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- Advances in the Treatment of Ankylosing Spondylitis

Dr. Mo-yin Mok

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- Early Diagnosis of Spondyloarthropathies **CME**
- Present Status on the Genetics of Ankylosing Spondylitis
- Surgical Interventions for Ankylosing Spondylitis
- Update in the Management of Ankylosing Spondylitis
- Current Management of Juvenile Idiopathic Arthritis

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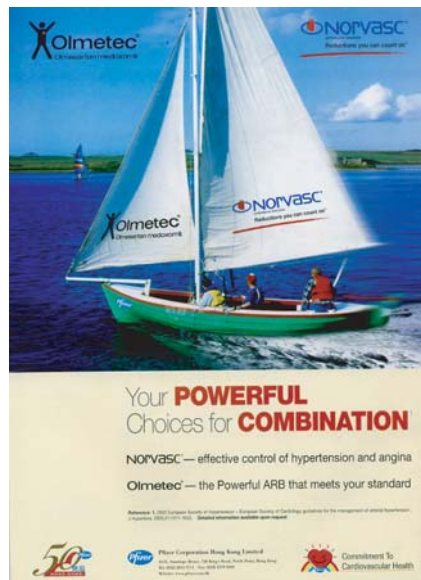
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Advances in the Treatment of Ankylosing Spondylitis

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Dr. Mo-yin Mok

Ankylosing spondylitis (AS) is a chronic inflammatory joint disease that affects the axial skeleton and is characterised by sacroiliitis and spondylitis. The disease onset typically occurs during the adolescence and early adulthood. AS typically presents with low back pain and stiffness which may be mistaken by these young people as musculoskeletal strains and sprains from sports or work activities. Not many are aware of possible underlying rheumatic diseases and present themselves for medical attention. With time, the ascending spondylitis results in significant stiffness of the lumbar, thoracic and cervical spine. A patient with advanced disease often adopts a stooped posture with limitation in chest expansion and restriction in movement of the neck. This often results in significant compromise in the activities of daily living. Some patients may also have peripheral arthritis, of which the hip joints are commonly involved and often indicates poor prognosis.

There have been struggles in the management of these patients in terms of pharmacological therapy. In contrast to rheumatoid arthritis, disease modifying anti-rheumatic agents in AS have not been shown to be efficacious in clinical studies. Patients have been left with no choice but regular non-steroidal anti-inflammatory drugs for symptomatic relief and non-pharmacological therapy to maintain the mobility of the spine.

The emergence of biologic agents has revolutionised the management of these patients. Tumour necrosis factor-alpha (TNF α), a pro-inflammatory cytokine has been found in sacroiliac joint aspirate from patients with AS. Various anti-TNF α biological agents have been shown to be efficacious in symptom control and radiological improvement. Early recognition of the disease and selection of patients based on the clinical profile and immunogenetics can hopefully help us to identify high risk patients for cost-effective treatment and to provide us with more information on predicting prognosis and clinical response to biologic treatment.

Novel surgical treatment has also shown early promising results in terms of correction of body posture and improvement in quality of life for these patients.



Early Diagnosis of Spondyloarthropathies

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This article has been selected by the Editorial Board of the Hong Kong Medical Diary for participants in the CME programme of the Medical Council of Hong Kong (MCHK) to complete the following self-assessment questions in order to be awarded one CME credit under the programme upon returning the completed answer sheet to the Federation Secretariat on or before 30 November 2006.

Introduction

Spondyloarthropathies are chronic inflammatory rheumatic disorders that are characterised by sacroiliitis, ascending spondylitis, enthesitis, extra-articular manifestation and genetic factor predisposition (HLA B27). They include ankylosing spondylitis (AS), psoriatic arthritis, reactive arthritis, and arthritis associated with inflammatory bowel disease.

Patients suffering from early spondyloarthropathies may not seek medical attention because of lack of awareness of their underlying conditions. Patients with advanced disease have significant restriction of movement of the trunk and neck leading to impairment in their activities of daily living. Early diagnosis can help counsel these patients and maintain spinal mobility by physiotherapy and achieve symptomatic control by the use of non-steroidal anti-inflammatory drugs. Recent advances in medical treatment using anti-tumour necrosis factor-(anti-TNF- α) have shown significant symptomatic and radiological improvement¹. Early diagnosis of spondyloarthropathies and referral to specialists is important in the management of these patients. Early diagnosis remains the current challenge in the context of different sets of diagnostic criteria which currently exist. It is important that the diagnostic criteria are useful to differentiate patients from the background population. Table 1 shows an example of such diagnostic criteria for which AS is commonly used. In this article clinical features that can help in early diagnosis of spondyloarthropathies at the level of the primary health care physicians are discussed.

Seronegative Spondyloarthropathies

Ankylosing spondylitis

This is a prototypic inflammatory arthropathy affecting joints of the axial skeleton. The male to female ratio is 3:1. The age at disease onset is around 20 years. The disease is extremely strongly associated with HLA B27. About 20% of these patients also have peripheral arthritis that involves particularly the hips, shoulders and knees. Enthesitis, inflammation affecting sites of insertion of ligaments, tendons and joint capsule into bone, is common. Fibrocartilage, such as sacroiliac (SI) joints and rib cartilages, is involved. Some patients may also suffer from extra-articular manifestations including iritis, aortitis and apical lung fibrosis.

Psoriatic arthropathies

Psoriasis affects 1-2% of the general population and around 10% of patients with skin psoriasis develop arthritis. The disease may start at any age. Joint involvement occasionally occurs prior to the development of psoriatic skin disease. About 70% of patients with psoriatic arthritis show evidence of nail dystrophy including pitting, ridging and onycholysis compared with only 20% of patients without arthritis. Psoriatic arthropathies may take one of the five patterns of joint involvement: distal interphalangeal joints, oligoarticular, rheumatoid arthritis like, spondyloarthropathy and arthritis mutilans.

Reactive arthritis

This inflammatory joint disease typically follows a genitourinary or gastrointestinal infection. Gram negative bacteria including Chlamydia trachomatis, Shigella, Salmonella, Yersinia and Campylobacter have been implicated in the underlying pathogenesis. There is typically arthritis involving lower limb joints that resolves within 3-6 months. Around 40% of patients develop persistent erosive arthritis.

Enteropathic arthropathies

Approximately 10% of patients with inflammatory bowel disease develop peripheral arthritis. Arthropathies are more commonly seen in patients with Crohn's disease than in ulcerative colitis. Oligoarticular involvement of lower limb joints may develop in some patients. AS occurs in around 5-10% of patients with Crohn's disease.

Early Diagnostic Features Of Spondyloarthropathies

Back pain

Limited spinal mobility is a cardinal feature of seronegative spondyloarthropathies. Low back pain is one the earliest symptoms of lumbar spondylitis. A distinction should be made in regard to the nature of pain being inflammatory or mechanical. Mechanical back pain is brought on by exercise. Inflammatory back pain should be alerted if it is of insidious onset in a patient younger than 40 years that persists for more than 3 months and is associated with morning stiffness that improves with exercise. Clinical history has been found to be useful as a screening tool for detection of patients with AS in the out-patient setting².



Inflammatory back pain gives satisfactory sensitivity (71.4%) and specificity (77.3%) in the diagnosis of early spondyloarthropathies³.

The early plain radiographic abnormalities of spondylitis may appear as marginal sclerosis with shiny corners at the margin of the intervertebral disc which may best be seen in MRI. New bone along the anterior vertebral margin results in squared appearance of lumbar vertebrae. With time, the spinal ligaments ossify forming vertically oriented bony bridges between the vertebral bodies called syndesmophyte. The posterior apophyseal and costotransverse joints become fused. In advanced disease the whole spine is rigidly fused and becomes a solid block of bone and is known as 'bamboo' spine.

Chest wall pain and limited chest expansion

Anterior chest pain may occur as a result of arthritis of the manubriosternal, sternoclavicular and costosternal joints. Together with limited chest expansion, chest wall pain is commonly seen in thoracic spinal involvement. Reduced chest expansion, especially of less than 5 cm, represents advanced forms of spondylitis and is of limited value in differentiating normal from early cases of spondylitis.

Restricted spinal movement

The clinical course of spondyloarthropathies is characterised by ascending spondylitis with gradual sequential involvement of the lumbar, thoracic and cervical spine. Limited spinal mobility is one of diagnostic criteria for spondyloarthropathies. Ankylosis is a late feature and is a result of ossification of ligaments, vertebrocostal and sternocostal joints. This eventually forms the classical "bamboo spine". Limitation in flexion and extension, rotation and lateral flexion of the lumbar spine may be detected in patients with early disease. However, the measurement is poorly standardised in clinical practice. Limited spinal motion appears to reflect the disease duration rather than a diagnosis of early disease.

Sacroiliitis

Unilateral or bilateral buttock pain is one of the earliest symptoms of sacroiliitis. The pattern of involvement of the SI joints being unilateral or bilateral may also give a clue to the underlying diagnosis. AS typically involves both SI joints whereas unilateral sacroiliitis is more usually found in psoriatic spondyloarthropathy, Reiter's disease and enteropathic spondyloarthropathies. There may be tenderness over one or both SI joints on palpation but radiological imaging offers higher sensitivity for detection. Plain X-ray of the SI joints is simple to perform. Despite the high specificity, it showed a poor sensitivity in diagnosing spondyloarthritis³. Radiological changes usually take three to seven years to develop and are the characteristics of advanced disease. A grading system has been devised depending on the chronic radiographic changes (Table 1). The earliest radiological change (Grade I) involve irregular fuzzy outlines of the joint margins that can be non-specific and may be difficult to differentiate from degenerative and infective changes of the SI joints. Grade 2 lesions show up as early erosion with sclerosis of the joint but may take years to develop. Eventually the process leads to obliteration of the joint space (Grade 4).

Computerized Tomography (CT) of the SI joints may allow detection of structural changes and is superior to conventional radiography for detecting bony changes related to sacroiliitis. Magnetic resonance imaging (MRI) can detect bone oedema and fatty conversion in the subchondral marrow, features of early sacroiliitis. It can also demonstrate joint inflammation in the synovial joint⁴. However, the MRI grading has not been standardised and their role in diagnosis is still under investigation. There is no firm consensus on the relative merits of CT versus MRI in the diagnosis of sacroiliitis. MRI is superior in the detection of both cartilage abnormalities and erosions whereas CT is superior to MRI in the detection of new bone formation and ankylosis. Scintigraphy is an alternative method to detect sacroiliitis but the sensitivity and specificity is lower than with other imaging techniques⁵. Areas of increased uptake of radioisotope may suggest pseudoarthrosis or fractures that may complicate the clinical course in patients with advanced disease.

Family history

The development of spondyloarthropathies is strongly linked to HLA B27 haplotype. The haplotype is prevalent in all forms of spondyloarthropathies especially AS and is inherited in an autosomal co-dominant fashion. The risk of developing AS in a person with positive family history is 20 to 40 times higher than the general population. Fifty percent of first degree relatives of the HLA-B27 positive individuals possess the antigen. The prevalence of HLA B27 among spondyloarthropathies and general population is shown in Table 2. HLA B27 is present in around 10% of normal population but in 90% of patients with AS. It has a high negative predictive value and is useful in early screening of the disease. The presence of HLA B27 and/or family history of spondyloarthropathies show high specificity in diagnosis when associated with inflammatory back pain³.

