An Update of Paediatric Neurological Disorders
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Editorial
- Editorial
  Dr Mario WK CHAK

Medical Bulletin
- Paediatric Cushing’s Disease
  Dr Eunice WY WONG & Dr Lap-ming WONG
- Autism Spectrum Disorder
  Dr Quinney KN CHAN
- MCHK CME Programme Self-assessment Questions
- A Family-based Sport and Nutrition Programme for People with Intellectual and Developmental Disabilities in Hong Kong
  Ms Sally SP POON, Ms Violet Hon MAN, Mr Charles MC LAW, Mr Kam-hung TAM & Ms Tsau-jin CHENG
- What are the Treatment Options for Paediatric Drug-resistant Epilepsy?
  Dr Mario WK CHAK
- Spina Bifida Occulta: When to Look for It and How to Manage?
  Dr Sui-To WONG
- Ketogenic Diet for Epilepsy and Other Medical Conditions
  Ms Candy SM WONG

Special Article
- Dermatology Quiz
  Dr Chi-keung KWAN

Medical Diary of July

Calendar of Events

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The Cover Shot

We have a lot to learn from flowers. They do not spend their time on weeds and predators around them, nor yield to difficulties. Like the sunflower, its goal is to find its way up for the sun so as to survive. "Keep your face to the sunshine and you cannot see the shadow. It’s what sunflowers do.” said Helen Keller. Be like a sunflower. Stand tall and stay focused. Accept who we are and open up ourselves to challenges. The might to survive will become unbendable strength. Time kneels before this might.

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Editor

It is my great pleasure to serve as the Issue Editor of this July issue
of the Hong Kong Medical Dairy. The theme of this issue is "An
Update on Paediatric Neurological Disorders". The reason I have
chosen this theme is that there are a lot of recent advances in paediatric
neurologically related disorders, including epilepsy, spinal bifida,
Down’s syndrome, autistic spectrum disorder, Cushing’s syndrome,
and as well as the development of dietary and nutrition management in
neurologically related disorders such as paediatric epilepsy, Down’s
syndrome and autistic spectrum disorder.

Our contributing authors are all distinguished local experts in their
respective fields. I myself, a Paediatric Neurologist, will present the
"Treatment options for paediatric drug-resistant epilepsy". Dr Lap-
ming Wong and Dr Eunice W. Y. WONG, both experts in Paediatric
Endocrinology, will share their experience in the management of
paediatric Cushing’s disease. Dr Siu-to WONG, an expert in Paediatric
Neurosurgery, will share his experience in the surgical management of
spinal bifida. Dr Quinney CHAN, an expert in Child Psychiatry,
will share her expertise in the management of autistic spectrum
disorder. Ms Candy WONG, an expert dietitian, will share her local
experience in using ketogenic diet in paediatric epilepsy. Ms Sally
POON, Ms Violet MAN, Mr Charles LAW, Mr Kam-hung TAM, expert
Dietitians and Ms Tsau-jin CHENG, an expert nutritionist, will share
their experience in "A family-based sport and nutrition programme for
people with intellectual and developmental disabilities in Hong
Kong". Last but not least, I must thank Dr Paul LEUNG for sharing
his beautiful photo of Sunflowers as the cover photo of this issue of
the Medical Dairy. Alike this cover photo, we hope this medical dairy
would convey a positive message, strength and energy to all medical
and allied health professionals to continue to try our very best to take
care of these patient groups. I sincerely trust that you all find these
articles interesting and useful in your clinical practice.
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References:

Meeting the special needs of neonates: A lipid emulsion combining the benefits of four different oils

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**Paediatric Cushing’s Disease**

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**INTRODUCTION**

Cushing’s syndrome is caused by sustained exposure to excess glucocorticoid. The clinical characteristics of Cushing’s syndrome, including stunted growth, truncal obesity, round face and striae, are often subtle initially and overlooked by patients and physicians. It is important to make an early diagnosis to reduce cardiovascular and metabolic morbidity.

Paediatric Cushing’s syndrome is most commonly caused by exogenous steroid exposure. After exclusion of exogenous steroidal exposure, endogenous Cushing’s syndrome can be further classified into adrenocorticotropic hormone (ACTH)-dependent and ACTH-independent subtypes. Cushing’s disease is characterised by the overproduction of ACTH by a pituitary corticotroph adenoma, which results in hypercortisolism.

**EPIDEMIOLOGY**

The incidence of endogenous Cushing’s syndrome has been reported to be about 0.7-2.4 per million people per year. In the paediatric population, Cushing’s disease accounts for 75-90% of endogenous Cushing’s syndrome, while ACTH-independent Cushing’s syndrome accounts for around 15%.1

In children below five years of age, endogenous Cushing’s syndrome is more commonly caused by an adrenal adenoma, carcinoma or hyperplasia, while in children over five years of age, endogenous Cushing’s syndrome is most commonly caused by Cushing’s disease. Children with Cushing’s disease present at a mean age of 12.3 to 14.1 years. A male preponderance is observed in children, with a prevalence of 63%.2

**CLINICAL FEATURES**

The clinical features of Cushing’s disease result from chronic hypercortisolism. The most common clinical features are weight gain and growth retardation, affecting more than 80% of the patients. Moon face has been reported in 46-100% of patients.2 Skin changes including facial plethora, acne, striae, bruises and hyperpigmentation are also commonly found. Some may experience neuropsychiatric disturbances, including fatigue, headache, irritability, depression and sleep disturbance. Pubertal disorders like menstrual irregularity, excessive virilisation, precocious or delayed puberty may also affect these patients. In cases of early hypertension, osteoporosis or metabolic disorder, physicians should proactively look for evidence of hypercortisolism, especially in children with decreasing height percentile but increasing weight. As the initial symptoms and signs could be non-specific, patients may experience two to three years of symptoms before the diagnosis is reached.2,3

**DIAGNOSIS**

A stepwise approach is recommended for the diagnosis of paediatric Cushing’s disease.4

**Clinical Suspicion**

Screening for Cushing’s syndrome is recommended by the Endocrine Society in the following circumstances5:

a. Patients with unusual features for age e.g. hypertension, osteoporosis  
b. Patients with multiple and progressive symptoms suggestive of Cushing’s syndrome  
c. Children with decreasing height percentile but increasing weight  
d. Patients with adrenal incidentaloma compatible with adenoma

One must not forget to take a thorough drug history to rule out exogenous glucocorticoid exposure before proceeding to further investigations.

**Establishing Endogenous Hypercortisolism**

The diagnosis of Cushing’s syndrome can be made if two or more of the following tests are suggestive of hypercortisolism. Midnight salivary and serum cortisol levels assess the circadian rhythm of cortisol production. Overnight dexamethasone suppression test and low-dose dexamethasone suppression test assess the suppressibility of the hypothalamic-pituitary-adrenal (HPA) axis. A 24-hour urinary free cortisol test quantifies the endogenous cortisol load.

a. **Midnight Salivary Cortisol**  
More than two samples should be taken between 11pm to 12 midnight by passive drooling or commercially available salivary collection device. A
High-dose dexamethasone suppression test (HDDST) and CRH test have been used to differentiate between Cushing’s disease and ectopic ACTH syndrome. In Cushing’s disease, ACTH production increases in response to CRH administration, while cortisol production is suppressible by a high dose of dexamethasone for two days.

For ACTH-dependent Cushing’s syndrome, the pre-test probability of pituitary origin is 80% overall and 90% in females. Ectopic ACTH syndrome is even rarer in the paediatric population. Therefore, the need for these tests is questionable and they are no longer recommended as routine.

**Localisation of Pituitary Corticotroph Adenoma In Cushing’s Disease**

After confirming the pituitary origin of hypercortisolism, it is important to localise the pituitary adenoma in order to plan for curative surgical treatment.

**a. Magnetic Resonance Imaging (MRI)**

MRI is the imaging method of choice for pituitary adenoma. The detection rate of pituitary adenoma in children with Cushing’s disease is reported to be 43-72%. This is because pituitary corticotroph adenoma in children is usually small and hypointense. The gadolinium uptake is less avid than adjacent pituitary tissue and often delayed, making the visualisation on MRI more difficult. The spoiled gradient-recall acquisition technique may improve spatial resolution compared to the conventional technique.

**b. Bilateral Inferior Petrosal Sinus Sampling (Bipss)**

Bilateral inferior petrosal sinus sampling aims to lateralise the pituitary ACTH-producing adenoma. It involves catheterisation of bilateral femoral veins and advancing catheter to petrosal sinuses. The position of the catheter is confirmed by contrast injection. CRH is administered while simultaneous central and peripheral blood sampling of ACTH and prolactin is performed.

A central-to-peripheral ACTH gradient confirms the pituitary source of ACTH overproduction. A central-to-peripheral prolactin gradient on each side confirms correct catheter placement. Inter-sinus prolactin-adjusted ACTH gradient of greater than 1.4 correctly diagnoses tumour location in 75% of patients.

**MANAGEMENT**

**Surgery**

The optimal treatment of Cushing’s disease is selective pituitary adenomectomy. This aims to reverse the physical changes, minimise cardiovascular and metabolic morbidity, and reduce the risk of disease recurrence, while preserving pituitary function as far as possible.
Transphenoidal microscopic surgery is the main approach to pituitary tumour resection. For those with inconclusive or normal MRI, surgery remains the first-line treatment as it has been shown that the diagnostic performance of intra-operative visualisation by surgeons is superior to MRI. When a microadenoma is successfully removed by surgery, the remission rate is 65-90%, while the recurrence rate of these patients is 10-20% at 10 years. Immediate remission rate after macroadenoma removal is lower and the long-term recurrence rate is also higher. When an adenoma cannot be identified intra-operatively, partial or total hypophysectomy may be required. The remission rate is about 70%, lower than selective adenomectomy, and hypophysectomy may be required. The remission rate cannot be identified intra-operatively, partial or total recurrence rate is also higher.

Some guidelines recommended testing of morning serum cortisol in the first post-operative week to assess remission. Suppressed morning cortisol below 50 nmol/L should be expected in successful surgery, as the normal pituitary corticotroph is suppressed by chronic hypercortisolism. Patients should be treated with a physiological dose of glucocorticoid to prevent glucocorticoid withdrawal. Meanwhile, other studies suggest testing of the HPA-axis at 6-12 weeks after surgery. They found that the cut-off of morning cortisol below 138 nmol/L at 6 to 12 weeks predicts cure with a sensitivity of 94% and specificity of 79%. A 24-hour urinary free cortisol level below 55 nmol suggests remission as well.

In case of persistent or recurrent disease, repeat pituitary surgery is the preferred treatment option. More aggressive removal of the gland may be required, which leads to a higher risk of hypopituitarism. Early repeat surgery within two months of the initial operation may be beneficial in minimising additional trauma before the formation of scar tissue and alteration of anatomical structures.

Radiotherapy

In patients with persistent or recurrent disease after repeated surgeries, fractionated external beam radiotherapy and stereotactic radiosurgery induce remission in 50-60% of patients in 3-5 years. They may cause pituitary failure, neurocognitive impairment and cerebrovascular complications. There is also a small risk of secondary cancer formation.

Medical Treatment

Several classes of medications have been used to control hypercortisolism. They include steroidogenesis inhibitors (e.g. ketoconazole, metyrapone, mitotane), centrally acting agents (e.g. cabergoline, pasireotide) and glucocorticoid receptor antagonist (e.g. mifepristone). The effectiveness of these agents range from 40-80%.

Bilateral Adrenalectomy

Bilateral adrenalectomy provides immediate control of hypercortisolism, but it carries the risk of surgical morbidity and permanent hypoadrenalism. The patient will need life-long replacement of glucocorticoid and mineralocorticoid, with careful titration of the medications during acute stress. Furthermore, removal of adrenal feedback may lead to further enlargement of the pituitary corticotroph tumour, resulting in Nelson’s syndrome. The mass effect of the pituitary tumour may cause compression of the adjacent neurological structures resulting in visual field defects, external ophthalmoplegia and headache. Elevated ACTH secretion can cause hyperpigmentation.

