaker: Dr. FONG Wing Chi; Dr. HO Chung Ping, MH, JP, Venue: Block M, Lecture Theatre, Queen Elizabeth Hospital,30 Gascoigne Road, Kowloon, Hong Kong	Miss Candice TONG Tel: 2527 8285
2:00 pm	**MPS Workshop – Mastering Adverse Outcomes** Organiser: The Hong Kong Medical Association, Speaker: Dr. LEUNG Kwok Ling, Ares, Venue: Level B3, Holiday Inn Goden Mile Hong Kong	Ms. Viviane LAM Tel: 2527 8452 2.5 CME points
29, 30, Oct 1& 2	**BodyTalk Fundamantals Seminar (Module 1 & 2)** Certification for BodyTalk Practitioner, Venue: White Lotus Center, Central (BodyTalk Free Introductory talk on 14th Sept at Holistic Central) www.bodytalksystem.com.hk	Ms. Angie TOURANI Tel: 6683 2755
30 SUN 8:00 pm	**HKMA Tennis Tornament 2012** Organiser: The Hong Kong Medical Association, Venue: Kowloon Tong Club, 113A Waterloo Road, Kowloon	Miss Phoebe WONG Tel: 2527 8285

Upcoming Meeting

27-28/10/2012	**20th Annual Scientific Meeting of Hong Kong College of Radiologists** Organiser: Hong Kong College of Radiologists, Venue: Hong Kong Academy of Medicine Jockey Club Building, 99 Wong Chuk Hang Road, Aberdeen, Hong Kong	Hong Kong College of Radiologists Tel: 2871 8788

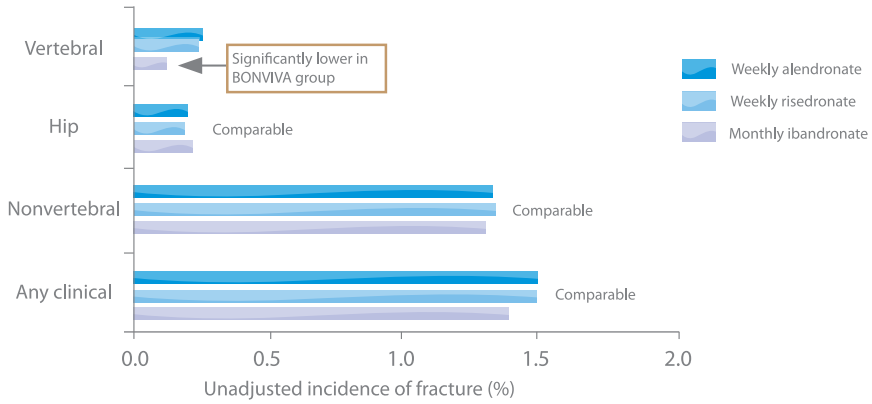
Bonviva® 邦維亞
ONCE-MONTHLY
ibandronic acid
There's only one
每月一粒 輕鬆護骨



The VIBE* Study

Proven efficacy: Once-monthly Bonviva vs. weekly bisphosphonates (BP)

One year retrospective observational fracture study[1]



Bonviva-treated patients had statistically lower incidence of vertebral fractures.[1]

BONVIVA
66%
significant lower risk vs. Alendronate (p=0.004)

BONVIVA
61%
significant lower risk vs. Risedronate (p=0.014)

*The eValuation of IBandronate Efficacy (VIBE) study was a retrospective claims database study with a 12-month observational period that included women ≥45 years of age (n=64,182), newly prescribed monthly oral ibandronate (Bonviva) (n=7345) or weekly oral BPs (alendronate 35 mg or 70 mg, or risedronate 35 mg) (56,837) for a period between April 1, 2005 and December 31, 2005.

Ref:1. Bone. 2009;44:758–765.

Full prescribing information available upon request

Takeda Pharmaceuticals (Hong Kong) Limited
Unit 3706-8, 37/F, AIA Tower 183 Electric Rd North Point Hong Kong 香港北角電氣道183號友邦廣場37樓3706-8室
Tel: 2133 9800 Fax: 2856 2728

HK/ML/BON/10/07-2011