Enthesitis

Inflammation of the entheses, the sites of ligamentous attachment to bones, is one of the prominent features of spondyloarthropathies. Patients commonly complain of pain over the heel or the sole of the foot on walking. Tenderness can be elicited on the Achilles tendon and plantar fascia for detection of enthesitis at these sites. Clinical examination has only low sensitivity in detecting enthesitis. The role of MRI and ultrasonography as a more accurate tool in detecting enthesitis is currently under evaluation.

Peripheral arthritis

Some patients with spondyloarthropathies also have peripheral arthritis and may present with dactylitis, asymmetrical monoarthritis, oligoarthritis or a pattern simulating rheumatoid arthritis. There is usually a predominant involvement of joints of the lower limbs. In Reiter's disease, few joints are involved and there may be calcaneal erosions with spur formation that can be detected on Xray.

Extra-articular features

Extra-articular manifestations of spondyloarthropathies include inflammatory bowel disease, psoriasis, urethritis and anterior uveitis. These specific features



help to differentiate the particular sub-types of spondyloarthropathies. For example, anterior uveitis is more common in patients with AS (a prevalence of 40%) and skin psoriasis and nail dystrophy suggest psoriatic arthropathy. Other features such as fibrosing alveolitis, aortic incompetence, amyloidosis, balanitis and iritis may aid in diagnosis of spondyloarthropathies.

Conclusion

With the development of new therapies, there is a need to recognise patients with early disease who have worse prognosis. The inflammatory nature of back pain obtained from clinical history is helpful in the early diagnosis of spondyloarthropathies. Clinical sacroiliitis lacks the specificity and radiological sacroiliitis is too insensitive to be useful in early diagnosis. The emerging technique of ultrasound and MRI are future tools in assisting early diagnosis. Other useful information includes tissue-typing and family history. Particular extra-articular features help to differentiate the sub-types of spondyloarthropathies.

With the development of new biologic therapies, early recognition of patients with early stage of disease, together with information from future researches on identifying patients with worse prognosis and better response to treatment for earlier therapy will be of great benefit.

Table 1. Modified New York criteria for ankylosing spondylitis.

Clinical criteria
Low back pain and stiffness for >6 months that improves with exercise but is not relieved by rest
Limitation of motion of the lumbar spine in both sagittal and frontal planes
Limitation of chest expansion relative to normal values for age and sex
Radiological criteria
> grade II bilateral sacroiliitis
Grade III or IV sacroiliitis unilaterally

Table 2. Grading of chronic radiographic changes of the sacroiliac joint in ankylosing spondylitis.

Grade	X-ray findings
0	Normal
1	Suspicious
2	Sclerosis, some erosion
3	Severe erosion, widening of joint space, minor ankylosis
4	Complete ankylosis

Table 3. Prevalence of HLA B27 haplotypes in various spondyloarthropathies

Spondyloarthropathies	Percentage (%)
Ankylosing spondylitis	90
Reactive arthritis	75
Psoriatic arthropathy	50
Enteropathic arthropathy	50
General population	10

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MCHK CME Programme Self-assessment Questions

Please read the article entitled "Early diagnosis of spondyloarthropathies" by Dr Ho-yin Chung, Dr. Mo-yin Mok and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheet via fax (2865 0345) or by mail to the Federation Secretariat on or before 30 November 2006. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please choose the best answer.

1. Which of the following diseases do not belong to spondyloarthropathies?
 - a. Ankylosing spondylitis
 - b. Rheumatoid arthritis
 - c. Psoriatic arthropathy
 - d. Inflammatory bowel disease related arthritis
2. What of the following is not a pathological characteristic of spondyloarthropathies?
 - a. Sacroiliitis
 - b. Enthesitis
 - c. Osteoarthritis
 - d. Spondylitis
3. Which of the following is not an early symptom of presentation of spondyloarthropathy?
 - a. Neck pain
 - b. Back pain
 - c. Buttock pain
 - d. Back stiffness



- 4. Which of the following is most sensitive in the detection of early sacroiliitis?
 - a. Plain X ray
 - b. Magnetic Resonance Imaging
 - c. Scintigraphy
 - d. Tenderness on sacroiliac joint
- 5. Which of the following pattern of peripheral arthritis is seen in spondyloarthropathies?
 - a. Oligoarticular
 - b. Rheumatoid arthritis-like
 - c. Monoarticular
 - d. All of the above
- 6. Which of the following are predictive of psoriatic arthritis in a patient with skin psoriasis?
 - a. Nail dystrophy
 - b. Extensive psoriatic skin plaques
 - c. Erythroderma type of skin psoriasis
 - d. Family history of skin psoriasis
- 7. Which of the following is not an extra-articular manifestation of spondyloarthropathies?
 - a. Cardiac valvular defect of aortic regurgitation
 - b. Uveitis
 - c. Generalised lymphadenopathies
 - d. Apical lung fibrosis
- 8. Which of the following is poor prognostic factor in spondyloarthropathies?
 - a. Male
 - b. Female
 - c. Hip involvement
 - d. Family history
- 9. Which of the following is compatible with advanced spondyloarthropathies?
 - a. Restricted movement of the neck
 - b. Limited chest expansion
 - c. Bamboo spine on Xray of the lumbosacral spine
 - d. All of the above
- 10. What is the biologic treatment that has currently been shown to be efficacious in the treatment of ankylosing spondylitis?
 - a. Anti-CD20 antibody
 - b. Anti-tumour necrosis factor-alpha therapy
 - c. Methotrexate
 - d. Mycophenolate mofetil

ANSWER SHEET FOR NOVEMBER 2006

Please return the completed answer sheet to the Federation Secretariat on or before 30 November 2006 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Early diagnosis of spondyloarthropathies

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Present Status on the Genetics of Ankylosing Spondylitis

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Prof. Jieruo Gu

Ankylosing spondylitis (AS) is a multifactorial chronic rheumatic disease. The precise aetiology remains unclear. It is likely to involve interactions between genetic and environmental factors as evidenced by the variable clinical morbidity in different racial groups, familial congregation and the strong association with HLA-B27 in the major histocompatibility complex (MHC) region. There are more evidences from aggregation studies suggesting that more than one gene are involved in AS, including genes in both MHC and non-MHC regions. Genome-wide linkage analysis and disease-association studies are the main approaches to identify susceptible genes.

Major histocompatibility complex (MHC), located on chromosome 6p, is a multigene family comprises of genes in close linkage disequilibrium. It is closely related to function of the immune system and the product of this gene is a highly complex extracellular transmembrane protein called MHC antigen. Genetic epidemiology study showed that 40%-50% of the genetic component may be contributed by genes in the MHC region. Rubin et al first demonstrated this strong linkage between MHC region and AS in 15 multiplex AS families. When the population association of HLA-B27 with AS was taken into account, the maximum lod score was 7.5 at $\alpha = 0.05$. In accordance with Rubin's finding, all subsequent whole genome linkage investigations demonstrated strongest linkage between MHC region and AS suggesting the major role on genetic influence of the MHC region on the development of AS.

The genetic marker, HLA-B27, is present in 80 to 98 percent of AS patients. HLA-B27 accounts for only 16 percent of the total genetic risk for the disease, whereas the MHC on its own accounts for about half of the genetic variability for AS. The precise role of HLA-B27 in the pathogenesis of AS remains unclear and is likely to be heterogeneous and involves more than one mechanism. HLA-B27 is a family of 31 different alleles. Studies indicate that the relatively common alleles (subtypes), HLA-B*2705, B*2704, and B*2702, are strongly associated with AS. HLA-B*2706 is prevalent in Southeast Asia. The strong association with most subtypes of HLA-B27 supports the view that the disease is due to a genetically determined immune response to environmental factors in susceptible individuals. Arthritogenic peptide and molecular mimicry are hypotheses on the antigen presenting function of HLA-B27 postulated to relate to disease development. Different subtypes of HLA-B27 may differ in their ability to present peptides to autoreactive cytotoxic T

cells. However, certain aberrant immunobiological features of HLA-B27, such as misfolding and heavy chain dimerisation suggest that the underlying pathogenic mechanisms may be unrelated to its physiological function. We hope that more data from X-ray diffraction studies on individual peptides in the different HLA-B27 alleles can explain the role of B27 molecule in the pathogenesis of AS. Other HLA subtypes may also contribute to the genetic susceptibility to AS. HLA-B60 has been demonstrated to be associated with susceptibility to AS in some studies, whereas other studies support a role for HLA-DRB1*0101 and 1501 and other HLA factors (B7-Creg, B38, B39, DR1, DR8).

Tumour necrosis factor- α (TNF- α) promoter allele polymorphism has been postulated to be involved in the predisposition to AS. TNF α has been shown to be involved in the pathogenesis of a number of autoimmune diseases. Genome scans revealed the location of TNF α gene in the susceptibility region of MHC segment in AS. Anti-tumour necrosis factor (TNF)- α therapies, infliximab and etanercept, have been shown in clinical trials to be efficacious in the treatment of AS. However, there are controversial findings on the association of TNF α and AS from different association analysis studies world-wide. We performed a meta-analysis on this subject and found no significant association of AS with TNF α promoter 308G/A and 238G/A polymorphism by stochastic effect model. As national publications in China on this subject are few and that TNF α and B27 linkage disequilibrium were not analysed together, we suggest further research on linkage disequilibrium in different races by strict match control.

Family studies strongly suggest additional genetic factors (including non-HLA genes) other than HLA-B27 or its subtypes, in predisposition to AS. Around 69 percent of the genetic effect may be contributed from outside the HLA region. Genome-wide scans from Oxford and the North American Spondylitis Consortium (NASC) and other studies have identified strongly implicated genes in other regions on chromosomes 1q, 2q, 3q, 5q, 6p, 11q, 16q, 10q, 16q, 17p, 19q and so on. However there has not been significant agreement in conclusions from the candidate gene analyses completed by NASC and other studies. Controversial results were found in regard to the relation between IL-1 and AS. Recently, Maksymowich et al genotyped AS samples in three Canadian populations using a panel including 38 SNPs across the IL-1 gene cluster, and found significant association with



AS in 18 SNPs, among which rs3783526 (IL1A) and rs1143627 (IL1B) are the most significantly linked. On the contrary, Kim et al found no difference of IL-1 gene cluster polymorphism between 205 AS patients and 200 controls. Djouadi et al also reported a negative finding. A weak association of AS with a variable number of tandem repeats (VNTR) in intron 2 of interleukin 1 receptor antagonist (IL1RN) and an association of 2 synonymous single nucleotide polymorphisms (SNP) in exon 6 of IL1RN and their haplotypes in a large Canadian cohort of AS patients has recently been described. However, the NASC study examining the same SNP, revealed no evidence for linkage of AS to IL1RN. Although the level of Matrixmetalloproteinase III (MMP3) is found to be elevated in synovial biopsies in AS patients with active disease, no association or linkage of MMP3 SNP could be demonstrated in the NASC families. Likewise, the gene of TGF-beta 1, a cytokine found elevated in serum of AS patients have been studied. These studies did not show significant association with genes that lie in chromosome 19 where the TGF-beta 1 gene is located. CYP2D6, a gene found

on chromosome 22q, is found weakly associated with AS in German and British patients. No correlation between the sex biases of AS susceptibility and X-chromosome has been found.

Current genetic research of genome-wide scans using microsatellite markers for AS have largely been disappointing. The MHC is likely the major contributor in susceptibility to AS. The biggest challenge ahead lies in identifying the non-MHC contribution to the pathogenesis of AS. Success in this area in future should focus on using dense SNP screening of the genome which can help identify individuals with poor prognostic factors and their response to novel treatments.