CONCLUSION

Cushing’s disease is a rare condition in children. Early recognition of suspicious features, such as obesity, growth retardation, hypertension and facial and skin changes can lead to prompt diagnosis and treatment. A stepwise approach is employed to reach the diagnosis. After establishing biochemical evidence of Cushing’s disease, localisation is achieved by MRI or bilateral inferior petrosal sinus sampling. Surgical resection of pituitary adenoma is the mainstay of treatment. In persistent or recurrent disease, repeat surgery with more extensive hypophysectomy, radiotherapy, medical treatment and bilateral adrenalectomy may be considered.

References

European Pharmacopeia monograph; silymarin was first isolated in 1968 by German scientists at the University of Munich and then described and patented as a specific treatment “against liver diseases”.

Based on in-vitro studies and/or animal studies.

Based on a drug monitoring program which included 2,637 patients with the clinical syndrome of toxic liver damage of different degree of severity and treated with Legalon® for 8 weeks.

References:

LEGALON 140 SUMMARY OF PRODUCT INFORMATION

1. TRADE NAME: Legalon 140
2. PRESENTATION: Each capsule contains 173.0-186.7 mg of dry extract from the fruits of milk thistle, equivalent to 140 mg of silymarin, calculated as silibinin.
3. INDICATIONS: Toxic liver damage; for supportive treatment in patients with chronic inflammatory liver conditions and hepatic cirrhosis.
5. WARNINGS & PRECAUTIONS: Drug therapy is not a substitute for the avoidance of causes damaging the liver (e.g., alcohol). In case of jaundice, a doctor should be consulted. Not be used in children aged under 12 years. Not suitable for treating acute poisoning.
6. PREGNANCY AND LACTATION: No experience available. Only be used after doctor consultation.

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Autism Spectrum Disorder

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THE HISTORY

Autism Spectrum Disorder (ASD) is a neurodevelopmental disorder, characterised by a deficit in reciprocal social interaction and communication, and a repetitive and restrictive behavioural (RRB) pattern. The characterisation of ASD dates back to 1943 when Kanner first introduced the concept of autistic disorder in 1943 and described children who presented with social aloofness, lack of communication and stereotypic behaviours. One year later, Hans Asperger in 1944 described a group of boys who demonstrated behaviour such as ‘a lack of empathy, little ability to form friendships, one-sided conversations, intense absorption in a special interest, and clumsy movements’.1 However, it did not gain much attention until 1981 when Lorna Wing coined the term Asperger’s Syndrome, which included individuals with social interaction deficits and restricted behavioural patterns but with normal cognitive development and language acquisition.4

The work by Kanner and Asperger laid the foundation for the establishment of the diagnostic entity of ASD; together with the important contribution from other lines of research in the subsequent decades, ASD was first included in the third version of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III) as Pervasive Developmental Disorder. There was further expansion of the diagnostic category of ASD in DSM 4th ‘Text Revision (DSM-IV TR) which included three phenotypes of ASD, namely the Autistic Disorder, Asperger’s Syndrome, Pervasive Developmental Disorder Not Otherwise Specified (PDDNOS); and two non-ASD disorders: Rett’s Disorder and Childhood Disintegrative Disorder.3

THE DSM 4th TEXT REVISION

Under the DSM-IV TR, there were twelve symptoms listed under ASD and they were grouped under three main domains: ‘impairment in social interaction’, ‘impairment in communication’ and ‘restricted, repetitive behavioural pattern (RRB)’. The patient has to fulfill the minimum number of symptoms in each domain in order to be legible to receive a diagnosis of Autistic Disorder, Asperger’s Syndrome and PDDNOS (see Table 1). For a diagnosis of Autistic Disorder, the patient has to have a total of six symptoms from the three domains, at least two of which from the ‘impairment in social interaction’, at least one from the ‘impairment in communication’ and at least one from the RRB domain. For a diagnosis of Asperger’s Syndrome, the patient has to display at least two symptoms from the ‘social’ domain and one symptom from the RRB domain, without any delay in language and cognitive development. For a diagnosis of PDDNOS, the patient has to demonstrate severe social impairment accompanied by either communication impairment or RRB. As there was no minimum number of symptoms required as the diagnostic criteria for PDDNOS, PDDNOS was described as a ‘catch-all’ ASD diagnosis.4

Table 1. DSM-IV TR diagnostic criteria of Autistic Disorder 3 (Personal collection)

<table>
<thead>
<tr>
<th>DSM-IV TR</th>
<th>Autistic Disorder (at least six symptoms in total)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Qualitative impairment in communication (at least one)</td>
<td>• Delay in, or total lack of, spoken communication</td>
</tr>
<tr>
<td></td>
<td>• Marked impairment in the ability to make conversation with others</td>
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<td></td>
<td>• Stereotyped and repetitive use of language or idiosyncratic language</td>
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<td></td>
<td>• Lack of varied, spontaneous pretend play</td>
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<tr>
<td>Qualitative impairment in social interaction (at least two)</td>
<td>• Marked impairment in the use of non-verbal communication (e.g. eye contact, gesture)</td>
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<td></td>
<td>• Failure to develop appropriate peer relationship</td>
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<td></td>
<td>• Lack of spontaneous sharing of interest, enjoyment, and achievement</td>
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<td></td>
<td>• Lack of social reciprocity</td>
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<tr>
<td>Restricted, repetitive behaviours, interest and activities (at least one)</td>
<td>• Preoccupation with restricted pattern of interest that is of abnormal intensity and focus</td>
</tr>
<tr>
<td></td>
<td>• Inflexible adherence to routine and habit</td>
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<td></td>
<td>• Motor mannerism (e.g. hand, finger flapping or twisting, tip toeing)</td>
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<td></td>
<td>• Persistent preoccupation about part object (e.g. playing with the wheels instead of the car)</td>
</tr>
</tbody>
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THE DSM V

The DSM V came into use in 2013, under which the Pervasive Developmental Disorder was renamed as Autism Spectrum Disorder (ASD). The distinction among Autistic Disorder, Asperger’s syndrome and PDDNOS was obsoleted. There were seven symptoms
listed for ASD grouped under two domains. The two domains in the DSM-IV TR, ‘impairment of social interaction’ and ‘impairment of communication’, were collapsed into one domain of ‘impairment of social communication’. The other domain remained to be ‘restricted, repetitive pattern of behaviours’, within which there was an additional item on sensory symptoms. The patient has to have at least five symptoms (three from the domain of ‘impairment of social communication’ and two from the RRB domain) to receive a diagnosis of ASD (see Table 2). Besides, under the DSM-V, the presence of speech and developmental delay was no longer used as a diagnostic feature distinguishing the subtypes of ASD (i.e. Autistic Disorder and Asperger Syndrome), rather it became a specifier. The DSM-V also changed the age of onset from ‘three years old’ to ‘early childhood’.

<table>
<thead>
<tr>
<th>Table 2. DSM V diagnostic Criteria of ASD(^1) (Personal collection)</th>
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<tbody>
<tr>
<td>DSM-V</td>
</tr>
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<td>---------------------</td>
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</tbody>
</table>
| Impairment in social communication (all three) | • Deficits in social reciprocity  
• Deficits in nonverbal communication  
• Deficits in developing relationship |
| Restricted repetitive of behaviours (at least two) | • Preoccupation with restricted pattern of interest that is of abnormal intensity and focus  
• Inflexible adherence to routine and/or habits, insistence on sameness and cognitive rigidity  
• Repetitive and stereotyped motor movement (i.e. motor mannerism), speech and use of objects  
• Hyper-reactivity, hypo-reactivity to sensory input or usual sensory interest (e.g. festinated about lights and moving objects, excessive response to sound, indifference to pain/temperature, excessive smelling and mouthing objects |

**CONTROVERSY ABOUT THE DSM-V**

Despite the good intention of the American Psychiatric Association’s attempt to make the diagnostic system simpler, clearer and hopefully to make the diagnosis of ASD more reliable across different centres, the changes are not without controversy.

The main concern is that some patients who meet the DSM-IV TR diagnosis of ASD would no longer meet the diagnostic criteria of the 5th edition.\(^{13,14}\) The DSM-V had a higher diagnostic requirement that five out of the seven ASD symptoms had to be fulfilled, whereas the DSM-IV TR only required six out of twelve. Furthermore, the diagnoses of Asperger’s Syndrome and PDDNOS required even fewer symptoms to be fulfilled. In particular, the PDDNOS diagnosis did not have a minimum requirement on the number of symptoms as long as a patient demonstrated deficits in social interaction coupled with either communication deficits or RRB.

**THE LOSS OF THE DIAGNOSTIC LABEL OF ASD**

A systematic review and meta-analysis by Kulage et al. in 2019 included 33 studies in their final analysis and reported that a significant number of individuals who were qualified for DSM-IV TR diagnosis of ASD would not meet DSM 5 criteria with the pooled reduction in ASD diagnosis of 20.8%. The DSM-IV TR ASD subtypes which were affected the most was PDDNOS, where there was a pooled reduction of 46.1% in the diagnosis (though the result was not statistically significant), while the reductions were 10.1% and 23.3% for those who were diagnosed as Autistic Disorder and Asperger’s Syndrome respectively.\(^{15}\) Patients lost the diagnosis of ASD usually because they either demonstrated an inadequate number of symptoms under the RRB domain or an inadequate level of impairment in the social communication domain. Yet, various studies had found that those who lost their ASD diagnosis had similar level of symptoms severity as compared to those who did not and that they continued to exhibit significant autism symptoms when compared to non-autistic control.\(^{16,17,18,19}\) The loss of diagnostic label could have the implication that these patients might not get the support and intervention they needed. The American Psychiatric Association had suggested for these patients, the diagnosis of Social Communication Disorder, a new diagnostic category in the DSM-V, might be a suitable alternative diagnosis. However, Kulage et al. demonstrated that only less than one-third of those who lost the DSM-IV TR ASD diagnosis qualified for the diagnosis of Social Communication Disorder, which means these patients still would not receive any diagnostic label to enlist the social and educational support and intervention they needed. Such lack of provisions may lead to poorer academic, social outcome and lower rate of employment.\(^{20}\)

**ASD AS A SPECTRUM OF DISORDER**

The rationale behind the change to the DSM V is due to the increasing evidence from research showing that the distinction among Autistic Disorder, Asperger’s Syndrome and PDDNOS present no meaningful differences especially when cognitive ability and language level were controlled for.\(^{6,7}\) These Disorders are currently viewed as belonging to the same spectrum with variable manifestation and severity across the life span, gender, intellectual level and language ability i.e. a categorical diagnosis with a dimensional aspect.\(^{9,7}\)

It was also known that there was arbitrariness and inconsistency in making the diagnoses of the three subtypes of ASD. Lord et al. showed that the best predictor of which ASD diagnosis a patient received was depending on which centre he/she went to.\(^{10}\) A survey in 2008 showed that half the young people receiving the diagnosis of Asperger’s Syndrome and PDDNOS in fact also met the criteria of Autistic Disorder.\(^{11}\) Gibbs et al. also mentioned that different centres in Australia had different ‘threshold’ for diagnosing PDDNOS.\(^{12}\) The overhaul made in DSM-V tried to eliminate the rigid delineation among outdated categorisation and rather opted for a dimensional spectrum-oriented approach.
**Lecture highlights**

- **2′-Fucosyllactose intake at 1 month of age is associated with cognitive development at 24 months of age in infants**

- **3′-Sialyllactose is associated with cognitive function, particularly language development in infancy**

- Various studies suggested that early intake of HMOs may influence neurodevelopment and cognitive functions

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**References:**


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THE RISING PREVALENCE

Despite the evidence from various studies that there might be a reduction in the number of patients diagnosed with ASD along with the introduction of DSM-V, the prevalence of ASD was noted to be on a rising trend. The Centers for Disease Control and Prevention reported the prevalence of ASD in the USA, using DSM-IV TR, was 113 in 10,000 children in 2008; while it reported the prevalence was 230 among 10,000 children in 2018 using the DSM-V. A recent systematic review in 2022 inclusive of 71 studies from 34 countries globally revealed a median prevalence of 100 in 10,000 children, where a systematic review in 2012 found that the median prevalence of ASD was 62 in 10,000 children. Despite the variation of prevalence in different studies, there was a consistent increase in the trend of the prevalence. The reason for the increase was postulated to be attributable to the increase in public awareness of ASD, the broadening of concepts of ASD, the increase in identification of milder form of illness and in the previously underdiagnosed group such as females.

THE LOCAL DATA

The most recent local data were provided by a meta-analysis of the prevalence of autism in mainland China, Taiwan and Hong Kong in 2013, which showed that the prevalence in the three regions was 26.6 among 10,000 children. The estimated prevalence was much lower than those of other regions because of the inclusion of only Autistic Disorder instead of the whole spectrum.

DIFFICULTY IN DIAGNOSIS OF ASD

It is challenging to diagnose ASD as it has heterogeneous manifestation and severity across the life span, gender, intellectual level, and language ability. There are no laboratory tests and neuroimaging techniques to diagnose ASD. The diagnosis of ASD is ideally to be made by a multi-disciplinary team. The team should collect clinical information from the direct observation of the child’s behaviour, history taken from the parent / care givers regarding the developmental history, taking into account of the other assessment results, such as IQ level and overall functioning level. The clinical information would then be mapped against the ICD 10 or DSM-V diagnostic criteria to see if they fulfil the symptoms and impairment requirement to reach a diagnosis of ASD. Thus, the reliability of diagnosis partly depends on whether the caregivers are capable of being aware of and reporting the symptoms of ASD. However, it may be difficult for them to identify the problem unless these were overtly abnormal or deviant from the typically developing children.

ASD symptoms severity and appearance are dependent on the environment. ASD symptoms may only partially or even may not manifest when social demands do not outweigh a patient’s ability, especially for those with milder severity of symptoms and normal IQ. Patients with normal IQ, particularly females, may also employ strategies to camouflage their social deficits, such as imitating facial expressions, gestures and phrases, pretending to be interested in social group’s topics etc., which may then lead to doubt in diagnosis.

Co-morbid psychiatric diagnoses such as Attention-Deficit /Hyperactivity Disorder may also mask ASD. ASD patients frequently have co-morbid psychiatric diagnoses. Lai et al reported in their meta-analysis that the prevalence of psychiatric comorbidities was in general higher in ASD than that of the general population; and that 28% of ASD patients were comorbid with ADHD, 20% with anxiety disorder, 13% with sleep-wake disorders and 11% with depressive disorder. It could be difficult for the clinician to delineate whether symptoms are due to ASD or other diagnoses.

TREATMENT

Current evidence shows that behavioural treatment is still the mainstay of treatment for the core symptoms of ASD. Pharmacological treatment in ASD has its value only in treating irritability, and to a lesser extent, in treating repetitive behaviours with two atypical antipsychotics: Risperidone and Aripiprazole. ASD patients comorbid with ADHD would benefit from medications such as psychostimulants (those registered for use in HK include Ritalin, Ritalin LA, Concerta, Lisdexamfetamine), non-stimulants (Atomoxetine) and Alpha 2 Adrenergic Agonists (e.g. Clonidine). Serotonergic drugs such as Serotonin Reuptake inhibitors (SSRI), Serotonin Noradrenaline Reuptake Inhibitors (SNRI) only play a role for those with comorbid depression and anxiety disorders.

CONCLUSION

ASD is a complex, heterogeneous neurodevelopmental disorder having a significant impact on a person’s overall functioning. Early diagnosis and thus intervention are crucial for a more desirable outcome. However, the diagnosis of ASD has never been easy and straightforward. Clinicians, as well as those involved in childcare, should raise their awareness on the subtle and heterogeneous presentations of ASD.

References

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The bioavailability and pharmacodynamics of different concentrations of omega-3 acid ethyl esters. Pronova Biocare, R&D, Vollsvieien 6, N-1327 Lysaker, Norway 2006.

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**MCHK CME Programme Self-assessment Questions**

Please read the article entitled "Autism Spectrum Disorder " by Dr Quinney KN CHAN 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 31 July 2022. 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. Asperger’s Syndrome is coined by Hans Asperger.
2. Rett’s Syndrome and Childhood Disintegrative Disorder are included in the autism spectrum.
3. The patients diagnosed with Asperger’s Syndrome have normal intelligence.
4. All patients diagnosed the Autistic Disorder have mental retardation.
5. ASD patients may manifest deficits in middle childhood.
6. ASD patients frequently have comorbid psychiatric disorders.
7. Impairment in social interaction can be cured by medication.
8. All ASD patients with restricted repetitive behaviours have to be treated with atypical antipsychotic.
9. There are consistent reports on the rising trend of the prevalence of ASD.
10. Patients who do not fulfil the DSM-V diagnostic criteria of ASD are normal individuals and do not suffer from impairment from ASD symptoms.

**ANSWER SHEET FOR JULY 2022**

Please return the completed answer sheet to the Federation Secretariat on or before 31 July 2022 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

**Autism Spectrum Disorder**

Dr Quinney KN CHAN  
MBBS(HK), FHKCPsych, FHKAM (Psychiatry)  
Specialist in Psychiatry  
Associate Consultant  
Department of Child and 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) HKDU No.: _________________ HKAM No.: ________________

Contact Tel No.:_____________________________ MCHK No. / DCHK No.: __________________(must fill in)

**Answers to June 2022 Issue**

Severe Asthma: Phenotyping and Its Implication for Treatment

A Family-based Sport and Nutrition Programme for People with Intellectual and Developmental Disabilities in Hong Kong

Ms Sally SP POON
Accredited Practising Dietitian (APD)
Chairman of Hong Kong Practising Dietitians Union

Ms Violet Hon MAN
Accredited Practising Dietitian (APD)
Honorary Secretary of Hong Kong Practising Dietitians Union

Mr Charles MC LAW
Accredited Practicing Dietitian (APD)
Honorary Treasurer of Hong Kong Practising Dietitians Union

Mr Kam-hung TAM
Accredited Practicing Dietitian (APD)
Love 21 Foundation

Ms Tsau-jin CHENG
Nutritionist
Love 21 Foundation

BACKGROUND

People with intellectual and developmental disabilities (IDD) tend to experience nutritional challenges from an early age and carry a greater risk of obesity and long-term health complications, resulting in higher morbidity and earlier mortality. In Hong Kong, it is estimated that there are about 77,000 – 90,000 people with intellectual disability and 22,400 people with autism spectrum disorder. The Centers for Disease Control and Prevention estimated that individuals with intellectual disabilities pose an average lifetime economic cost at USD 1,014,000 per person, which is the highest per person cost amongst individuals with any type of developmental disability.

Individuals with IDD currently enjoy longer lifespan than in the past and most are residing in the community rather than in institutional settings. Therefore, the demand for primary care clinicians for health care will increase with the increasing number of these patients. Dietitians play an important role as part of the multi-disciplinary team in addressing and managing the multiple health and nutrition issues faced by these patients, such as feeding difficulties, allergies, thyroid disorders, growth and/or developmental problems, overweight/obesity, gastrointestinal dysfunction, sleep disturbances, cardiovascular disease, diabetes mellitus, and osteoporosis. Major factors contributing to overweight and obesity include poor eating habits (high in fat and sugar, low in fruit and vegetables), lack of physical activity, the tendency towards sedentary behaviours, and weight gain from commonly prescribed psychotropic medications. Effective components of obesity intervention programmes include attention to diet, promotion of physical activity and family support.

The aim of this paper is to report the clinical outcomes of the "Jockey Club Love Healthy Life Sport and Nutrition Programme", which has been targeted at people with IDD living in the community.

PROGRAMME DESIGN

The programme was carried out for 11 months from January to November 2021. The intervention comprised monthly one-on-one dietetic consultations, regular running of exercise classes, monthly cooking workshops and videos demonstrating dietitian-approved recipes, and monthly nutrition talks and educational workshops for the participants’ family members.

Participants were recruited via flyers circulated within the Love 21 community and by word of mouth among beneficiary families. The programme was offered free of charge to participants. There were no prerequisites for joining the programme and any member of Love 21 was eligible.

A total of 58 individuals (male = 41, female = 17, age 23±7.7 years) were recruited for the programme (Table 1). The study group comprised 63.8% individuals with Down’s syndrome, 22% with autism spectrum disorder and 13.7% with intellectual and other disabilities. Most participants have mild (67.2%) to moderate (29.3%) intellectual disability. Participants either attended school (39.7%) or worked in sheltered workshops (37.9%), while others engaged in other forms of part-time employment (6.9%) or were unemployed (10.3%).

DATA COLLECTION

Anthropometric assessments were performed monthly to assess the health status of participants. Key measurements including the body mass index (BMI), skeletal muscle mass, body fat mass and body fat percentage were obtained using the body composition analyser InBody 120. Waist circumference was also recorded as an indicator of central obesity.

In addition to observing changes in body composition, we also obtained resting blood pressure, and resting and recovery heart rate through the YMCA 3-minute step test.
Table 1: Descriptive characteristics of the study population at baseline (Unpublished data from the “Jockey Club Love Healthy Life Sport and Nutrition Programme” and released with permission from Love 21 Foundation and Hong Kong Jockey Club)

<table>
<thead>
<tr>
<th>Demographic</th>
<th>Overall (n=58)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>41</td>
<td>70.7</td>
</tr>
<tr>
<td>Female</td>
<td>17</td>
<td>29.3</td>
</tr>
<tr>
<td>Age</td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 18 years old</td>
<td>17</td>
<td>29.3</td>
</tr>
<tr>
<td>≥ 18 years old</td>
<td>41</td>
<td>70.7</td>
</tr>
<tr>
<td>Developmental disability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Down’s syndrome</td>
<td>37</td>
<td>63.8</td>
</tr>
<tr>
<td>Autism spectrum disorder</td>
<td>13</td>
<td>22.4</td>
</tr>
<tr>
<td>Intellectual disability</td>
<td>6</td>
<td>10.3</td>
</tr>
<tr>
<td>Others</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>Grades of intellectual disability</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mild</td>
<td>39</td>
<td>67.2</td>
</tr>
<tr>
<td>Moderate</td>
<td>17</td>
<td>29.3</td>
</tr>
<tr>
<td>Severe</td>
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<td>0</td>
</tr>
<tr>
<td>Unidentified</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>Occupations</td>
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</tr>
<tr>
<td>Student</td>
<td>23</td>
<td>39.7</td>
</tr>
<tr>
<td>Full- or part-time work</td>
<td>4</td>
<td>6.9</td>
</tr>
<tr>
<td>Sheltered workshop</td>
<td>22</td>
<td>37.9</td>
</tr>
<tr>
<td>Social enterprise</td>
<td>2</td>
<td>3.4</td>
</tr>
<tr>
<td>None</td>
<td>6</td>
<td>10.3</td>
</tr>
<tr>
<td>Other</td>
<td>1</td>
<td>1.7</td>
</tr>
</tbody>
</table>

Table 2: Changes in anthropometry, biochemistry, cardiovascular fitness and lifestyle measures before and after programme (Unpublished data from the “Jockey Club Love Healthy Life Sport and Nutrition Programme” and released with permission from Love 21 Foundation and Hong Kong Jockey Club)