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Surgical Interventions for Ankylosing Spondylitis

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Queen Mary Hospital, The University of Hong Kong.*



Dr. WY Cheung

Introduction

Ankylosing spondylitis is an inflammatory condition of the spine usually starting in young adulthood. The predominant symptom is pain, later followed by stiffness. The sacro-iliac joints and the spine are most commonly affected but the peripheral joints may also be involved. In the study of 100 patients, Ho et al found peripheral joint involvement in 58 patients, the most common being the hips and knees.¹

As the spine is concerned, there are three aspects in ankylosing spondylitis that are of particular surgical interest. They are severe kyphosis deformity, pseudarthrosis and spinal fractures. For the peripheral joints, total hip arthroplasty has become a well established treatment for patients with significant hip involvements.

Kyphosis in Ankylosing Spondylitis

Kyphosis may affect the cervical and thoracic spine. The kyphotic posture put the spine in mechanical disadvantage. Owing to the increased level arm, more force is required to maintain the up-right posture which makes patients tiring in walking and standing (Fig 1). Sagittal mal-alignment together with the stiff spine also impairs the visual angles of the patients; making them difficult to look forward on standing and walking. In order to maintain a good forward visual arc, patients need to flex their knees, thus resulting in a very tiring posture (Fig 2) the severe kyphosis may also cause difficulty in sitting, feeding, sleeping, impair diaphragmatic breathing, and psycho-social function. Surgical interventions should be considered in patients with severe fixed kyphosis that causes significant symptoms or disabilities.

Three types of extension osteotomies have been described to correct kyphosis in ankylosing spondylitis, namely Smith Peterson opening wedge osteotomy (Fig 3), Thomason closing wedge osteotomy (Fig 4) and poly-segmental dorsal wedge osteotomy (Fig 5). For thoraco-lumbar kyphosis, the osteotomy is usually at the lumbar spine for lesser chance of neurological complications and more effective in correcting the sagittal mal-alignment compared with osteotomy at thoracic levels² (Fig 6). For cervical or cervico-thoracic kyphosis, the osteotomy is usually at cervico-thoracic junction to correct the gaze angle and maintain the sagittal alignment of the spine³ (Fig 7) Kim et al prospectively studied 45 patients having received extension osteotomies for kyphosis in

ankylosing spondylitis, there were significant improvements in sagittal balance of the spine, gaze angle, overall function, indoor activities levels, outdoor activities levels and back pain after the operation.⁴ Van Royen et al reviewed 856 patients underwent extension osteotomy for kyphosis and ankylosing spondylitis in 41 published articles. The overall neurological complication was two to three percents. Four patients had aortic rupture and ended up with mortality. All aortic ruptures happened in the Smith-Peterson opening wedge osteotomy group and the ruptures were attributed to the opening up of the anterior column as the aorta is just lying in front of the thoraco-lumbar spine, suggesting this method is less safe compared with the other two methods.⁵

Spinal Pseudarthrosis in Ankylosing Spondylitis

This condition was first described by Romanus and Yden in 1953. It appears as disco-vertebral destructive lesions commonly in thoraco-lumbar junction in patients with ankylosing spondylitis (Fig 8). Initially it was thought to be caused by inflammation or infection of the spine. Fang et al did en-block excision of the lesions in 35 patients for histopathological analysis. They showed that the lesions were fibrous tissue and/or fibrocartilage showing fibrinoid necrosis and cystic degeneration characteristic of pseudarthrosis.⁶ there are three possible causes for formation of the pseudarthrosis. Firstly, the segment in question may have escaped fusion while other levels became ossified. The process of spinal ossification in ankylosing spondylitis is multifocal and not contiguous, so this process may leave short mobile segments between long ankylosed segments. This set the scene for high stress and mechanical failure. Secondly, there is a distinct possibility of an acute fracture through an already fused segment which ended up with non-union. Thirdly, the mechanics of a stiff kyphotic spine result in high stresses, especially near the thoraco-lumbar junction. Repeated stress may lead to fatigue fracture as in stress fractures of long bones. Both acute or stress fractures are predisposed to non-union by the long level arm of the kyphotic ankylosed spine.

Not all pseudarthrosis are symptomatic. In patients whose lesions are painful, the pattern of pain may vary. A patient with ankylosing spondylitis may present initially with increasing pain and stiffness for a number of years, and subsequently there is gradual decrease of the amount of pain. A recent increase in pain or the pain



becomes more acute and perhaps more localised, may suggest the development of pseudarthrosis. The second pattern is noted in patients whose disease has already burnt out so that there is no pain, but with residual stiffness and deformity associated with a tiring posture. The pain, which can recur, may be localised or more acute. This also suggests development of pseudarthrosis. Healing of the pseudarthrosis may rarely occur with plaster cast or spinal brace immobilisation or without any treatment. The indication for surgical treatment is persistent and significant pain not responding to conservative treatment. Another indication although uncommon, is the presence of neurological symptoms. Fang et al reported 18 lesions in 16 patients who underwent anterior spinal fusion. Solid fusion was achieved in 16 lesions. 15 patients had well to complete relief of the back pain.⁷

Spinal fracture in ankylosing spondylitis.

Advanced ankylosing spondylitis creates a kyphotic, stiff and brittle spine that is prompt to fracture. Most of the spinal fractures involve three spinal columns predisposing them to displacement and neurological complications. Surgical stabilisation is usually indicated to prevent neurological complications and allow early mobilisation and rehabilitation. (Fig 9)

Hairline fractures can result in a patient with extensive ossification of the spine. The fracture may occur as a result of a fall or with very minor injury. In the process of trying to break the fall, there is sudden and strong contraction of paraspinal muscles resulting in a fracture. Hairline fractures commonly occur at the cervicothoracic junction. Plain x-ray may not reveal the fracture line. Clinical suspicion together with marked tenderness may alert the physician to such a problem. MRI and CT scan are more sensitive in diagnosing the condition (Fig 10). Despite the fracture is undisplaced, it is unstable and may result in neurological injury if left untreated. Surgical fixation is generally recommended in this condition.⁸

Ankylosing spondylitis with hip involvement.

Apart from the spine, ankylosing may also involve the hips. Total hip replacement is a well established treatment for ankylosing spondylitis patients with severe hip involvements. (Fig 11) The indications for surgery include significant hip pain, stiffness and flexion deformity that cause limitations in functions. Tang et al reported 96 total hip replacements in 56 ankylosing spondylitis patients, majority patients had good to excellent results.⁹ Joshi et al reported 181 total hip arthroplasty in 103 patients with ankylosing spondylitis. Ninety-six percent patients had minimal or no hip pain and seventy percent of patient had well to excellent function after surgery.¹⁰

Conclusion

Surgical interventions are indicated in some patients suffering from ankylosing spondylitis. The indications for surgery include: Firstly, severe kyphotic deformity, which corrective spinal osteotomy can improve function and

decrease back pain. Secondly, patients with spinal pseudarthrosis and back pain which failed conservative treatment, spinal fusion can achieve bone union and decrease back pain in majority of patients with this condition. Thirdly, patients with spinal fractures, surgical stabilisation can prevent neurological injury and allow early mobilisation and rehabilitation. Fourthly, for patients with severe hip involvements, total hip arthroplasty can decrease hip pain and improve function.

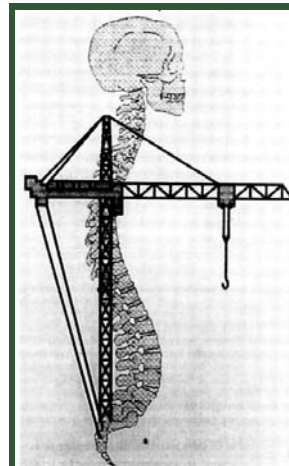


Fig 1: Increased kyphosis shift the centre of gravity anteriorly. More force is required from the posterior back muscles to maintain the up-right posture.

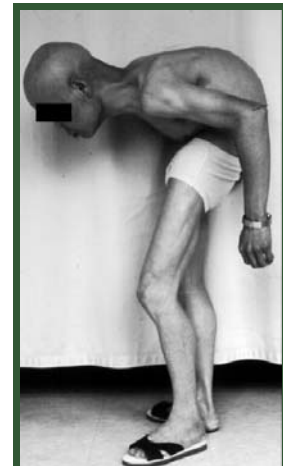


Fig 2: A patient with ankylosing spondylitis and severe kyphotic deformity.

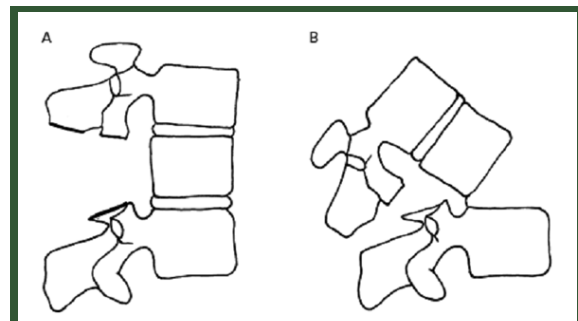


Fig 3: Smith Peterson opening wedge osteotomy. Laminae and facet joints were taken down. Lordosis is achieved by closing the posterior column and creating an opening wedge at the anterior column.

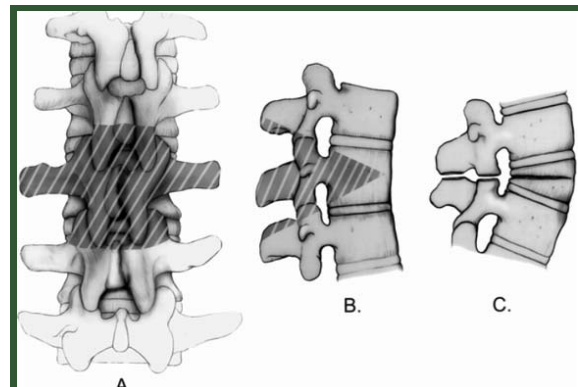


Fig 4: Thomason closing wedge osteotomy. Laminae, facet joints together with a wedge of the vertebral body are taken. Lordosis is achieved by closing the anterior and posterior column.

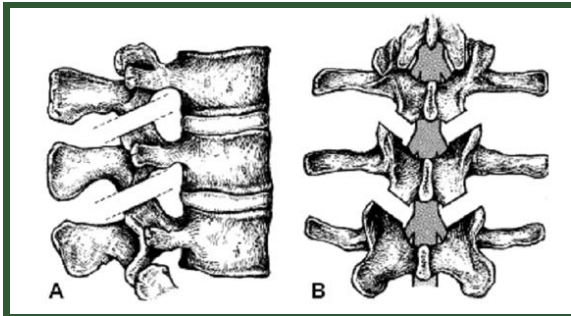


Fig 5: Poly-segmental dorsal wedge osteotomy. V-shape laminae and facet joints were taken at multiple levels. Lordosis was achieved by closing the posterior column without opening up the anterior column.

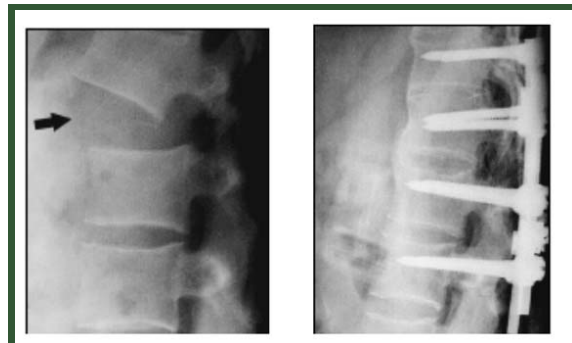


Fig 9: Fracture of lumbar spine in ankylosing spondylitis treated with posterior instrumented fusion.