<table>
<thead>
<tr>
<th></th>
<th>Before programme (Mean±SD)</th>
<th>After programme (Mean±SD)</th>
<th>Mean difference (CI)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anthropometry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Body Weight (kg)</td>
<td>62.6±11.9</td>
<td>60.8±10.5</td>
<td>-1.8 (-2.7 to -0.9)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>25.4±3.9</td>
<td>24.5±3.6</td>
<td>-0.9 (-1.2 to -0.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Skeletal Muscle Mass (kg)</td>
<td>24.3±5.1</td>
<td>24.8±4.9</td>
<td>0.5 (0.04 to 0.9)</td>
<td>0.031</td>
</tr>
<tr>
<td>Body Fat Mass (kg)</td>
<td>18.4±6.6</td>
<td>15.9±6.3</td>
<td>-2.5 (-3.2 to -1.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Body Fat Percentage (%)</td>
<td>28.9±7.9</td>
<td>25.8±8.3</td>
<td>-3.1 (4.1 to -2.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>86.0±10.1</td>
<td>83.9±9.5</td>
<td>-2.1 (-3.3 to -1.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Biochemistry</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Alanine Transaminase (U/L)</td>
<td>50.2±27.2</td>
<td>38.9±19.6</td>
<td>-11.3 (-17.1 to -5.6)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>5.2±0.5</td>
<td>5.0±0.3</td>
<td>-0.2 (-0.25 to -0.05)</td>
<td>0.004</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>4.9±0.9</td>
<td>4.7±0.9</td>
<td>-0.2 (-0.4 to -0.06)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>High Density Lipoprotein (mmol/L)</td>
<td>1.30±0.2</td>
<td>1.33±0.3</td>
<td>0.03 (-0.02 to 0.07)</td>
<td>0.212</td>
</tr>
<tr>
<td>Low Density Lipoprotein (mmol/L)</td>
<td>3.1±0.7</td>
<td>2.9±0.7</td>
<td>-0.2 (-0.3 to -0.03)</td>
<td>0.019</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.2±0.6</td>
<td>1.0±0.5</td>
<td>-0.2 (-0.3 to 0.07)</td>
<td>0.003</td>
</tr>
<tr>
<td>Uric Acid (mg/dL)</td>
<td>7.0±1.7</td>
<td>6.9±1.7</td>
<td>-0.1 (-0.3 to 0.2)</td>
<td>0.484</td>
</tr>
<tr>
<td>Thyroid Stimulating Hormone (mIU/L)</td>
<td>2.9±3.7</td>
<td>2.5±2.9</td>
<td>-0.4 (-0.8 to 0.04)</td>
<td>0.079</td>
</tr>
<tr>
<td><strong>Cardiovascular Fitness</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>113.4±13.5</td>
<td>106.2±15.2</td>
<td>-7.2 (-11.7 to -3.0)</td>
<td>0.001</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>74.6±13.2</td>
<td>72.1±8.9</td>
<td>-2.5 (7.0 to 8.0)</td>
<td>0.120</td>
</tr>
<tr>
<td>Resting Heart Rate (bpm)</td>
<td>82.2±16.1</td>
<td>76.6±9.4</td>
<td>-5.6 (-9.9 to -1.2)</td>
<td>0.013</td>
</tr>
<tr>
<td>Recovery Heart Rate (bpm)</td>
<td>101.7±16.3</td>
<td>92.4±13.3</td>
<td>-9.3 (-14.3 to -4.3)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td><strong>Lifestyle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Exercise Time (hours/week)</td>
<td>7.9±6.0</td>
<td>10.1±5.4</td>
<td>2.2 (0.4 to 4.0)</td>
<td>0.016</td>
</tr>
<tr>
<td>Seating Time (hours/day)</td>
<td>8.3±3.1</td>
<td>8.2±3.4</td>
<td>-0.1 (-1.3 to 1.1)</td>
<td>0.826</td>
</tr>
<tr>
<td>Sleeping Time (hours/day)</td>
<td>8.5±1.1</td>
<td>7.9±0.9</td>
<td>-0.6 (-0.9 to -0.3)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Table 3: Changes in dietary habits before and after the programme (Unpublished data from the “Jockey Club Love Healthy Life Sport and Nutrition Programme” and released with permission from Love 21 Foundation and Hong Kong Jockey Club)

<table>
<thead>
<tr>
<th></th>
<th>Before programme (%)</th>
<th>After programme (%)</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>More than six glasses of water daily</td>
<td>45</td>
<td>70</td>
<td>56</td>
</tr>
<tr>
<td>Less than once a week of sugary beverages intake</td>
<td>69</td>
<td>76</td>
<td>10</td>
</tr>
<tr>
<td>Breakfast daily</td>
<td>85</td>
<td>93</td>
<td>9</td>
</tr>
<tr>
<td>More than two servings of fruits daily*</td>
<td>29</td>
<td>54</td>
<td>86</td>
</tr>
<tr>
<td>More than three servings of vegetables daily**</td>
<td>24</td>
<td>67</td>
<td>179</td>
</tr>
<tr>
<td>More than one serving of dairy daily***</td>
<td>45</td>
<td>87</td>
<td>93</td>
</tr>
<tr>
<td>More than one serving of wholegrains daily****</td>
<td>15</td>
<td>70</td>
<td>367</td>
</tr>
<tr>
<td>Less than once a week of processed meat intake</td>
<td>69</td>
<td>93</td>
<td>35</td>
</tr>
<tr>
<td>Less than once a week of high-sugar and/or high-fat snacks intake</td>
<td>86</td>
<td>94</td>
<td>9</td>
</tr>
</tbody>
</table>

* 1 serving of fruit = 1 medium-sized fruit (e.g. apple, orange)
** 1 serving of vegetables = half bowl of cooked vegetables or 1 bowl of raw vegetables
*** 1 serving of dairy = 1 glass of milk/ calcium-fortified soymilk or 1 pot (150ml) of yogurt or 2 slices of cheese
**** 1 serving of wholegrains = 1 bowl of cooked wholegrains (e.g. brown rice, oatmeal) or 2 slices of whole wheat bread

Measurements: 1 glass = 240ml; 1 bowl = 250-300ml

SD = Standard Deviation, CI = 95% Confidence Interval
once every three months for assessing the cardiovascular fitness of the participants.

Voluntary blood tests were carried out before and after the intervention. Eight biomarkers including alanine transaminase (ALT), fasting glucose, total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL), triglycerides, uric acid and thyroid stimulating hormone, had been selected to help identify whether the participants were at risk of developing diet-related diseases, and to help manage any pre-existing conditions or complications.

Each month, the participants were asked to submit a monthly exercise record and a 3-day food diary to facilitate dietetic consultations. Once every three months, exercise and diet questionnaires were administered to record the levels of physical activity and sedentary behaviours, hours of sleep, and dietary intakes (food group consumption and diet quality) for parallel assessment.

Last, the participants and their parents or carers were asked to complete a programme satisfaction survey every three months based on three areas that the programme has set out to study, namely (1) behavioural and attitude changes, (2) knowledge increment in sports skills, nutrition, and diet; and (3) overall feedback on the programme and support provided.

OUTCOME MEASURES

By the end of the programme, a large proportion of participants had improvements in the anthropometry measures (Table 2). The body weight, BMI, body fat mass, body fat percentage and waist circumference reduced significantly by 1.8 kg, 0.9 kg/m², 2.5 kg, 3.1% and 2.1 cm respectively. Muscle mass increased significantly by 0.5 kg.

As shown in Table 2, biochemical measurements showed an overall improving trend: total cholesterol, LDL and triglycerides were all reduced significantly by 0.2 mmol/L; ALT and fasting glucose were reduced significantly by 11.3 U/L and 0.2 mmol/L respectively by the end of the programme. No significant changes were observed in the level of HDL, uric acid and thyroid stimulating hormone. The systolic blood pressure reduced significantly by 7.2 mmHg; however, the reduction in diastolic blood pressure was insignificant. Both resting and recovering heart rates decreased significantly by 5.6 bpm and 9.3 bpm by the end of the programme.

Increased physical activity time and decreased seating and sleeping time were noted among the participants. Physical activity increased from 7.9 hours per week at baseline to 10.1 hours per week by the end of the programme. A remarkably positive and significant average increase in exercising time by 2.2 hours per week was observed. The mean exercise time of 10.1 hours per week meets the World Health Organization recommendations for teens and adults with disability. In the meantime, seating time averagely decreased by 0.1 hours per day. The decrease is desirable though relatively non-significant. Interestingly, we saw a significant drop in sleeping time by the end of the programme, an undesirable 0.6 hour drop per day compared to baseline. We have the impression that the drop was probably due to a change in daily schooling/work routines among the participants. Nevertheless, the mean sleeping time of 7.9 hours a day is close to the sleep recommendation for teens and adults. Last but not least, data in the exercise and diet questionnaires are subject to recall bias as they were self-reported.

In retrospect, the improvements are the result of a number of measures strictly adhered to in our programme, namely an in-depth understanding of the participants’ problems; the formulation of feasible and practical strategies together with the participants and their family members for implementation; timely consultation and monitor of progress; and a strictly family-based approach in which family members were involved in intervention measures.

We have a deep conviction that a family-based approach is pivotal to the success of intervention measures set out to help individuals with IDD. To our knowledge, the "Jockey Club Love Healthy Life Sport and Nutrition...
Certificate Course in

Allergy 2022

(Video Lectures)

Jointly organised by

The Federation of Medical Societies of Hong Kong
The Hong Kong Institute of Allergy

Objectives:
To provide an updated understanding in hot topics of allergy.

<table>
<thead>
<tr>
<th>Date</th>
<th>Topics</th>
<th>Speakers</th>
</tr>
</thead>
</table>
| 21 July 2022 | Allergen specific immunotherapy: the clinical applications | Dr. Alson W. M. CHAN
Specialist in Paediatric Immunology
Allergy & Infectious Diseases |
| 28 July 2022 | Allergy, diet & nutrition                       | Ms. Sabrina W. S. MOK
Registered Dietitian                      |
| 4 Aug 2022  | Oral immunotherapy for food allergy             | Dr. Gilbert T. CHUA
Clinical Assistant Professor
Department of Paediatrics & Adolescent Medicine
The University of Hong Kong |
| 11 Aug 2022 | Urticaria: new treatment updates                | Dr. Marco H. K. HO
Specialist in Paediatric Immunology
Allergy & Infectious Diseases |
| 18 Aug 2022 | Anaphylaxis: the new developments               | Dr. Agnes S. Y. LEUNG
Assistant Professor
Department of Paediatrics
The Chinese University of Hong Kong |
| 25 Aug 2022 | Updates in allergy diagnostics                 | Dr. Adrian Y. Y. WU
Specialist in Allergy & Immunology           |

Date: 21, 28 July & 4, 11, 18, 25 August 2022 (Every Thursday)
Duration of session: 1.5 hours (6 sessions)
Time: 7:00 pm - 8:30 pm
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Language Media: Cantonese (Supplemented with English)
Course Fee: HK$1,000
Certificate: Awarded to participants with a minimum attendance of 70% (4 out of 6 sessions)
Deadline: 14 July 2022
Enquiry: The Secretariat of The Federation of Medical Societies of Hong Kong
Tel.: 2527 8898    Fax: 2865 0345    Email: vienna.lam@fmshk.org

CME / CNE / CDE (Dietitians) Accreditation in application
Online Application from website: http://www.fmshk.org
Programme” is one of the first family-based intervention programmes targeted at individuals with IDD in Hong Kong. We found that a key strength of our programme was its acceptability to families, 98% of whom had found it satisfactory. Their feedback is that the programme has enabled them to understand basic nutrition principles and to put the principles to practical use in their family. The high attendance for dietetic consultations (98.5%) and the zero-dropout rate are clear and convincing indicators of the importance of such an approach in intervention.

We had taken into account key challenges for addressing the population with IDD, such as intellectual limitations (e.g. lack of knowledge, difficulty in understanding), cognitive and social emotional barriers (e.g. lack of motivation, lack of self-efficacy, poor outcome expectations), and issues of accessibility (e.g. money, accessibility of equipment). With social distancing measures during the COVID-19 pandemic, we swiftly managed to modify our classes and consultation sessions to become online, so that we could still maintain our participants’ motivation and commitment to the programme. We also made offers when needs arose to deliver fresh produce and provided basic cooking equipment (e.g. portable blender) throughout the programme as our encouragement to them to practice home cooking for better health.

Further larger long-term randomised controlled trials are warranted to confirm the findings of this programme. Worth noting is the scarcity in studies on physical activity and nutrition health interventions for the individual with IDD. Heller et al. found that from 1986 to 2006, only a total of 11 articles comprising 12 studies were found that were looking into the issue. Heller et al. opined that the interventions in most of these studies need more rigorous testing because the evidence to date, while promising, lacks a strong empirically tested evidence base. Given the long duration of our programme, the information thus far obtained is promising empirical evidence in support of claims made in those studies in which physical activity and nutrition health interventions are upheld for coping with obesity problems encountered by individuals with IDD.