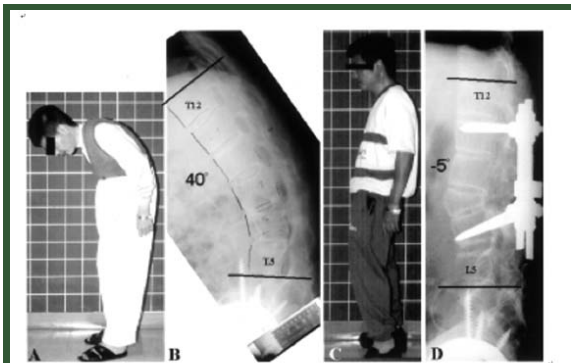


Fig 6: Thoraco-lumbar kyphosis before and after surgery²



Fig 10: Hair-line fracture of cervical spine in ankylosing spondylitis⁸.

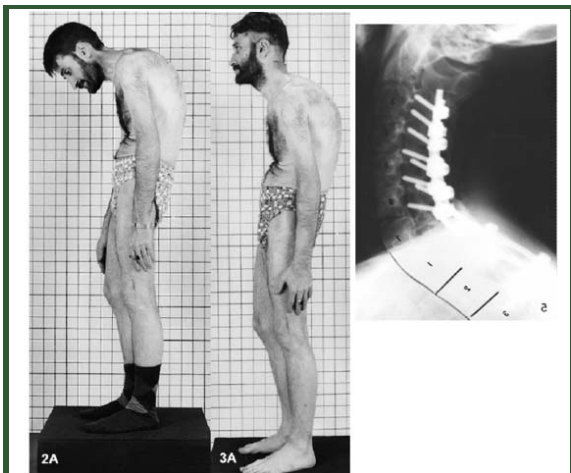


Fig 7: Cervico-thoracic kyphosis before and after surgery.³



Fig 8: Disco-vertebral destructive lesion at L1/2 compatible with pseudarthrosis.

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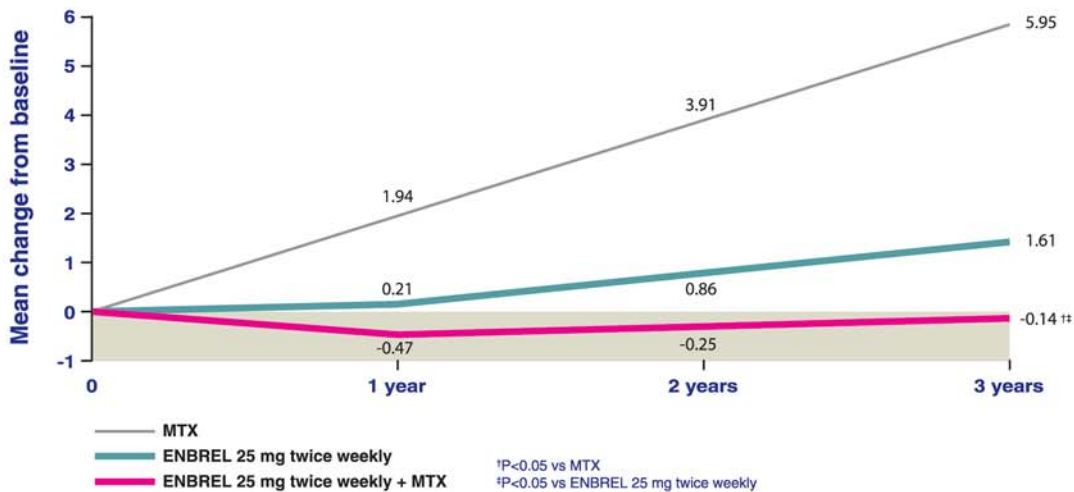
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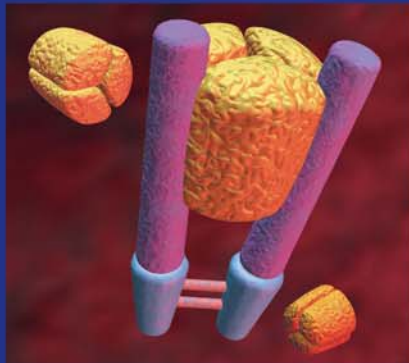
*Modified Total Sharp Score is based on combined scores of joint erosion in the hands on a scale of 0 to 5, feet on a scale of 0 to 10 (0=no damage) and joint space narrowing. All radiographic data based on ITT analysis of patients with an acceptable baseline and postbaseline radiograph. Linear extrapolation methodology was used.

Reference: van der Heijde D, Klareskog L, Pedersen R, et al. Assessment of functional status among patients with active rheumatoid arthritis in a double-blind trial of etanercept and methotrexate, alone and combined (Year 3 TEMPO trial results) [abstract]. Presented at EULAR 2005, June 8-11, 2005, Vienna, Austria.

In postmarketing use, serious infections and sepsis, including fatalities, have been reported. Discontinue ENBREL in patients with serious infections or sepsis. Do not start ENBREL in the presence of sepsis, infection (including chronic or localized), or allergy to ENBREL or its components. Use caution in patients predisposed to infection.

Cases of CNS demyelinating disorders have been reported, although the causal relationship to ENBREL remains unclear. Rare case of pancytopenia, including aplastic anemia, some fatal, have been reported in patients with rheumatoid arthritis (RA). Exercise caution in patients who have a previous history of significant hematologic abnormalities. Although the causal relationship to ENBREL remains unclear, advise patients to seek immediate medical attention if they develop signs or symptoms of blood dyscrasias or infection. If significant hematologic abnormalities are confirmed, discontinue ENBREL. Long-term effects of ENBREL therapy on the development or course of infection and malignancy are unknown.

The most frequent adverse events in five double-blind, controlled clinical trials in patients with RA were infections (49% of patients), injection-site reactions (31%), headaches (12%), and respiratory disorder (10%). Malignancies were rare.



ENBPA-004-AUG05



Update in the Management of Ankylosing Spondylitis

Dr. Hing-sum Tsui MBBS(HK) FHKCP FHKAM (Medicine) FRCP (Edin) FRCP (London)

Private Rheumatologist



Dr. Hing-sum Tsui

Introduction

Ankylosing Spondylitis (AS) is a chronic inflammatory disease of unknown aetiology, characterised by sacroiliitis and spondylitis. It typically affects the spine, but other joints and organs are sometimes involved, especially the hips. AS can be a severe disease and lead to serious disability.

Medication, physical therapy and exercise are the main stays of treatment.

For a long period of time, non-steroidal anti-inflammatory drug (NSAID) was the only available option for symptom alleviation in AS. In recent years, however, considerable progress has been made in the pharmacotherapy of AS. Anti-Tumour Necrosis Factor (anti-TNF) agents had been shown to be highly effective in controlling disease activity. Other medications that may be useful include sulphasalazine, methotrexate, pamidronate, thalidomide and intraarticular steroid.

Nonsteroidal Anti-inflammatory Drugs (NSAID)

NSAIDs are effective in control of pain and stiffness in AS patients. Indomethacin was once thought to be more effective than the other NSAIDs. It is necessary to give the maximum dose of 150mg to 200 mg per day in divided doses. Incidence of side effects such as headache, gastrointestinal upset and fluid retention are common. One recent trial showed indomethacin and aceclofenac were equally effective. Perhaps most NSAIDs in adequate doses are equipotent. Different NSAIDs may work best for different individual patients.

To assess the usefulness of a NSAID, it should be given at a sustained dose on a regular basis for about two weeks. After the maximum effect has been observed, further use may be as needed for symptom control.

A recent study showed AS patients who were continuously on NSAID were half as likely to develop radiological progression when compared to those who use NSAID on as needed basis. This made a suggestion for continuous use of NSAID, regardless of the symptom control. More large scale studies are needed to confirm this observation.

COX2 inhibitors had been shown to be useful in double blind controlled trials. Celecoxib 100 mg BD was found to be more effective than placebo. Etoricoxib (90 mg/ day

or 120 mg/ day) was also found to be effective. Actually, etoricoxib at this dose had been shown to be more efficacious than naproxen 500 mg BD. Increase in cardiovascular risk is a concern when COX2 inhibitor is used for prolonged period of time though the actual number of serious adverse cardiovascular events was small.

Tumour Necrosis Factor Alpha Antagonists

Etanercept, infliximab and adalimumab are anti-TNF agents that are commercially available. Both etanercept (25mg sc twice weekly) and infliximab (5 mg/ kg infusion at week 0, 2, 6, 12, 18) had been shown to be very effective in AS in double blind placebo controlled studies. Results of adalimumab trials are expected to be published soon. Preliminary data suggest anti-TNF agents can reverse bone marrow changes shown on magnetic resonance imaging (MRI) and prevent progression of radiological spinal changes as well. However, potential side effects such as the increased risk of pyogenic infections, reactivation of latent tuberculosis and rarely development of lymphoma, should be considered when using these agents.

The very high cost of anti-TNF therapy is a major impediment to their widespread use and different countries have different guidelines for its usage.

To put AS patient on anti-TNF therapy, they should meet the following criteria:

1. Firm clinical diagnosis of AS
2. Active disease
The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is one common tool used by rheumatologists to assess the disease activity of AS patients.
3. Exclusion of contraindications
 - Active infections
 - Untreated latent tuberculosis
 - Demyelinating disease (eg. Multiple sclerosis, optic neuritis)
 - Heart failure
 - Pregnancy and breast feeding

AS response rate to an anti-TNF agent is up to 80 percent and the response is typically rapid, usually within six weeks of treatment. Positive predictors of response to TNF blockade include

- Young age
- Shorter disease duration
- Good functional status, as measured by the Bath Ankylosing Spondylitis Functional Index (BASFI)
- Elevated ESR and C-reactive protein



Sulphasalazine

There had been many trials on the usefulness of sulphasalazine (SSZ) in AS. The trial with the largest sample and that with the longest treatment duration produced similar results. SSZ had benefit in subset of AS patients with peripheral arthritis. Across all AS patients, SSZ demonstrated some benefits in reducing ESR and easing morning stiffness, but no significant improvement in physical function, pain, spinal mobility, enthesitis, patient and physician global assessment. The literature concluded that patients at early disease stage, with high level of ESR (or active disease) and peripheral arthritis might benefit from SSZ but not those with only symptoms and signs of axial disease.

Methotrexate

Methotrexate (MTX) is one of the most widely used disease modifying anti-rheumatic drugs in the treatment of Rheumatoid Arthritis. However, there is uncertainty in its usefulness for treating AS.

A 2004 systematic review of the effectiveness of MTX in AS found no evidence of benefit. However only two studies met criteria for inclusion and these studies used relative small doses of MTX (7.5 and 10 mg weekly respectively). Furthermore, there were only a total of 81 patients in these two studies. More well designed randomised controlled trials with sufficient patient number and study duration, perhaps with higher dosage regime as well, are needed to establish the role of MTX in the treatment of AS.

Pamidronate

Because of some evidence of anti-inflammatory activity, pamidronate has been evaluated in the treatment of AS. In a double blind RCT, 84 patients with active AS despite NSAIDs were randomised to pamidronate infusion 60mg monthly or 10 mg monthly each for a period of 6 months. The decrease in BASDAI was significantly greater with the higher dose therapy. Pamidronate appears to be an option when other medications are not feasible or useful.