Though a global problem, there are yet few sustainable solutions realised for obesity control. Community-based interventions are predominantly short term and limited in scope. Hong Kong is no exception. Given the positive outcomes in weight management, cardiovascular health, lifestyle and diet quality, it is apparent that the “Jockey Club Love Healthy Life Sport and Nutrition Programme” is a feasible framework worthy of further consolidation to make it even more applicable and resourceful to the community with IDD. It is probable, too, that as the programme further goes, empirical data so accumulated will serve as a valuable database for developing the project into a long-term, community-based, and sustainable intervention programme. Bearing in mind the huge average lifetime economic cost (USD 1,014,000) per person for people with intellectual disabilities, it is worth the while to do the utmost we can to curb their obesity problem at its very root. Effective prevention is better than mending.

Established in 2016, Love 21 Foundation Limited (Love 21) is a registered charity in Hong Kong dedicated to empowering members of the Down’s syndrome, autistic, and neurodiverse communities to reach their full potential through sports, nutrition, and holistic support.

Sports are at the core of the charity’s mission, with over 360 classes hosted each month throughout 2021 that promote the physical and mental health benefits of sports-related activities. A wide range of sports activities are offered, including fitness, tennis, rugby, football, basketball, yoga, dance, boxing, karate as well as outdoor activities such as hiking, surfing and dragon boat.

With the support from the Hong Kong Jockey Club Charities Trust, Love 21 has been running the “Jockey Club Love Healthy Life Sport and Nutrition Programme” since 2021 to promote, encourage and sustain healthy lifestyle changes for Love 21 members. In addition, families are also offered holistic support through one-on-one counselling. The figure below represents a summary of Love 21’s achievement between 1st April 2021 and 31st March 2022. All of Love 21’s programmes are offered free of charge to beneficiary families and are mainly held at the organisation’s community centre, Love 21 Space, in San Po Kong.

CASE SHARING 1

Ms A is an adult female with mild intellectual disability and obesity. She suffered from constipation, oligomenorrhoea, recurrence of canker sores, face acne and hidradenitis suppurativa. Her usual dietary habit was excess in refined carbohydrates, sugar, and animal protein. Her water intake was inadequate. Her lifestyle was quite sedentary before joining the programme. Ms
A’s goals were to get slimmer and better skin for photo shooting. Ms A’s mother was aware of her overweight issue; however, she did not know how to help Ms A and was worried that Ms A would not get enough nutrients during weight loss. During the programme, Ms A showed good compliance with the dietitian’s dietary advice. She drank more water, consumed more wholegrains, fruit and vegetables; and less animal protein, refined carbohydrates and sugar. In meal preparation, her mother followed our tailor-made diet plan for food portioning and purchased fewer takeaway meals. Ms A increased her hours on physical activities. The patient’s health parameters improved as below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before programme</th>
<th>After programme</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>63.4</td>
<td>60.3</td>
<td>-4.9</td>
</tr>
<tr>
<td>Muscle Mass (kg)</td>
<td>22.2</td>
<td>24.0</td>
<td>8.1</td>
</tr>
<tr>
<td>Body Fat Mass (kg)</td>
<td>22.8</td>
<td>17.0</td>
<td>-25.4</td>
</tr>
<tr>
<td>Body Fat Percentage (%)</td>
<td>35.9</td>
<td>28.1</td>
<td>-21.7</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>25.0</td>
<td>23.7</td>
<td>-5.2</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>92.5</td>
<td>87.8</td>
<td>-5.1</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>130</td>
<td>104</td>
<td>-20.0</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>85</td>
<td>71</td>
<td>-16.5</td>
</tr>
<tr>
<td>Recovery Heart Rate (bpm)</td>
<td>125</td>
<td>100</td>
<td>-20.0</td>
</tr>
<tr>
<td>Alanine Transaminase (U/L)</td>
<td>56.0</td>
<td>29.0</td>
<td>-48.2</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>5.70</td>
<td>5.10</td>
<td>-10.5</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>5.70</td>
<td>3.90</td>
<td>-31.6</td>
</tr>
<tr>
<td>High Density Lipoprotein (mmol/L)</td>
<td>1.3</td>
<td>1.27</td>
<td>-2.3</td>
</tr>
<tr>
<td>Low Density Lipoprotein (mmol/L)</td>
<td>3.52</td>
<td>2.12</td>
<td>-39.8</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>1.92</td>
<td>1.10</td>
<td>-42.7</td>
</tr>
<tr>
<td>Uric Acid (mg/dL)</td>
<td>7.95</td>
<td>6.91</td>
<td>-13.0</td>
</tr>
</tbody>
</table>

During the programme, Ms A had fewer canker sores and much milder face acne. Hidradenitis suppurativa did not occur. Her bowel movement and menstruation became regular. Ms A is satisfied with the improvement, and her mother has more confidence now in meal preparation for her daughter. The whole family has benefitted from the programme.

CASE SHARING 2

Mr B, an adult male, is overweight and mildly autistic. He is on Epilim and Trileptal. He lives with his family and works in a sheltered workshop. Before joining the programme, he danced and ran 2-3 times a week, and spent 2.4 hours a day on electronic devices. His intake of fruit, vegetables, wholegrains, fatty fish, dairy and fluid was inadequate; however, the intake of refined carbohydrates and meat was excessive. His nutrition goals were to reduce weight and waistline, and to eat healthily. He attended our monthly dietetic consultation with his mother. In the consultations, we worked out attainable nutritional goals with him and his mother on a monthly basis. The patient’s health parameters improved as below:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before programme</th>
<th>After programme</th>
<th>Change (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Body Weight (kg)</td>
<td>90.7</td>
<td>80.1</td>
<td>-11.7</td>
</tr>
<tr>
<td>Muscle Mass (kg)</td>
<td>39.4</td>
<td>37.0</td>
<td>-6.1</td>
</tr>
<tr>
<td>Body Fat Mass (kg)</td>
<td>21.6</td>
<td>14.8</td>
<td>-31.5</td>
</tr>
<tr>
<td>Body Fat Percentage (%)</td>
<td>23.8</td>
<td>18.5</td>
<td>-22.3</td>
</tr>
<tr>
<td>Body Mass Index (kg/m²)</td>
<td>26.9</td>
<td>23.8</td>
<td>-11.5</td>
</tr>
<tr>
<td>Waist Circumference (cm)</td>
<td>95.6</td>
<td>84.7</td>
<td>-11.4</td>
</tr>
<tr>
<td>Systolic Blood Pressure (mmHg)</td>
<td>127</td>
<td>111</td>
<td>-12.6</td>
</tr>
<tr>
<td>Diastolic Blood Pressure (mmHg)</td>
<td>78</td>
<td>69</td>
<td>-11.5</td>
</tr>
<tr>
<td>Recovery Heart Rate (bpm)</td>
<td>95</td>
<td>82</td>
<td>-13.7</td>
</tr>
<tr>
<td>Alanine Transaminase (U/L)</td>
<td>25.0</td>
<td>22.0</td>
<td>-12.0</td>
</tr>
<tr>
<td>Fasting Glucose (mmol/L)</td>
<td>4.50</td>
<td>4.40</td>
<td>-2.2</td>
</tr>
<tr>
<td>Total Cholesterol (mmol/L)</td>
<td>3.80</td>
<td>3.10</td>
<td>-18.4</td>
</tr>
<tr>
<td>High Density Lipoprotein (mmol/L)</td>
<td>1.16</td>
<td>1.22</td>
<td>5.2</td>
</tr>
<tr>
<td>Low Density Lipoprotein (mmol/L)</td>
<td>2.22</td>
<td>1.57</td>
<td>-29.3</td>
</tr>
<tr>
<td>Triglycerides (mmol/L)</td>
<td>0.92</td>
<td>0.68</td>
<td>-26.1</td>
</tr>
<tr>
<td>Uric Acid (mg/dL)</td>
<td>4.49</td>
<td>3.80</td>
<td>-15.4</td>
</tr>
</tbody>
</table>

In the programme, Mr B did follow the prescribed meal plan for him. He increased his intake in fruits, vegetables, dairy, wholegrains, fatty fish and fluid and reduced his refined carbohydrates and meat consumption. Bowel movements improved from every 1-2 days with pellet stools to daily with soft and formed ones. He also increased his exercise level and reduced his time spent on electronic devices to 0.5 hour a day. His mother is extremely pleased with his son’s achievements and appreciative of our health advice, which has enabled her to make better food choices for her family.
References


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香港醫學組織聯會

VOL.27 NO.7 JULY 2022
Indication: VYVANSE® is indicated for the treatment of Attention Deficit / Hyperactivity Disorder (ADHD)²

- Novel Prodrug formulation in ADHD treatment²
- Once daily, Capsule or Capsule free administration²
- Long acting efficacy for up to 13 Hours in children 6-12 year old³ & up to 14 hours in adults⁴

* Study design: Study 311 was a randomised, double-blind, multicentre, placebo-controlled, crossover, analogue-classroom study of 34 children (6-12 years) with a primary diagnosis of ADHD. Following screening (≥3 weeks) and washout (up to 1 week), eligible subjects received open-label VYVANSE, titrated from 30 mg QD, to reach an optimal dose in 4 weeks. Afterwards, 17 patients were randomised (1:1) to receive VYVANSE at the optimised QD dose × 1 week followed by placebo QD × 1 week or vice versa, in a double-blind manner. The primary end point was the SKAMP-D subscale score at 15 hours post-dose on the last day of each phase, closed at 7 a.m.³

# Study design: Study 316 was a randomised, double-blind, placebo-controlled, 2-way crossover study of 127 adults (18-55 years) with a primary diagnosis of ADHD, conducted in a simulated work environment. Following a 4-week, open-label dose-optimisation phase, 127 patients were then randomised to receive their optimised dose of VYVANSE × 7 days followed by placebo × 7 days or vice versa. The efficacy end point was the total PERMP scale score averaged over all post-dose time points during the visits at week 5 and 6.

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Indication: VYVANSE® is indicated for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). Dosage: The recommended starting dose is 30 mg once daily in the morning. In patients aged 6 and above, dosage may be adjusted in increments of 10 mg or 20 mg at approximately weekly intervals up to a maximum dose of 70 mg/day. Administration: Take VYVANSE by mouth in the morning with or without food. Avoid afternoon doses because of the potential for insomnia. Swallow VYVANSE capsules whole, or open capsules, empty and mix the entire contents with yogurt, water or orange juice. Do not take anything less than one capsule per day. A single dose should not be divided. Contraindications: Known hypersensitivity to amphetamines or other ingredients of VYVANSE. Patients taking monoamine oxidase inhibitors (MAOIs) or within 14 days of stopping MAOI. Warnings & Precautions: Potential for abuse and dependence, serious cardiovascular reactions, blood pressure and heart rate increases, psychiatric adverse reactions, suppression of growth, peripheral vasculopathy including Raynaud’s phenomenon, serotonin syndrome, Adverse Reactions (Incidence ≥5% and at a rate at least twice placebo): reported in children, adolescents, and/or adults were anxiety, decreased appetite, decreased weight, dizziness, dry mouth, irritability, insomnia, nausea, upper abdominal pain, and vomiting. Full prescribing information is available upon request.


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What are the Treatment Options for Paediatric Drug-resistant Epilepsy?

Dr Mario WK CHAK

VOL.27 NO.7 JULY 2022

HOW COMMON IS DRUG-RESISTANT EPILEPSY?

The condition is also referred to as intractable, medically refractory, or pharmaco-resistant epilepsy. As many as 20-40 per cent of patients with epilepsy are likely to have refractory epilepsy.

Options for the Management of Drug-Resistant Epilepsy Include:

• Continuing trials of anti-seizure medications or specific treatment according to specific underlying aetiologies including metabolic, genetic, immunological causes, etc.
• Epilepsy Surgery
• Dietary Therapy
• Vagus Nerve Stimulation
• Other Palliative Surgical Options, e.g. Corpus Callosotomy for drop attack

WHAT IS THE CHANCE OF SEIZURE FREEDOM WITH MEDICATIONS AFTER 2 FAILED TRIALS?

After two anti-seizure medications fail, the chance of the third failing is 95%. It is true that in Kwan and Brodie’s seminal 2000 study, only 4% of the entire study cohort achieved seizure freedom after two failed medications. And in the 2018 follow-up by Chen et al., only 4.4% of the study cohort became seizure free on a third medication regimen. Now we noted that seizure free rated after two failed medications are much higher than misstated 5%. The 2018 follow up study found that among people who tried a third medication, 23.6% achieved seizure freedom. Similar seizure freedom was achieved in 15% of those trying a fourth medication, 14.1% trying a fifth and 14% trying a sixth. From the result of the above study, in clinical practice, it is worthwhile to continue to try third, fourth, fifth and sixth different anti-epileptic drugs for individual patients who failed the first and second anti-epileptic drugs. The crucial message for clinicians and patients is that seizure freedom is possible, even if the first two medications don’t work.

said Blond. “Seizure freedom makes a huge difference in terms of quality of life and survival,” Blond said, “if you can help someone achieve that, you can change their life.”

PAEDIATRIC EPILEPSY SURGERY

Such surgery refers to the resection/disconnection of brain epileptogenic tissue with the aim of improving seizure control.

Goal

At present, the goal of surgery in children is to achieve seizure control, with the potential for the added benefit of improved neurodevelopment.

Indications for Referral

• Children with seizures that are uncontrolled by medical treatment (i.e. failure of two or three appropriate drugs) or are disabling (including medication side effects)
• Patients with MRI findings of a lesion potentially amenable to surgical removal
• Patients with stereotyped or lateralised seizures or other evidence of focality that cannot be definitely attributed to idiopathic partial epilepsies
• Childhood epilepsy that cannot be classified as a clearly defined electro-clinical epilepsy syndrome (ILAE classification)

Common Surgical Remedial Syndrome in Children

• Hippocampal Sclerosis
• Developmental Tumour (DNET, Ganglioglioma)
• Hemispheric Syndrome (Rasmussen’s Encephalitis, Unilateral Procephalic Cyst/MCA infarct, Hemispheric Cortical Dysplasia, Hemimegalencephaly)
• Sturge-Weber Syndrome
• Focal Cortical Dysplasia
• Cavernous Haemangioma
Special Considerations in Children

- Children with intellectual disability, developmental delay, psychiatric disease, or at a very young age should not be excluded from being considered surgical candidates.
- A developmental arrest or progressive disturbances in cognitive function, behaviour, and psychiatric state (epileptic encephalopathy) are common findings in pre-epilepsy surgery assessment and these findings can influence the decision for surgical management.
- Early surgical intervention is critical such as in infants with catastrophic epilepsy, for whom surgical intervention needs to be prompt in order to avoid developmental arrest/regression.
- A subgroup of Paediatric epilepsy surgery candidates, namely those patients with extremely complex presentation or early catastrophic seizures, should be served at Paediatric Surgical centres with advanced technologic capability and dedicated multidisciplinary expertise.

PAEDIATRIC EPILEPSY SURGERY CENTRES LEVEL 1 & 2

Pre-surgical evaluation and surgery in the paediatric age group are unique in challenges related to caring for the very young, range of aetiologies, choice of appropriate investigations, and surgical procedures. Accepted standards that define the criteria for levels of pre-surgical evaluation and epilepsy care do not exist. Through a modified Delphi process involving 61 centres with experience in pediatric epilepsy surgery across 20 countries, including low-, middle-, and high-income countries, consensus has been established for two levels of care. Levels have been based on the age, aetiology, and on the complexity of pre-surgical evaluation and surgical procedure. Competencies have been assigned to the levels of care relating to personnel, technology, and facilities. Criteria were established when consensus was reached (>/= 75% agreement).

Level 1 Care

- Level 1 care applies to children aged nine years and older, with discrete lesions including hippocampal sclerosis, undergoing lobectomy or lesionectomy. The lesion is preferably located on the cerebral convexity and not close to the eloquent cortex. Care is provided by a team comprising a paediatric epileptologist, a paediatric neurosurgeon, and a paediatric neuroradiologist with access to video electroencephalography and 1.5-T magnetic resonance imaging (MRI).

Level 2 Care

- Encompassing level 1 care, Level 2 care applies to patients across the age span and across a wide range of aetiologies (including tuberous sclerosis complex, Sturge Weber syndrome, hypothalamic hamartoma) associated with MRI lesions that may be ill-defined, multi-lobar, hemispheric, or multifocal, including children with normal MRI findings or children with foci in/abutting the eloquent cortex. Necessary level 2 technologies include 3-T MRI, other advanced magnetic resonance technology including functional MRI and diffusion tensor imaging (tractography), positron emission tomography and/or single photon emission computed tomography, source localisation with electroencephalography or magnetoencephalography, and the ability to perform intra- or extra-operative invasive monitoring and functional mapping. Necessary specialised personnel includes a large multidisciplinary team with expertise in paediatric epilepsy, neurophysiology, neuroradiology, epilepsy neurosurgery, neuropsychology, anaesthesia, neuro-critical care, psychiatry, and nursing. Such advanced level of care will improve patient safety and outcomes for paediatric epilepsy surgery and will set standards for personnel and technology to achieve these levels.

VAGAL NERVE STIMULATION

In children and young people who are refractory to anti-epileptic medications but who are not suitable for resective surgery, vagal nerve stimulation (VNS) is indicated for use as adjunctive therapy in reducing the frequency of seizures.

This group of patients includes children and young people whose epileptic disorder is dominated by focal seizures (with or without secondary generalisation) or generalised seizures.

Side effects are usually transient and well-tolerated and include voice alteration, hoarseness of voice, cough, stomach upset, pain, tingling sensations, nausea, and headache.

It is a palliative procedure with a response rate of 50% reduction in seizure frequency in one-third to one-half of patients.

Ketogenic Diet

The ketogenic diet is a treatment option for people with epilepsy, typically for those whose seizures are not controlled with anticonvulsant medications.

What is a Ketogenic Diet?

It is a special high-fat, low carbohydrate, and moderate protein diet that is carefully controlled. Keto = ketone, genic = producing. The typical ketogenic diet, called the "long-chain triglyceride diet", provides 3 to 4 grams of fat for every 1 gram of carbohydrate and protein. A ketogenic diet "ratio" is the ratio of fat to combined carbohydrate and protein (both in grams).
How Does the Diet Work?12

Usually the body uses carbohydrates (such as sugar, bread, pasta) for its fuel but in KD, fats become the primary fuel. Ketones are one of the possible mechanisms of action of the diet. Other possible theories include glucose stabilisation, adenosine, polyunsaturated fatty acids, etc.

Whom is the Diet Suitable For? 12

It is recommended for people whose seizures have not responded to several different anti-seizure medicines.

Highly Beneficial Clinical Entities as Recommended by The International Ketogenic Diet Study Group12

- Angelman Syndrome
- Complex 1 Mitochondrial Disorders
- Tuberous Sclerosis Complex
- Dravet Syndrome
- Doose Syndrome
- Glut-1-deficiency Syndrome
- Infantile Spasms
- Febrile Infection Related Epilepsy Syndrome (FIRES)
- Solely Formula Fed Infants or Children with Drug Resistant Seizure
- Ohtahara’s Syndrome
- Pyruvate Dehydrogenase Deficiency
- Super Refractory Status Epilepticus (SRSE)

Moderately Beneficial Clinical Entities12

- Childhood Absence Epilepsy
- Cortical Malformation
- Juvenile Myoclonic Epilepsy
- Lennox Gastaut Syndrome
- Rett’s Syndrome

Development of Local Paediatric Epilepsy Surgery Service

Since 2005, a multidisciplinary Paediatric Epilepsy Surgery team has been established in Tuen Mun Hospital to have regular case conferences to evaluate each child and adolescent with drug-resistant epilepsy, with the aim to identify the underlying aetiologies and any epileptogenic focus, by offering investigations such as Long term Video EEG monitoring, structural and functional imaging etc. Suitable candidates will be selected for curative surgical treatment. For those who are not candidates for resective surgery, the team will try to optimise medical treatment or consider for Vagus Nerve Stimulator Implantation and Ketogenic Diet.

References

3. Epigraph Vol.22isssue 4, summer 2020 Setting the record straight on the chances of seizure freedom after two medications fail
12. ILAE Website Ketogenic Diet Basic
# Certificate Course in Ophthalmology 2022

## Video Lectures

**Objectives:**
This course aims to provide an overview and update on the diagnosis and management of common and important eye diseases. After attending the course, attendees will learn how to deal with common ophthalmic conditions and when to refer patients to ophthalmologists.

<table>
<thead>
<tr>
<th>Date</th>
<th>Topics</th>
<th>Speakers</th>
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</thead>
<tbody>
<tr>
<td>16 August 2022</td>
<td>Cataract and Cataract Surgery Update</td>
<td>Dr. HO Wing Lau FHKAM (Ophthalmology)</td>
</tr>
<tr>
<td></td>
<td>Refractive Errors, Presbyopia and Refractive Surgeries</td>
<td>Dr. CHAN Chung Yan, Tommy FHKAM (Ophthalmology)</td>
</tr>
<tr>
<td>23 August 2022</td>
<td>Corneal and External Eye Diseases</td>
<td>Dr. WAN HO Nam, Kelvin FHKAM (Ophthalmology)</td>
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<tr>
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<td>Glaucoma and Glaucoma Surgery Update</td>
<td>Dr. WONG Ka Wai, Jasper FHKAM (Ophthalmology)</td>
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<tr>
<td>30 August 2022</td>
<td>Neuro-Ophthalmology</td>
<td>Dr. HO Wing Lau FHKAM (Ophthalmology)</td>
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<td>Squint, Paediatric Ophthalmology</td>
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<tr>
<td>6 September 2022</td>
<td>Update in Orbital Diseases and Oculoplastic Surgery</td>
<td>Dr. LAM Stacey Carolyn FHKAM (Ophthalmology)</td>
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<td></td>
<td>Red Eyes, Ocular Trauma and Emergencies</td>
<td>Dr. CHOY Nga Kwan, Bonnie FHKAM (Ophthalmology)</td>
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<tr>
<td>13 September 2022</td>
<td>Retinal Detachment and Diabetic Retinopathy</td>
<td>Dr. LAI Hiu Ping, Frank FHKAM (Ophthalmology)</td>
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<tr>
<td></td>
<td>Common Macular Diseases and Treatment</td>
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<tr>
<td>20 September 2022</td>
<td>Ophthalmic Imaging</td>
<td>Dr. MOHAMED Shaheeda FHKAM (Ophthalmology)</td>
</tr>
<tr>
<td></td>
<td>Use of Laser in Ophthalmology</td>
<td>Dr. YUEN Shi Yin, Nancy FHKAM (Ophthalmology)</td>
</tr>
</tbody>
</table>

**Date:** 16, 23, 30 August & 6, 13, 20 September 2022 (Tuesday)

**Duration of session:** 1.5 hours (6 sessions)

**Time:** 7:00 pm – 8:30 pm

**Course Feature:** Video lectures (with Q&A platform for participants to post the questions)

**Quiz for doctors:** DOCTORS are required to complete a quiz after the completion of each lecture

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---

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Spina Bifida Occulta: When to Look for It and How to Manage?

Dr Sui-To WONG
MBBS(HK), MMedSc, FRCSed(Surgical Neurology)
Consultant, Department of Neurosurgery, Tuen Mun Hospital

INTRODUCTION

Spina bifida occulta (aka closed spina bifida) remains a common condition in current neurosurgical practice, even though spina bifida aperta (aka open neural tube defect and myelomeningocele) has become a rare entity. Spina bifida occulta encompasses an assemblage of spinal anomalies of different complexities. Neurosurgeons prefer the term "closed type of spinal dysraphism" to "spina bifida occulta" because the bony "spina bifida" itself is of least clinical importance.