Thalidomide

One abstract reported an open study of thalidomide (200-300 mg per day) in 30 patients. After one year, 80 % of patients had improved more than 20 % in 4 of 7 clinical outcome measures (BASFI, BASDAI, early morning stiffness, total body pain score, spinal pain, patient global and physician global assessment). Well defined, controlled studies are needed to define the role of thalidomide in the treatment of AS. The cutaneous and neurological adverse effects are of concern in its long term usage.

Steroid

Long-term systemic steroid is not recommended for AS patient. Intraarticular steroid for peripheral arthritis and local injection to painful plantar fasciitis can be helpful. Injection of long acting steroid to sacroiliac joint may be beneficial to patients unresponsive to other measures.

Physical therapy and exercise

It has been demonstrated that supervised group and individual physical therapy can lead to symptomatic relief and significant improvement and maintenance of spinal mobility. An initial evaluation and treatment by physical therapist should be part of every therapeutic regimen. Physical therapy involves postural training, range of motion exercises, and hydrotherapy. All AS patients should be advised on regular specific home exercises. In addition, pain relief measures such as local heat or cold can be tried.

Conclusion

Recent advances in our understanding of ankylosing spondylitis and the availability of potent therapeutic options call forth a change from the traditional approach to the management of the disease. Primary care physicians and specialists alike should adopt an expeditious rather than an expectant approach in the diagnosis, referral and treatment of patients suffering from ankylosing spondylitis in order to prevent irreversible functional disability.

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Current Management of Juvenile Idiopathic Arthritis

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Dr. Tsz-leung Lee

Introduction

Juvenile Idiopathic Arthritis (JIA) is the most common form of chronic rheumatic disease in children. There is wide variation in the epidemiological studies of JIA in different countries. It is estimated that the overall prevalence of JIA is from 0.07 to 4.01 per 1000 children. From most outcome studies of JIA, active disease often persists into adult life in all subtypes of JIA. Several long term studies conducted from 1960s to 1990s showed that 31% to 55% patients with JIA have active disease when followed for at least 10 years. Persistently active disease is associated with poor outcome and long term disability. Thus, the current management of JIA is to diagnose early, treat early and be aggressive earlier in order to limit permanent disability. This article focuses on the current medical therapies of JIA.

Definition

JIA is defined as presence of arthritis (swelling or effusion, limitation of range of motion, tenderness or pain on motion, and increased heat) in one or more joints. The age at onset is less than 16 years old. The duration of arthritis lasts for 6 weeks or longer and other causes of arthritis (e.g. septic arthritis, malignancy) are excluded.

Classification

JIA is a new ILAR (International League Against Rheumatism) classification of juvenile arthritis. (Table 1)

Treatment

A. Multi-disciplinary Approach

A coordinated multi-disciplinary team care consisting of paediatric rheumatologist, nurse specialist, social worker, physical therapist, occupational therapist, orthopaedic surgeon and clinical psychologist is the key to success of management of JIA. Uveitis is an important extra-articular complication in children with JIA. Children with JIA should have regular slit-lamp screening by ophthalmologists. The aims of treatment are to preserve cartilage, control pain and preserve range of motion, muscle strength and function; to manage systemic complications; to facilitate normal nutrition, growth, and physical and psychological development.

B. Medical Therapy

Non-steroidal Anti-inflammatory Medications (NSAIDs)

Traditional NSAIDs are the first line therapy for all types of JIA. Naproxen is effective in management of joint inflammation in a dose of 15-20 mg/kg/day in two divided doses. Other NSAIDs include ibuprofen (35 mg/kg/day in 4 divided doses), tolmetin (25-30 mg/kg/day in 3 doses) and diclofenac (3-5 mg/kg/day in 4 doses). Other NSAIDs have specific indications but are not officially approved for use in children.

Disease Modifying Anti-Rheumatic Medications (DMARDs)

a. Methotrexate (MTX)

Methotrexate remains the remission-inducing agent of first choice for persistent and active arthritis. Most paediatric rheumatologists will initiate methotrexate therapy early in the disease course, sometime within 8 weeks of initiation of NSAID therapy. The starting dose is usually 15 mg/m²/week per oral route. Daily folic acid supplementation (1 mg/day) may alleviate the side effects of nausea, vomiting, gastrointestinal upset and mucosal stomatitis without compromising the therapeutic effect. If the response is inadequate, it could be stepped up with an increment of 2.5 mg/week. Subcutaneous route is advised if the dose reaches 20 mg/week or more.

Most studies have demonstrated no severe liver damage in children taking methotrexate for extended periods. There is no clear evidence that methotrexate increases the risk of malignancy in children. In our hospital, a retrospective study (from 1996 to 2005) of 40 children with JIA was performed to review the treatment outcome and adverse effects associated with use of MTX. We concluded that MTX was safe and well tolerated in the majority of patients, but treatment response varied with different JIA subtypes. Methotrexate is teratogenic and adolescent patients are advised about prevention of pregnancy and total abstinence from alcohol drinking. Patients should be informed of the nature, toxicities, precautions, expected duration of therapy and education of subcutaneous injection technique.

b. Leflunomide

Methotrexate is the mainstay of therapy, but recently, combination DMARD therapy such as methotrexate and leflunomide has been shown to have better clinical outcomes when methotrexate monotherapy fails. Headache, diarrhoea, abdominal pain, elevated liver enzymes, reversible hair loss and skin rash are the reported side effects. Leflunomide is teratogenic and patients should not take alcohol to minimise hepatotoxicity.



c. Corticosteroid:

Systemic Corticosteroid

Moderate or high dose systemic corticosteroid therapy should be reserved for patients with systemic arthritis with severe systemic symptoms that cannot be controlled with NSAID, such as macrophage activation syndrome, symptomatic serositis and myocarditis. Systemic corticosteroid is not recommended for all other subtypes of JIA.

Intra-articular Corticosteroid Injection

Intra-articular corticosteroid is a safe and effective treatment in managing synovial inflammation in a child with monoarticular or oligoarticular arthritis. It is sometimes indicated in treatment of particular symptomatic joints in a child with polyarticular arthritis. It provides sustained anti-inflammatory effect on synovium lasting for 4 to 6 months in most cases. It has been shown by magnetic resonance imaging studies that intra-articular steroid therapy resulted in significant suppression of inflammation and pannus formation while cartilage integrity is well preserved.

d. Sulphasalazine (SSZ)

SSZ has been shown to be effective in children with oligoarthritis or spondylitis at doses 30-50 mg/kg/day (maximum dose 2000 mg/day). The adverse effects are gastrointestinal intolerance, rash, leukopenia and hypogammaglobulinaemia.

e. Cyclosporine A (CsA)

There are no controlled trials on the use of CsA in JIA treatment. A few open studies suggest that it may have a role in the treatment of systemic symptoms of systemic-onset JIA and steroid sparing effect but less convincing efficacy for arthritis control. The usual dose is 3-5 mg/kg/day. Adverse effects include hypertension, hand tremor, impaired renal function, gingival hyperplasia and hypertrichosis.

f. Combination DMARD Therapy

If conventional treatment with a single DMARD fails to adequately control clinical symptoms or to prevent disease progression, combination DMARD therapy is indicated. In such cases, rheumatologist referral is strongly recommended.

g. Biologic Agents

It has been shown that tumour necrosis factor and other cytokines like interleukin 1 and interleukin 6 are important mediators of joint and synovial inflammation. Targeted monoclonal antibody therapies have been developed recently.

i. TNF Inhibitors

Etanercept, a TNF receptor antagonist, is the first biologic to be approved by the FDA for use in JIA. In a randomised, prospective, placebo-controlled trial in children who had severe JIA not controlled by methotrexate, etanercept induced a rapid, significant improvement in the clinical and laboratory features of JIA. The median improvements ranged from 40% to 95%. Etanercept is well tolerated in children, with headache, upper respiratory tract infections, and injection site reactions being the toxicities reported most commonly. Rare but serious infections such as

sepsis and varicella meningitis have been reported. Other infections, such as TB, histoplasmosis, and listeriosis, have been reported in people taking anti-TNF-alpha drugs. Neurologic disorders, retrobulbar optic neuropathy, cutaneous vasculitis, and pancytopenia have been reported. Data on the long-term toxicity of etanercept are not available. Other anti-TNF-alpha biologics such as infliximab and adalimumab have been given to children who have JIA, with improved response.

ii. Anti-IL 6

Anti-IL-6R, termed tocilizumab, has been tried in children who had systemic arthritis with some success.

iii. Anakinra

i. Anakinra is a recombinant form of agonist to interleukin-1 receptor (IL-1Ra) and its use in arthritis treatment is associated with reduction in mononuclear cell infiltration of the synovial membrane. A few anecdotal reports indicate good responses to the use of anakinra (IL-1 receptor antagonist) in JIA.

h. Thalidomide

1. Thalidomide is a potential agent that looks promising in treatment of inflammatory joint disease.

C. Autologous Stem Cell Transplantation (ASCT)

Despite the emergence of new therapeutic agents which appear to be more effective in treating JIA, there are still some patients who remain resistant to medical therapies. Autologous stem cell transplantation has been considered in recalcitrant cases. Drug-free remissions of disease have been reported, but the procedure carries a significant mortality risk, usually from macrophage activation syndrome. Stem cell transplantation should be performed only after all other treatment options have failed. In our hospital, we have performed autologous stem cell transplantation for two patients. One is in complete remission with follow up more than 6 years and the other relapsed 9 months after transplantation, and remission is achieved with combination therapy of leflunomide, cyclosporine and thalidomide. At present, this treatment should be considered experimental and should be reserved for those patients who have most severe disease unresponsive to standard treatment.

Conclusion

Progress in achieving international consensus concerning the classification of JIA has been made. There are many promising developments in the understanding and improved treatment options in JIA. In order to prevent long term disability, earlier and more aggressive therapy is advised for those with persistent arthritis. A multidisciplinary team approach is very important in management of JIA. It is hoped that with increased awareness of the long term morbidity of JIA and the availability of new treatment options in JIA, the outcome of patients with JIA could be further improved.

**Table 1 ILAR Classification of JIA**

Systemic arthritis	Arthritis daily fever for at least 2 weeks evanescent nonfixed erythematous rash generalised lymphadenopathy hepato/splenomegaly serositis.
Oligoarthritis	Arthritis of one to four joints during the first 6 months of disease.
o Persistent	Affects no more than four joints throughout the disease course.
o Extended	Affects more than four joints after the first 6 months.
Polyarthritis (*RF-negative)	Affects five or more joints in the first 6 months of disease. Tests for RF are negative.
Polyarthritis (*RF-positive)	Affects five or more joints in the first 6 months of disease.
Enthesitis-related arthritis	Arthritis and enthesitis or arthritis or enthesitis with at least two of: sacroiliac tenderness and/or inflammatory spinal pain, human leukocyte antigen (HLA) B27-positive, family history in a first- or second-degree relative of medically confirmed HLA B27-associated disease.
Psoriatic arthritis	Arthritis and psoriasis or arthritis and at least two of: dactylitis, nail abnormalities, family history of psoriasis in at least one first-degree relative.
Other	Arthritis of unknown cause persisting for at least 6 weeks that either does not fulfill criteria for any categories or fulfills criteria for more than one category

* RF=rheumatoid factor

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Use of Thalidomide in Rheumatic Diseases

For the vast majority who won't start it

Dr. Moon-ho Leung MBBS, MRCP, MSc(Rhu)(Birm), FHKCP, FHKAM (Medicine)

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Dr. Moon-ho Leung

Ended with tragic side effects & revived for desperate conditions

Thalidomide was synthesized in 1954 and prescribed as a sedative, tranquiliser, and anti-emetic for morning sickness. It is chemically similar to barbiturate, but with much less hang-over, and thus soon became very popular. However, after the emergence of reports of teratogenicity, in particular foetal limb malformation, including pregnant women who took as little as a single dose of the drug, it was withdrawn from the European and Canadian markets in 1961 - 62.