These anomalies are of interest to clinicians simply because they pose a threat to the nervous system, chiefly by the tethering effect on the spinal cord, sometimes by the presence of dermoid, epidermoid tissues or sinuses, also rarely through local mass effect.

The clinical manifestations of the neurological damage in spina bifida occulta depend on the spinal level of a particular lesion. In the most prevalent lumbosacral lesions, symptomatic patients have various degrees of asymmetrical lower limb motor and sensory impairment, limb deformity, and bladder and bowel dysfunction.

Treatment, when indicated, is by open surgery. The majority of the surgeries are prophylactic in nature - to prevent new onset of neurological deficits and limb deformities, and/or to prevent existing neurological deficits from deteriorating. Prophylactic surgery is advocated for most cases because limb deformities, once present, are permanent, chronic neurological deficits are usually irreversible, and even acute neurological deteriorations are only partially reversible. Neurological deficits that are present at birth are mostly due to dysgenesis of functional neural tissue, thus cannot be rectified by surgical procedures; only in exceptional situations that the "congenital" deficits are due to tethering or local mass effect such that they may be partially corrected by surgery.

CLASSIFICATION

Here, I present a classification of spinal dysraphism that is currently being used by the international community of paediatric neurosurgeons treating spina bifida: Table 1.7,13 This classification has been refined in the past three decades, through a better understanding of the underlying patho-embryogenetic mechanisms of these spinal anomalies. Knowing the patho-embryogenetic mechanism of a lesion helps the surgeon to understand the patho-anatomy of the lesion, which is a prerequisite for performing safe surgery on these patients.8 It will be beneficial to the general practitioner to appreciate the heterogeneity of these anomalies from the classification, even without going into the fine details of each individual entity.

Table: All except myelomeningoceles/open neural tube defect in this table are closed type of spinal dysraphism. (Developed by the author)

Table 1: All except myelomeningoceles/open neural tube defect in this table are closed type of spinal dysraphism. (Developed by the author)

<table>
<thead>
<tr>
<th>Spinal Dysraphism: Classification by Embryogenesis Theories</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disorders of gastrulation</td>
</tr>
<tr>
<td>Spinal cord malformations</td>
</tr>
<tr>
<td>Neurenteric cyst</td>
</tr>
<tr>
<td>Disorders of primary neurulation</td>
</tr>
<tr>
<td>Incomplete neural tube closure</td>
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<td>Myelomeningocele/Open neural tube defect</td>
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<td>Incomplete disjunction</td>
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<td>Focal spinal nondisjunctural disorders</td>
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<tr>
<td>(Limited dorsal myeloschisis, Dermal sinus tract and cyst, Mixed lesions)</td>
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<td>Premature disjunction</td>
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<td>Spinal cord lipoma</td>
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<td>Disorders of secondary neurulation</td>
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<td>Spinal cord lipoma</td>
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<td>Retained medullary cord</td>
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<td>Terminal myelodystocie</td>
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<td>Filum abnormalities</td>
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Table 2: Indications for MRI of the Spine (Developed by the author)

Indications for MRI of the Spine
1. Infants with flat buttocks, low intergluteal cleft, champagne bottle legs.
2. Imperforate or stenotic anus.
3. Male with hypospadias, bifid scrotum, ambiguous genitalia.
4. Female with salpingo-uterovaginal atresia, bicornuate or didelphic uterus.
5. Renal agenesis, horseshoe kidney, double ureters.
6. Known caudal agenesis.
7. Neonates with unexplained recurrent urinary tract infection and reflux.
8. OEIS complex, VACTERL association, or bladder extrophy.
WHEN AND HOW TO SCREEN

The dogma of screening all patients with a midline skin lesion for tethering cord lesions is still true. Many skin stigmata cannot be missed (Fig. 1). Discharging sinuses with/without surrounding signs of infection are rare but can have dreadful consequences if missed (Fig. 1). Nowadays screening is also done for minor signs such as deviated or forked gluteal crease (Fig. 2). Some patients with spina bifida occulta may have no clinically identifiable skin stigmata. Thus in patients with neurological deficits, as well as in syndromal patients and in patients with vertebral anomalies (Table 2), magnetic resonance imaging (MRI) of the spine should be done.

As for the method of screening, to be definitive, MRI without gadolinium injection is the choice (Fig. 3). Ultrasound cannot deliver a definitely negative result; while in ultrasound positive cases, an MRI is still needed. X-ray plays no role in the screening process, because as mentioned above, a bony bifid per sec carries no clinical significance.

WHEN TO TREAT

The management of spina bifida occulta exemplifies the assessment of the benefit-to-risk ratio when contemplating surgery for patients. First, all patients are assessed for whether they are symptomatic of the condition with a full clinical history, physical examination, and appropriate investigations, especially urological studies. To assess the surgical risks, MRI images are studied to delineate the surgical anatomy.
the configuration of neural tissues, components of the tethering tissues, and their interfaces. A thorough understanding of the surgical anatomy will help the surgeon estimate the operability of a lesion.

In general, symptomatic patients are indicated for surgery, unless the residual neurological functions are not worthy of preservation. Patients with dermoid, epidermoid, or sinus tract in their lesions should also undergo surgery. Patients with large protruding mass should be operated on.

As mentioned in the Introduction, a high percentage of surgeries for spina bifida occulta are prophylactic surgery because of the irreversibility of the pre-operative neurological deficits and limb deformities. However, whether or not to recommend surgery for a particular patient depends on the result of the assessment of the benefit-to-risk ratio for that patient, based on the above-mentioned evaluations, and the best available natural history data of the type of lesions being evaluated. When the natural history data are lacking, the patient or guardians should be informed so; and the decision is made based on best estimates.

The value of prophylactic surgery declines with patients’ age. However, even young adults are likely to benefit from prophylactic surgery in most instances, as patients in this age group do present with new onset neurological deficits in ignored cases.

HOW TO TREAT

The goals of surgery in spina bifida occulta are the untethering of the spinal cord and total extirpation of any ectodermal tissue if present. Untethering of the spinal cord includes freeing the functional neural tissue completely from the surrounding tissues, and also reconstructing of the dural sac to house the untethered spinal cord in order to maintain the untethered milieu. Reconstruction is the key step in the prevention of re-tethering due to the formation of adhesions between the untethered spinal cord and the dural sac. The complexity of this reconstruction process varies in different subtype anomalies. In some anomalies, it is just a simple closure. In others, it could be a very difficult task, as in spinal cord lipomas.

In contemporary practice, an integral part of untethering surgery is advanced level intra-operative physiological monitoring, with which surgical risks are much reduced.

As a general rule, surgery on filum lesions can be considered technically the simplest, a procedure for trainee surgeons under supervision. Still there are filum lesions that with suboptimal handling, the patient may come back years later with re-tethering symptoms.

For the other lesions, although one might arbitrarily put them in some ascending order of technical complexity, I refrain from doing so to avoid giving a false impression that some of them could be handled without full attentiveness. All types of spina bifida occulta lesions need to be dealt with with the same degree of meticulousness. For the benefit of the patients, it is advisable that they are managed by experienced hands, because poor outcomes in this kind of prophylactic surgery take years to emerge, and by then not only limb deformities, but neurological deficits may well be irreversible.

A VERY SPECIAL ENTITY: SPINAL CORD LIPOMA

Spinal cord lipoma (aka lipomyelomeningocele) is a typical example of spina bifida occulta albeit the most-challenging-case scenario. It has the most complex patho-anatomy. Thus even surgeons specialised in the management of spinal cord lipomas need extra effort in each operative case, and recognise the high level of training required to master a safe and goal-achieving operation. Each step of the operation (opening, untethering, and reconstruction) is technically highly demanding. In order to achieve the goal of preventing re-tethering due to formation of adhesions, it is an overtly tedious operation. Suboptimal technique in a single step could cost the whole operation. The fact is that suboptimal surgery is worse than no surgery. Suboptimal surgery has a slim chance of rectifying someone’s "wreckage"; thus it is best to do it right the first time.

Furthermore, there is a subset of spinal cord lipomas, called Pang’s chaotic lipomas, that observation is currently the recommended approach in asymptomatic patients. The surgeon also needs to be able to recognise such conditions and to honour that a non-operative approach is the best option for the patient.
CONCLUSION

Spina bifida occulta is still a very relevant condition for clinicians to look out for. Many patients can benefit from proper surgery; though bear in mind that suboptimal surgery can be worse than no surgery.

References


Ketogenic Diet for Epilepsy and Other Medical Conditions

Ms Candy SM WONG

WHAT IS a KETOGENIC DIET?

A ketogenic diet is a therapeutic diet with high fat, low carbohydrate and sufficient protein content, with an aim to mimic the metabolism of fasting and result in chronic ketosis in the body. The Classical Ketogenic Diet (KD) was first used to treat epilepsy in the 1920s, with little variation hence constraining its compliance. In the past decades, the diet has evolved into other types, such as the Modified Atkin’s Diet (MAD), allowing greater diet flexibility and hence better tolerance and compliance.

USE OF KETOGENIC DIET IN REFRACTORY EPILEPSY

A ketogenic diet is an effective and safe treatment option for paediatric patients with drug-resistant epilepsy. A Cochrane review published in 2020 identified 13 randomised controlled trials with 932 participants: 711 children and 221 adults. Up to 55% of children achieved seizure freedom with a classical 4:1 ketogenic diet after three months whilst up to 85% of children achieved seizure reduction. Up to 25% of children were seizure free with MAD and up to 60% achieved seizure reduction. Another systematic review and meta-analysis published in 2017 included 70 studies to compare the short-term and long-term efficacy of classical KD and MAD in children and adolescents with epilepsy. In the classical KD group, the percentage of patients achieving ≥ 50% seizure reduction was 62, 60, 52, 42, and 46% at month-1, 3, 6, 12 and 24 and for the MAD group was 55, 47, 42, and 29% at month-1, 3, 6, and 12, respectively. This review concluded that classical KD does not differ substantially from MAD in achieving ≥ 50% and ≥ 90% reduction of seizure frequency.

The above-mentioned 2020 Cochrane review commented that the evidence for the use of KD in adults remains uncertain, while another meta-analysis of observational studies published in 2018 identified 16 studies, including 338 adult patients with intractable epilepsy. The results of the meta-analysis showed that the combined efficacy rates of all the symptoms of seizure freedom, seizure reduction by 50% or more, and seizure reduction below 50% in adults with intractable epilepsy were 13%, 53%, and 27%, respectively.

KD may be an effective treatment option for infants with drug-resistant epilepsy. A systematic review and meta-analysis published in 2020 included 33 studies with a total of 534 infants. Meta-analyses of uncontrolled studies estimate 59% of infants achieved ≥ 50% seizure reduction and 33% of infants achieved seizure freedom. The most commonly reported side effects were dyslipidaemia, and GI symptoms such as vomiting, constipation, gastroesophageal reflux, and diarrhoea. However, there are few studies focusing on infants treated with KD, and high-quality evidence is lacking. High-quality randomised-controlled trials are needed to confirm the effectiveness, safety, and tolerability of dietary treatment in this vulnerable age group.

MONITORING OF KETOGENIC DIET FOR REFRACTORY EPILEPSY

The precise mechanism of how a ketogenic diet works to reduce seizures remains unknown. It may be due to the direct action of the ketone bodies producing an anticonvulsant effect, or the metabolic changes associated with ketosis.

A ketogenic diet is recommended to be continued for at least 2-3 months to evaluate its efficacy. Routine monitoring of ketosis (in the form of urine or blood ketone checking) and of changes in seizure pattern is encouraged. Patients should be regularly reviewed by dietitians, and the KD should be regularly fine-tuned based on the nutritional assessment and laboratory data, such as blood urate, lipid profile and micronutrient levels.

Side effects of using a KD are usually mild and mostly limited to elevations of lipid profile and gastrointestinal symptoms. However, most of these side effects can be resolved with dietary modifications. Micronutrient deficiencies could also be an issue due to the restrictive nature of the diet. It is therefore crucial for the patients on a KD to have thorough assessments, careful meal planning, and regular follow-up by a dietitian trained in the area of KD.

In patients whose seizure control is successful, KD is recommended to be continued for two years. Weaning from KD to a normal diet is usually performed in a stepwise fashion over 3-4 months, with the ketogenic ratio slowly reduced every few days or weeks.

Multidisciplinary input from an experienced team of neurologists, neurology nurses, and ketogenic dietitians to manage these complicated patients with refractory epilepsy is fundamental to the successful control and
monitoring of seizures, while minimising the side effects of treatment and optimising the quality of life.

CONCLUSION

A ketogenic diet has been proven to be an effective and safe therapeutic diet for patients with drug-resistant epilepsy, especially in the paediatric population. Given the restrictive and unbalanced nature of the diet, it is crucial that the KD should be carefully planned, guided and monitored by a team of trained medical professionals. Patients and carers should have fully understood the benefits and risks before starting a ketogenic diet.

References

5. Lyons L and Schoeler NE et al. (2020) Use of ketogenic diet therapy in infants with epilepsy: A systematic review and meta-analysis. Epilepsyi, 61, 1261–1281

Dermatology Quiz

Dr Chi-keung KWAN
MBBS(HK), MRCP(UK), FRCP(Lond, Glasg, Edin), Dip Derm(Glasg), PDipID(HK), FHKCP, FHKAM(Medicine)
Specialist in Dermatology and Venereology

This 68-year-old lady complained of having an erythematous rash on the left vulval region for six months, with a gradual increase in size. There was a mild itch with some flaking. The patient had some tingling sensation. Physical examination revealed a relatively ill-defined erythematous patch on the left vulval region which had mild weeping and scaling on the surface. There was no ulcer or erosion (Fig. 1).

Questions

1. What are the differential diagnoses of her skin lesion?
2. What investigation are you going to order?
3. How do you treat this patient?

(See P.36 for answers)
The Medical Licentiate Society of Hong Kong (香港執照醫生學會) is delighted to be admitted as an ordinary member of The Federation of Medical Societies of Hong Kong. Our society is an independent, non-profit recognised professional body comprised of the LMCHK doctors (Licentiates of the Medical Council of Hong Kong). Our doctors graduated from medical schools from over 20 different licensing jurisdictions outside of Hong Kong including (in order by relative numbers of doctors): the UK, Mainland China, Australia, Ireland, USA, India, Canada, New Zealand, Chinese Taipei, Philippines, South Africa, Czech Republic, Germany, Italy, Korea, Nepal, Netherland-Antilles, Portugal, Singapore, Turkey, and Venezuela!

We were founded in 2017 as an association to support and represent the community of non-locally trained doctors and to engage with the public and other medical professionals both within and outside of Hong Kong.

Our aim is to promote the highest standards of health care, professionalism, safety and education in Hong Kong. Over the course of the last five years, we have worked with multiple media outlets to voice our support in retaining and improving the Hong Kong Medical Licensing Exam (HKMLE). We organise periodic seminars and clinical training experience for the HKMLE candidates. We reached out to the overseas medical communities and hosted multiple joint webinars on medical careers in Hong Kong, and offered assistance in preparation for the HKMLE. Senior doctors in our community are also active in public education.

We are fully aware of the needs of non-locally trained doctors, and have been offering advice and mentoring to our junior colleagues from career guidance to professional assistance. For the more senior doctors we are a platform for networking. And for all our members, one of our key objectives is socialising!

We are the only incorporated entity (HK Certificate No. 2896589) dedicated to non-locally trained doctors and the LMCHK community.
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**Events:**
- **Zoom Live:**
  - HKMA-HKSH CME Programme 2021-2022 (Online)
  - Topic: Scra, can it be better
  - Zoom Live:
  - Common Benign Perianal Diseases - Online
  - Zoom Live:
  - Certificate Course for GPs 2022 - Psychological effects of COVID-19 Pandemic - Online
  - Zoom Live:
  - Updates on Management of Thyroid Eye Disease - Online
- **Zoom Live:**
  - HKMA Annual General Meeting
  - The Hong Kong Neurosurgical Society Monthly Academic Meeting - To be confirmed
  - Zoom Live:
  - More Than Just a Number, What We Know About Hypertension? - Online
- **Zoom Live:**
  - Migraine - More Than a Simple Headache - Online
  - Zoom Live:
  - SGLT2 Inhibitors: Delivering More Evidences in Cardiorenal Protection - Online
  - Zoom Live:
  - Certificate Course for GPs 2022 - Cancer Screening - Oncologists’ Perspectives - Online
  - Zoom Live:
  - Vaccination safety and effectiveness in immunocompromised patients - Online
  - Zoom Live:
  - More Than Just a Number, What We Know About Hypertension? - Online
- **Zoom Live:**
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  - Vaccination safety and effectiveness in immunocompromised patients - Online
  - Zoom Live:
  - More Than Just a Number, What We Know About Hypertension? - Online

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<td>6 WED 2:00 PM</td>
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<td>HKMA Annual General Meeting Venue: HKMA Wanchai Premises, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong</td>
<td>Ms Candy YUEN 2527 8285</td>
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<td>13 WED 7:30 AM</td>
<td>The Hong Kong Neurosurgical Society Monthly Academic Meeting - To be confirmed Organiser: Hong Kong Neurosurgical Society Speaker: Dr CHINGLING Yuk-hong, Eric</td>
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<td>Zoom Live Vaccination safety and effectiveness in immunocompromised patients - Online Organiser: Hong Kong Medical Association Speaker: Dr SO Ho</td>
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Answers to Dermatology Quiz

Answers:

1. The main differential diagnoses are inflammatory dermatoses and infections such as eczema, irritant dermatitis, inverse psoriasis, fungal infection, intertrigo, cellulitis, erythrasma and so on. However, these lesions are often bilateral involving both sides. Unilateral involvement leads to consider other differential diagnoses, especially malignancy such as Extra-Mammary Paget’s Disease (EMPD).

As the lesion is unilateral, it makes inflammatory dermatoses or infections unlikely. Examination of other areas is still necessary to look for other clues suggesting inflammatory dermatoses such as eczema or psoriasis. Skin scraping for fungal smear and culture may be helpful to rule out dermatophytes infection. Since unilateral involvement suggests other serious diagnoses, a skin biopsy is preferred in this patient. Skin biopsy revealed, in the epidermis, Paget tumor cells which are large vacuolated cells with have a bluish cytoplasm. This suggests Extra-Mammary Paget’s Disease (EMPD).

Surgical excision including wide local excision or Mohs surgery is the mainstay of treatment. Sometimes radical vulvectomy may be required. Sentinel lymph node biopsy is also considered if the Paget cells have extended into the reticular dermis. Imiquimod cream, 5-fluorouracil cream, cryotherapy, CO2 Laser ablation, or photo-dynamic therapy may be considered in small lesions at initial presentation or for those who are not fit for surgery. Radiotherapy can be used alone or as adjuvant therapy.

2. As the lesion is unilateral, it makes inflammatory dermatoses or infections unlikely. Examination of other areas is still necessary to look for other clues suggesting inflammatory dermatoses such as eczema or psoriasis. Skin scraping for fungal smear and culture may be helpful to rule out dermatophytes infection. Since unilateral involvement suggests other serious diagnoses, a skin biopsy is preferred in this patient. Skin biopsy revealed, in the epidermis, Paget tumor cells which are large vacuolated cells with have a bluish cytoplasm. This suggests Extra-Mammary Paget’s Disease (EMPD).

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3. Surgical excision including wide local excision or Mohs surgery is the mainstay of treatment. Sometimes radical vulvectomy may be required. Sentinel lymph node biopsy is also considered if the Paget cells have extended into the reticular dermis. Imiquimod cream, 5-fluorouracil cream, cryotherapy, CO2 Laser ablation, or photo-dynamic therapy may be considered in small lesions at initial presentation or for those who are not fit for surgery. Radiotherapy can be used alone or as adjuvant therapy.

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Taking Good Care of the KIDS

An effective management on irritability for children with Autism

From week 3 through study endpoint, ABILIFY® shown significance in:
1. Efficacy in treating irritability
2. Improvement in CGI-I
3. Greater response rate

Data are expressed as least squares mean (standard error). *P<0.05; **P<0.01 versus placebo

Low incidence rates with ABILIFY® in:
- Prolactin elevation
- Weight gain
- Changes in triglycerides
- Changes in blood glucose

ABILIFY® Dosing and Administration

<table>
<thead>
<tr>
<th>Indication</th>
<th>Initial dose</th>
<th>Recommended dose</th>
<th>Maximum dose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irritability associated with Autistic Disorder</td>
<td>2mg/day</td>
<td>5-10mg/day</td>
<td>15mg/day</td>
</tr>
</tbody>
</table>


Abilify Prescribing Information:
See prescribing information before administering ABILIFY. ABILIFY may cause(d) or aggravate mania or hypomania. ABILIFY may cause suicidal thoughts or behavior. Suicidal thoughts or behavior may occur in children, adolescents, or adults at any time during treatment with ABILIFY. Symptoms and/or clinical features of suicidal behavior may include: agitation, intent to run away, unexplained anxiety, depression, irritability, and increased usage of energy. The potential benefits of treatment should be weighed against the risks of treatment. ABILIFY may cause an increase in weight. Some patients may experience problems in the eye such as blurred vision, dry eyes, or an increase in eye pressure. A rise in blood glucose levels may occur. Hyperkalemia may occur. Prolactin levels may increase. Other side effects may occur. Some patients experience dizziness, somnolence, or voice changes. Some patients may experience a decrease in blood pressure. Other side effects may occur. Some patients may experience problems in the eye such as blurred vision, dry eyes, or an increase in eye pressure. A rise in blood glucose levels may occur. Hyperkalemia may occur. Prolactin levels may increase. Other side effects may occur. Some patients experience dizziness, somnolence, or voice changes. Some patients may experience a decrease in blood pressure. Other side effects may occur. Some patients may experience problems in the eye such as blurred vision, dry eyes, or an increase in eye pressure. A rise in blood glucose levels may occur. Hyperkalemia may occur. Prolactin levels may increase. Other side effects may occur. Some patients experience dizziness, somnolence, or voice changes. Some patients may experience a decrease in blood pressure.

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HK004-A82-202006-4D1
THIS IS AIMOVIG.
THIS IS HEAD-TO-HEAD DATA.
THIS IS PREVENTION.

MORE DAYS WITHOUT MIGRAINE FOR MORE PATIENTS

• Significantly reduces migraine frequency and severity.¹

• Results may even improve over time among responders.² ⁴

MORE YEARS OF EVIDENCE THAN EVER BEFORE

• Evaluated to 5 years in the longest-running study of an anti-CGRP.⁴

• Most experience in the real world,⁵ ⁷ and results in this setting may exceed those seen in trials.⁶ ⁹

MORE CONFIDENCE FOR SIMPLE MANAGEMENT

• Proven superiority over topiramate for patient adherence, efficacy, and quality of life¹


ABBREVIATED PRESCRIBING INFORMATION: Aimovig® (triptan) is a dopamine D₂ receptor agonist. It is indicated for the acute treatment of migraine headaches. See Prescribing Information for complete prescribing information.

1. For migraine headache: for the acute treatment of migraine headache in adults and children 12 years and older. Use of this product in the pediatric population has not been established.
2. Use of this product for the acute treatment of 3 or more headaches per week may increase the likelihood of developing medication overuse headache.
3. Aimovig is contraindicated in patients who are hypersensitive to Aimovig or its components.
4. Aimovig is a Pregnancy Category C drug. The drug has not been studied in pregnant women, and it is not known whether it will cause fetal harm when given to pregnant women. Use is not recommended in pregnant women.
5. The most common adverse reactions to Aimovig in clinical trials were nausea, vomiting, irritability, and dizziness.
6. Always store in a dry place. Keep out of the reach of children.

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The materials for Aimovig® contained in this virtual material are approved for use only in Hong Kong. Prescribing information may vary among regional and countries. Your practice or local guideline is recommended. The information presented is based on the prescribing information of Aimovig®.

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