A few years later, an Israeli physician administered some old supplies of thalidomide to a patient with leprosy and mania for sedation. Surprisingly, it gave dramatic and near complete resolution of the patient's cutaneous symptoms. However, it was not until the discovery to thalidomide's anti-tumour necrosis factor- α (TNF α) activity in 1991 and experimental evidence of its ability to interfere with vasculogenesis in 1994 that interest in re-emergence of the drug was rekindled. Now it has been extensively studied for use in many refractory malignant or inflammatory conditions.

Between nasty poison and last card - immunomodulatory action

The immunomodulatory effects of thalidomide are complex and incompletely understood. Its key ability is to inhibit the production of TNF α , primarily on monocytes and also T-lymphocytes, alveolar macrophages, lamina propria mononuclear cells and microglial cells. How thalidomide inhibits TNF α production remains unclear but it seems to involve the enhancement of TNF α mRNA degradation and inhibition of NF (nuclear factor)- κ B activation. Besides its effects on TNF α production, thalidomide can also enhance the production of IL (interleukin)-4 and IL-5, while inhibiting IL-12 production. It also acts as a T-cell co-stimulant, which is potentially beneficial to anti-tumour activity. Moreover, it is capable of inhibiting angiogenesis induced by vascular endothelial derived growth factor and basic fibroblast growth factor.

The molecule

Thalidomide is a derivative of glutamic acid. It is administered clinically as a 1:1 racemic mixture of S and R enantiomers (mirror image isomers) that interconvert under physiological conditions. It is well absorbed after oral administration, eliminated by spontaneous

hydrolysis to multiple chemically inactive metabolites, and has a half-life of around five hours.

Recent convert of an ex-convict

Thalidomide is particularly useful in treatment of mucocutaneous diseases. Erythema nodosum leprosum was the first approved indication by Food and Drug Administration of the United States. Resistant oral aphthous ulceration, whether idiopathic or associated with human immunodeficiency virus infection, and the granulomatous skin lesions of sarcoidosis all respond very well to thalidomide.

Another major application of thalidomide is in haematological malignancies. The most promising results to date have been in the treatment of multiple myeloma. Up to 35% response rate in refractory cases had been reported. Thalidomide can also be useful in high-risk myelodysplasia, acute and chronic myeloid leukaemia, and other myeloproliferative disorders. In contrast, the efficacy of thalidomide in solid organ tumours is less well documented, because increased thromboembolic disease has also been reported. Thalidomide has also been reported to be beneficial in Crohn's disease, wasting and cancer cachexia.

Use of thalidomide in rheumatic diseases

In non-randomised studies, thalidomide was moderately effective for the treatment of **refractory cutaneous lesions of lupus**, which otherwise had inadequate response to treatment with anti-malarial agents, steroid or other immunosuppressive drugs. Overall, clinical response rates ranged from 84% to 100% at daily doses of 50 - 400 mg, with the possibility of subsequent maintenance therapy after initial response. The effects of thalidomide on visceral and articular involvement of lupus are conflicting. In short, thalidomide is considered second-line therapy in cutaneous lupus, as its usefulness is mainly limited by potential neurotoxicity and extent of relapse after discontinuation of therapy.

Ankylosing spondylitis, a chronic inflammatory disease of axial skeleton (spine and particularly sacroiliac joints) and occasionally other peripheral joints, also shows good response to thalidomide. An open-label study was conducted in Mainland China which involved 30 male patients suffering from severe and active ankylosing spondylitis refractory to non-steroid anti-inflammatory



drugs, sulphasalazine, methotrexate and even corticosteroid. Thalidomide 200 mg daily was used. As a result, 80% of the 26 patients who completed the study experienced at least 20% improvement in the functional and disease indices. Prompt improvement was noticed at 3-6 months. Nine patients (30%) became pain-free. Decreased expression of several pro-inflammatory genes, including TNF α and IL-1 in peripheral blood mononuclear cells from these patients after thalidomide treatment was also noted. The common side effects in this study were slight drowsiness and dry mouth, and these gradually subsided upon continued treatment. Only one patient in this study stopped thalidomide at 12th month because of tingling sensation over fingers for few seconds daily lasting for three days.

Behcet's disease is an inflammatory disease of unknown aetiology characterised by episodic exacerbation of oral ulcers, genital ulcers, uveitis, arthritis, erythema nodosum and other skin lesions. Several uncontrolled studies have shown that thalidomide is effective in both treatment and prevention of recurrence of orogenital ulceration in Behcet's disease. In a placebo controlled trial, oral and genital lesions of Behcet's disease improved after treatment with thalidomide (100mg or 300mg) versus placebo, with complete response rates of 9% on treatment versus 0% on placebo. Typically, oral lesions healed in 3 - 4 weeks, but recurrences were common after stopping the drug. Despite its effectiveness in orogenital ulcers, thalidomide appears to offer little help on uveitis in Behcet's disease.

For some unclear reasons, the effect of thalidomide is not so impressive in refractory rheumatoid arthritis, a chronic inflammatory arthropathy mediated in part by TNF α . Thalidomide has also been tried, but without major success, in a limited number of patients suffering from other rheumatic diseases such as Still's disease, scleroderma and Sjögren's syndrome.

Side effects

Thalidomide is notorious for being extremely **teratogenic**. In utero exposure of the drug, with even a single 50 mg dose taken in first trimester, could cause 10% - 50% risk of birth defects. Common foetal abnormalities are phocomelia (short limbs) or amelia (absent limbs), central skeletal or craniofacial abnormalities and visceral malformation. The mechanisms of teratogenicity may involve free radical mediated embryonic DNA oxidative damage, and disturbed cellular recognition through interaction with adhesion molecules.

Peripheral neuropathy is the next serious side effect and it occurs at a rate ranging from 1% to 70% in different series, depending on whether it is documented on clinical ground or with more sophisticated electrophysiological studies. Age and cumulative dose were identified to be associated factors in a large prospective study, though not so in another retrospective study. Typical presentation is painful or burning sensory neuropathy in association with mild proximal myopathy. Upon cessation of thalidomide, weakness rapidly resolves but sensory changes are usually slow to recover and in some cases may be irreversible.

Other side effects include somnolence (ironically the originally intended "effect"), constipation, dizziness, macular rash, decreased libido and rarely neutropenia.

Taming the shrewd - Precautions

Thalidomide should only be used to treat severe disabling conditions refractory to conventional treatment. In many public hospitals and clinics, the drug is available on a named patient basis. Patients should be encouraged to take part in the decision making process of resorting to thalidomide therapy. They should be well informed to consider such major undertaking, by striking the balance between possible benefit of controlling a refractory disease versus potential side effects and the absolute willingness to prevent pregnancy.

Any women of childbearing potential must be aware of the risk of birth defects and they should have a negative pregnancy test done shortly before starting thalidomide. They must abstain from intercourse or use two forms of contraception at the same time, which must begin one month before starting thalidomide and continued for at least one month after stopping treatment. Male patients must use a condom every time they have intercourse, even if they have undergone vasectomy.

Baseline nerve conduction studies may be useful, and patient should be advised to stop thalidomide should any neuropathic symptom arise. Bedtime dosing can minimise the side effect of somnolence.

The case for a special role in Asia

Roughly speaking, thalidomide can be regarded as an oral anti-TNF α agent, and supposedly less expensive than biologic agents specifically designed for such purpose. Indeed, anti-TNF α therapy is currently the breakthrough for treating refractory ankylosing spondylitis. However, TNF α is also a key cytokine in the body's defense against infection. Sepsis, including active tuberculosis, is a contraindication to anti-TNF α treatment. Chronic hepatitis carriers were excluded from clinical trials on use of anti-TNF α agents in refractory ankylosing spondylitis in western countries, as there were reported cases of fatal hepatitis C exacerbation after such treatment. There are only scattered reports on the safety of thalidomide use in hepatitis B and hepatitis C carriers in the literature. Here is the tantalising question - Is thalidomide a "safer" anti-TNF α agent in concomitant tuberculous infection and chronic hepatitis carriers? More intriguing is whether thalidomide can be a temporary substitute for biologic agents, the cost of which is certainly prohibitory.

Conclusion

Thalidomide has been demonstrated to be useful in some rheumatic conditions such as cutaneous lupus, ankylosing spondylitis and Behcet's disease when conventional treatment fails. However, contraception must be faithfully exercised, as teratogenicity remains the ultra concern.

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Clinical Quiz

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Clinical History

M/53
C/O Bone Pain
XR Pelvis for comment

Radiological Findings:

- 1) Generalised bone sclerosis
- 2) Multiple lytic lesions over the pelvic bones
- 3) Lytic lesions over both proximal femoral shafts with endosteal scalloping

(See P. 23 for answers)

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On Staying Fit

Dr. Axel SJ Hsu BSc, MBBS, MRCP

Department of Medicine, Queen Mary Hospital



Dr. Axel SJ Hsu

Having just completed Basic Physician Training requirements in Medicine at the Queen Mary Hospital, I was able to sit back and relax, contemplating on what to do with my limited free time. As an avid sports enthusiast, I spend most of my time after work with outdoor sports and family commitments.

Following along the footsteps of my father, I have learned to appreciate the game of golf since the age of 8. Although there aren't many places to play in Hong Kong, golf as a serious - and often expensive - hobby has become my pride and joy. I practise regularly at any driving range I can find, and travel up to the Mainland for the infrequent game of golf with peers or relatives. My goal is to achieve a handicap (card) and to play in golf courses elsewhere in Asia. Golf advice on staying fit: *avoid golf carts, carry your own clubs.*

On the contrary, a much cheaper alternative is to pursue one of the leisure trailwalking excursions in Hong Kong. As a doctor with a borderline high-normal BMI, I feel that there is no excuse for "no time for exercise". I like to hike, in groups or alone, in rain or in sun. The breath of fresh air re-invigorates me and allows me to capture a glimpse of what Hong Kong's natural beauty has to offer. Hiking and trail-walking is both mentally and physically challenging at times.

I was able to knock off 6 pounds of extra weight just from trailwalking alone. Trailwalking advice on staying fit: *if you walk and your long-range pager has no signal, you have probably walked enough.*

To water sports. Be it swimming, wakeboarding or diving, water sports are another area of interest of mine. I frequently venture out to the remote areas of Sai Kung to swim, dive or wakeboard. Although Hong Kong's weather can be very temperamental, these activities reiterate one thing - outdoor activities are truly fun and exciting. As I have yet to tear a ligament or fracture a bone, I will continue to try wakeboarding as much as I can. Diving advice on staying fit: *wakeboarding is fun as long as you don't try tricks.*

As I continue to try and find time to enjoy these activities, I am compiling a book with many photographic scenes on Hong Kong's untapped outdoors. From the remote and abandoned villages in the New Territories to the little idyllic islands off the Mainland, there are so much to see and so much to do. So to stay fit and rejuvenated, get away from the hustle of city life and put your body to the test. And if you are going to sit there and remain sedentary all your life, then you will regret what you are missing out on...

Answer to Clinical Quiz

Diagnosis:

MULTIPLE MYELOMA

Discussion:

Classical multiple myeloma most commonly appears as multiple osteolytic lesions scattered throughout the skeletal system, particularly in the vertebrae, skull, ribs and pelvis. It is rarely osteoblastic.

Bone sclerosis is a rare primary roentgenographic manifestation of myeloma (1-3%) and may occur as a sclerotic margin surrounding a lytic lesion, an increase in bony trabeculation or a diffuse sclerosis. Sclerosis sometimes occurs after chemotherapy, radiotherapy or fluoride administration, and also when the myeloma is complicated by fracture, amyloidosis or Paget's disease.

Osteosclerotic myeloma is a rare variant, and the patients are usually younger and less sick, often with a peripheral neuropathy and a more indolent disease course. They rarely complain of bone pain but rather the pain of peripheral neuropathy. Although less than 5% of patients with multiple myeloma have neuropathy, 50% with osteosclerotic myeloma develop it, with or without associated findings of organomegaly and endocrinopathy. The POEMS syndrome consists of a plasma cell dyscrasia with polyneuropathy, organomegaly, endocrinopathy, M-protein and skin changes.

Dr. Wendy WM Lam

Consultant, Department of Radiology, Queen Mary Hospital



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Abstracts from the Federation's Annual Scientific Meeting 2006 : Stem Cells From Bench to Bedside

Neural Stem Cells: Basic and Clinical Studies

Dr. Wutian Wu

Department of Anatomy, LKS Faculty of Medicine, The University of Hong Kong

Neural stem cells (NSCs) can be expanded and induced to differentiate into neurons and glia, which provides a potential therapeutic application for many neurodegenerative diseases and brain injury, such as Parkinson's disease, brain ischaemia and spinal cord injury. Transplantation of NSCs may replace the loss of neurons and glia due to the above neurodegenerative diseases. Although there have been several clinical studies using NSCs or other cells for the treatment of CNS diseases, several unsolved issues need to be addressed before NSCs transplantation can be considered for the clinical application. These issues include (i) the ideal NSCs source for transplantation for a given neurodegenerative diseases, (ii) the route of NSCs administration, (iii) the survival, differentiation and persistence of NSCs in the targeted area, (iv) the integration of transplanted NSCs with the host CNS. The present study investigated the survival and differentiation of NSCs isolated from embryonic or new-born CNS tissues in both in vitro and in vivo models. The potential application of NSCs in spinal cord injury is discussed.

Use of "Adult Stem Cells" in Children: the Current Status and Future Potentials

Dr. Godfrey CF Chan

Department of Paediatrics & Adolescent Medicine, Queen Mary Hospital, The University of Hong Kong

Human stem cells are known to have vast potentials in treating human diseases. However, there are different kinds of stem cells being studied or applied clinically. Some of them, such as embryonic stem cells which can be prepared by nuclear transfer technology, have the genuine multipotent differentiating capacity but unfortunately, are restricted by the ethical and legal boundary for clinical application. While adult stem cells, which include haematopoietic stem cells (HSCs), mesenchymal stem cells (MSCs), neural stem cells etc., are not as versatile in their differentiating ability but they are widely accepted for clinical use.

Among adult stem cells, HSCs are the most extensively used clinically. HSCs can be derived from bone marrow, cord blood or mobilized peripheral blood. Previously, HSCs transplant are confined to the treatment of haematological illnesses such as leukaemia, marrow failure or thalassaemia. It can also serve as a marrow support after megadose chemotherapy in selected solid tumours treatment. In recent decade, HSCs have been successfully applied to a wide range of non-haematological inherited diseases including metabolic disorders, storage diseases, primary immunodeficiency, bone disease (i.e. osteopetrosis). In addition, chemotherapy + CD34 selected autologous HSCs can now be used for many forms of poor risk autoimmune diseases including scleroderma, multiple sclerosis,

refractory SLE or JIA. The experience of our centre in applying HSCs to these diseases will be discussed.

Recently, bone marrow derived MSCs emerged as another important adult stem cells that can be applied to a wide spectrum of clinical diseases. Since they can form bone, cartilage, muscle and even cross lineage barrier into neurons and hepatocytes, they are intensively studied for the bioengineering purpose of replacing damaged tissues such as degenerated disc/cartilage or infarcted heart muscle. In paediatric setting, they have been tried for the treatment of osteogenesis imperfecta. In addition to their differentiating potential, they also have a potent immunosuppressive effect and recently, MSCs have been used in treating refractory graft versus host disease in organ transplant setting. Our laboratory has been studying the biology of human marrow derived MSCs for the past few years and some of the MSCs' unique biological properties will be discussed.

Techniques of Cord Blood Collection

Dr. Dominic FH Li

Specialist in Obstetrics & Gynaecology

Since the first case of cord blood transplant was performed in France on a boy with Fanconi's Anaemia in 1988, a lot of interest was generated on Cord Blood Collection and Transplantation around the world. Cord blood storage offers expectant parents an once-in-a-lifetime opportunity to collect and store their newborns' umbilical cord blood for potential life-saving use in future. This can be considered as a unique and highly innovative form of biological insurance. Cord blood banking is a safe, simple and convenient way to provide family members with insurance on life. Scientists recently are aware that cord blood can be successfully used as alternative to bone marrow for transplantation as cord blood is also rich in stem cells. This can be used on the child himself or herself, other family members (usually brothers and sisters who have similar HLA make-up as the cord blood) or other unrelated persons, children or adults, who are HLA-compatible with the cord blood. Collection of cord blood is easy and there is absence of risk to the donors (mother and newborn). There are less viral contaminations e.g. CMV etc and lower risks of rejection and GVHD. Incomplete HLA identity matching is possible and there is the advantage of immediate availability. The techniques of collection, processing and storage of cord blood will be discussed.

"Stem Cells - From Bench to Bedside" - Neurological Application

Dr. Gilberto KK Leung

Department of Neurosurgery, Queen Mary Hospital

The application of stem cell therapy in the treatment of central nervous system disorders is a natural extension of the recently developed concept of restorative neurology. Unlike



neuroprotection, which aims at minimising cellular injury, the restorative approach is concerned with the restoration of lost neuronal populations and functions by means of either the induction of endogenous neurogenesis or the implantation of progenitor neuronal stem cells. The latter approach, so-called 'neurotransplantation', is a particularly exciting field which has attracted a significant amount of attention and research effort in recent years.

Conceptually, stem cell therapy may have potential roles in the treatment of a wide range of neurological disorders, including ischaemic cerebral infarction, head trauma, spinal cord injury, brain tumours, and neurodegenerative diseases such as Parkinson's disease. Experimental studies have generated some promising results although many questions are still unanswered. Despite the apparent functional benefit observed in experimental animals following transplantation, the exact fate and behaviour of the transplanted stem cells are still unclear, and the mechanism by which transplantation may confer benefit is poorly understood. Practical issues such as the ideal cell source, the optimal timing and location of implantation, the choice of patients, and the role of immunosuppression are yet to be determined. Safety issues including infection and tumourigenicity of the implanted cells are other major concerns. Available data so far have not demonstrated any significant clinical benefit in human subjects.

In this review, the author aims at providing an overview of the recent development in stem cells therapy for the treatment of neurological disorders.

Stem Cell Therapy in Cardiovascular Diseases

Dr. Hung-fat Tse

Department of Medicine, the University of Hong Kong, Queen Mary Hospital

Despite the major efforts to prevent and treat cardiovascular diseases, they remain the most common cause of death in the western world and China. The main culprit is congestive heart failure, which can be caused by myocardial infarction, hypertension or any other insults to the heart. Human heart loses most of their regeneration capacity in the postnatal development, and is not able to replace any defects after damage to the myocardium. Currently, the only available curative therapy for patients with end-stage heart failure is heart transplantation, but is limited by the severe shortage of donor organs and transplant rejection. Stem cell transplantation has been explored as potential therapy to limit the progression of heart failure. Our recent clinical studies have highlighted the potential capacity to regenerate new blood vessels for the heart by intramyocardial injection of bone marrow stem cells. However, due to the limited developmental plasticity of these adult bone marrow stem cell, this approach may not be sufficient to replace cardiomyocyte (CM) loss due to heart attack. Direct CM replacement therapy is an obvious and promising option but is also limited by the availability of transplantable human CMs. Human embryonic stem cells (hESCs), isolated from the inner cell mass of human blastocysts, can propagate indefinitely in culture while maintaining their pluripotency, including the ability to differentiate into CMs; therefore, hESCs may provide an unlimited ex vivo source of CMs for transplantation and other cell-based therapies. In combination with recent advances in biomedical engineering techniques, hESCs have therefore enabled researchers to pursue the revolutionary paradigm of regenerative medicine for repairing, replacing or enhancing organ function in such aging-related diseases as heart failure.

Ethical Considerations of the Uses of Human Stem Cells

Prof. Edwin C Hui

Medical Ethics Unit, LKS Faculty of Medicine, The University of Hong Kong

The ability to produce and culture pluripotent human stem cells has created a brand new field called regenerative medicine whereby tissues that are previously considered to be without the capacity to regenerate themselves when damaged, notably the brain and the heart, can now be replaced by stem cells coaxed to become the damaged tissue. This has raised hope for those with terminal heart disease, Parkinson's disease, multiple sclerosis, spinal cord injuries and others. But at the same time, the use of human stem cells has also sparked intense debate in different countries as well as in the international scene. For all practical purposes, there are five different sources of human stem cells, and only two are ethically controversial as their derivations entail the destruction of human embryos. At the same time stem cells from the inner cell mass of the embryo are most potent. When cultured in the proper medium, these cells can multiply indefinitely as immortal cells; or under proper coaxing conditions they can be directed to become any one of the 220 cell types of the human body. There are 3 different sources of human embryos available for stem cell harvesting, and the moral assessment for each is significantly different. These include: (1) 'surplus' embryos following in vitro fertilisation (IVF) for infertility treatment; (2) embryos created through IVF specifically for the purpose of harvesting stem cells; (3) embryos created through somatic cell nuclear transfer (NT) specifically for the purpose of harvesting stem cells. The two other sources of stem cells whose derivations are unrelated to the destruction of embryo are (1) stem cells from "adult" somatic tissues including the bone marrow, adipose tissue, central nervous system, muscle, placenta and umbilical cord blood, and (2) stem cells from primitive foetal gonadal tissues (foetal germ cells). There is a rough hierarchy of contentiousness ordering the different ways of producing human stem cells, and in the order of decreasing degree of contentiousness: (1) embryonic stem cells created by NT; (2) embryonic stem cells from embryos specifically created for stem cell harvesting; (3) embryonic stem cells from 'surplus' embryos; (4) foetal germ cells; (5) adult stem cells. This paper discusses the ethical considerations for different sources of stem cells and some public policy concerns they raise.

Intervertebral Disc Regeneration

Prof. Kenneth MC Cheung

Division of Spine Surgery, Department of Orthopedic Surgery, The University of Hong Kong

Intervertebral disc degeneration and its consequences is a highly significant cause of low back pain and sciatica. Current treatment for severe back pain usually involves fusion of the spine, while more experimental procedures, such as replacement by an artificial intervertebral disc may have a role.

However a biological solution would be more ideal and considerable research work has been carried out in this area by our Division as well as others.

This presentation will provide an overview of the current science, and outlines where the likely future advances will be.



Unrelated Stem Cells Source

Dr. Cheuk-kwong Lee

Hong Kong Red Cross Blood Transfusion Service

Stem cells are primal undifferentiated cells that retain the ability to divide and differentiate into other cell types. They have been the focus in clinical medicine for the past few decades because of the potential to change the face of human disease by being used to repair specific tissues or to grow organs.

At present, the most common and clinically proven application is on the use of haematopoietic stem cells (adult or cord blood) for bone marrow transplantation which has shown an exponential growth in the number of procedures performed in the last two decades. Moreover, since the millennium, exciting reports also appeared on the applications of stem cells in clinical conditions like Parkinson's disease, myocardial infarction/ heart failure and spinal cord damage.

Although it is now known that we are able to isolate and obtain stem cells from other tissues such as human embryo, oocytes and adipose tissue, the present discussion will limit to unrelated haematopoietic stem cell source for bone marrow transplantation only. In Hong Kong, the Blood Transfusion Service is the organisation providing such service. A centralised cord blood bank was established in

1998 whereas Hong Kong Bone marrow Donor Registry has started its service since 1 September 2005 on donor recruitment, searching, and co-ordination of haematopoietic stem cell donation.

Safety of donation, donors and recipients remains the most important concern. In the unrelated setting, the donation risk should always be minimal to the voluntary non-remunerated donors whereas the transplantation risk should be acceptable to the recipient. Therefore, it appears to have a need of consensus on requirement of stringent donor eligibility and quality control on the collection, testing and storage and their applications. Lastly, one should not overlook the importance in ethical consideration of recruitment, donor confidentiality in searching, matching and donation and of course their clinical uses.

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Soccer Five Tournament 2006

Match results for 23 September 2006

Score

GSK	2 : 1	Eli Lilly
Sanofi-Aventis	1 : 3	HKMA
Janssen	1 : 0	HKDA
Bayer	4 : 1	Abbott

Match on 23 September 2006

There were 4 exciting matches between pharmaceutical companies on 23 September 2006. All teams played well with support from their friends.



GSK team from back row left to right: Jocky Chan, Shek, Nixon Nip, Anthony Ho, Keith Cheng, front row left to right: Gary Chan, Ricky Wan, Wilson Yuen, Garick Ho

Match results for 24 September 2006

Score

AVC	0 : 5	HKOS
IDS	0 : 3	Schwarz
AstraZeneca	0 : 2	Jacobson
Wyeth	0 : 2	Schering-Plough

Match on 24 September 2006

There were 4 exciting matches between medical societies and pharmaceutical companies on 24 September 2006. There were impressive performances by HKOS and Schwarz teams with 5 and 3 goals respectively.



From left to right: Dr Anthony Chan and Dr Michael Lai (HKOS)

Match results for 15 October 2006

Score

Boehringer I/Cardio Soc	2 : 1	AVC
T. Mountain	1 : 3	IDS
Eli Lilly	0 : 3	P&G
Janssen	1 : 0	Schering-Plough

Match on 15 October 2006

There were 4 exciting matches between pharmaceutical companies on 15 October 2006. All teams played well with IDS scoring the most goals on the day.



T. Mountain team from left to right: Chris Cheung, Frankie Chan, Lai Ka Ho, Wong Tak Po and Sam Liu



News from Member Societies

Australian Doctors and Dentists Association of Hong Kong

New office-bearers for the year are as follows: Chairman: Dr. Dominic WOO, Hon. Secretary: Dr. Francis LEE, Council Representative: Dr. Dominic WOO.

Hong Kong Institute of Medical Laboratory Sciences Ltd.

New office-bearers for the year are as follows: Chairman: Mr. Yiu-lam TSIM, Hon. Secretary: Ms. Po-chu LAM, Hon. Treasurer: Mr. Bosco Wan-lung YAU, Council Representative: Mr. Tat-tang CHEUNG.

The New Medico-Legal Society of Hong Kong

New office-bearers for the year are as follows: President: Mr. Kamlesh Arjan SADHWANI, Hon. Secretary: Mr. Patrick M. BURKE, Hon. Treasurer: Ms. Kimie BURKE.

The FMSHK would like to send its congratulations to the new office-bearers and look forward to working together with their societies.



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
<ul style="list-style-type: none"> HKMA Tennis Tournament Practical Tips & Pitfalls in Minimally Invasive Surgery Advances in Paediatric Critical Care 7th Asian Congress on Oral and Maxillofacial Surgery, ACOMS <p>5</p>	<ul style="list-style-type: none"> Certificate Course on Drug Dispensing in Office Clinics 家務助理陪月服務訓練課程 (TC-PNC-0206) <p>6</p>	<ul style="list-style-type: none"> HKMA CME Luncheon Lecture on Comorbidity of Anxiety and Depression - New Insight on Diagnosis and Treatment HKMA Newsletter Editorial Meeting <p>7</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) Integrative Medicine Forum 2006 Hong Kong Neurosurgical Society Monthly Academic Meeting - An Update on Neuroanaesthesia <p>8</p>	<ul style="list-style-type: none"> HKMA Council Meeting HKMA Lecture Series with Kennedys Part II: The Standard of Expert Reporting <p>2</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) Certificate Course on Quality Management (TC-QM-0106) <p>3</p>	<ul style="list-style-type: none"> Practical Management of Major Sexually Transmitted Infections in Social Hygiene Service HKMA Refresher Course for Health Care Providers 2006/2007 (III) - Urinary Incontinence in Females HKMA, 8th Beijing - Hong Kong Medical Exchange HKOA Annual Congress 2006 - Knee Surgery 2006: In Pursuit of Excellence <p>11</p>
<ul style="list-style-type: none"> HKMA Tennis Tournament The Federation's Soccer Five Tournament 2006 HKMA Structured CME Programme Year 06/07 (VIII) - Psychiatry 2nd Certificate Course in Recent Medical Advances for General Practitioners <p>12</p>	<ul style="list-style-type: none"> 醫療護理常用英語初階 (SUSMH 025 0 B) <p>13</p>	<ul style="list-style-type: none"> HKMA CME Luncheon Lecture on Medico-legal Seminar Clinical Nurse Specialist Group Evening Forum - Lecture on Incontinence (SCNSG-06-03) 13th Hong Kong International Cancer Congress & 3rd Annual Meeting of Centre for Cancer Research <p>14</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) Integrative Medicine Forum 2006 醫療護理常用英語初階 (SUSMH 025 0 B) 健康服務助理員訓練課程 (TC-HCA-0306) HKMA CME Luncheon Lecture on The Long-term Cardiovascular Safety for a COX-2 Specific Inhibitor, Etoricoxib - The MEDAL Program <p>22</p>	<ul style="list-style-type: none"> 13th Hong Kong International Cancer Congress & 3rd Annual Meeting of Centre for Cancer Research (1) An Atypical Disease Presenting Atypically (2) An Elderly Gentleman With Lung Infiltrates and Renal Impairment Advanced Wound Care Management (TC-AWCM-0106-CNSG) <p>16</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) 13th Hong Kong International Cancer Congress & 3rd Annual Meeting of Centre for Cancer Research <p>17</p>	<ul style="list-style-type: none"> Research Symposium - Topic: Research Partnership Among Service, Education and Research Sectors <p>18</p>
<ul style="list-style-type: none"> HKMA Tennis Tournament HKMA Family Sports Day <p>19</p>	<ul style="list-style-type: none"> 醫療護理常用英語初階 (SUSMH 025 0 B) <p>20</p>	<ul style="list-style-type: none"> Management Interest Group - Seminar on "消消怨氣, 開開心心工作無煩憂" (SMIG-04-06) <p>21</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) Integrative Medicine Forum 2006 醫療護理常用英語初階 (SUSMH 025 0 B) <p>22</p>	<ul style="list-style-type: none"> Advanced Wound Care Management (TC-AWCM-0106-CNSG) <p>23</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) HKMA CME Luncheon Lecture on The Long-term Cardiovascular Safety for a COX-2 Specific Inhibitor, Etoricoxib - The MEDAL Program <p>24</p>	<ul style="list-style-type: none"> Research Symposium - Topic: Research Partnership Among Service, Education and Research Sectors <p>25</p>
<ul style="list-style-type: none"> HKMA Tennis Tournament HKMA Structured CME Programme Year 06/07 (VIII) - Endocrinology <p>26</p>	<ul style="list-style-type: none"> 醫療護理常用英語初階 (SUSMH 025 0 B) <p>27</p>	<ul style="list-style-type: none"> Management Interest Group - Seminar on "消消怨氣, 開開心心工作無煩憂" (SMIG-04-06) <p>28</p>	<ul style="list-style-type: none"> 健康服務助理員訓練課程 (TC-HCA-0306) Integrative Medicine Forum 2006 醫療護理常用英語初階 (SUSMH 025 0 B) <p>29</p>	<ul style="list-style-type: none"> Advanced Wound Care Management (TC-AWCM-0106-CNSG) <p>30</p>		



Date / Time	Function	Enquiry / Remarks
8:30pm - 12:30 pm (3,8,10,15,17,22,24,29)	健康服務助理員訓練課程 (TC-HCA-0306) Organised by: College of Nursing, Hong Kong	Sugar Tel: 2572 9255 Fax: 2838 6280
1 7:30 pm to 9:30 pm (8,15,22,29) WED	Integrative Medicine Forum 2006 Organised by: Hong Kong Association for Integration of Chinese-Western Medicine Chairman: Prof. Edwin Chau Leung YU # Lecture Theatre, 10/F, TWGHs Yu Chun Keung Memorial Centre, Kwong Wah Hospital, 25 Waterloo Road, Kowloon	Miss Y.C. YEUNG Tel: 3119 1858 Fax: 2301 2414
2 8:00 pm 2:00 pm THU	HKMA Council Meeting Organised by: The Hong Kong Medical Association # HKMA Headquarter Office, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong HKMA Lecture Series with Kennedys Part II: The Standard of Expert Reporting Organised by: The Hong Kong Medical Association Chairman: Dr. K CHOI Speaker: Mr. J WALLACE # HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Ms. Christine WONG Tel: 2527 8285 Ms. Nina HUNG Tel: 2861 1979 1 CME Point
3 FRI (10,17,24)	Certificate Course on Quality Management (TC-CQM-0106) Organised by: College of Nursing, Hong Kong	Sugar Tel: 2572 9255 Fax: 2838 6280
5 7:30 pm (12,19,26) SUN	HKMA Tennis Tournament Organised by: The Hong Kong Medical Association Chairman: Dr. C.W. CHIN # Kowloon Tong Club, 113A Waterloo Road, Kowloon Tong, Kowloon Practical Tips & Pitfalls in Minimally Invasive Surgery Organised by: Minimally Invasive Centre, Union Hospital & Hong Kong Society of Minimal Access Surgery Chairman: Anthony P.C. YIM Speaker: Various # Minimally Invasive Centre, Union Hospital Advances in Paediatric Critical Care Organised by: Hong Kong College of Paediatricians Chairman: Dr. N.S. TSOI Speaker: Various # Lecture Theatre, M Floor, HAHO, Kowloon 7th Asian Congress on Oral and Maxillofacial Surgery ACOMS Organised by: Hong Kong Association of Oral and Maxillofacial Surgeons Chairman: Prof. Nabil SAMMAN Speaker: Various # Hong Kong Convention and Exhibition Centre, Wanchai	Ms. Dora HO Tel: 2527 8285 Miss Almen LAM Tel: 2608 3382 Email: almen@union.org.hk Ms. Jenny CHAN Tel: 2871 8871 Fax: 2785 1850 Mr. Daniel CHOK Tel: 2871 8896 Fax: 2871 8898
6 MON (13,20,27) 6:00 pm - 9:00 pm (9,13,16,20,23,27,30)	Certificate Course on Drug Dispensing in Office Clinics Organised by: The Federation of Medical Societies of Hong Kong Chairman: Dr. HUNG Kwan Ngai Speaker: Dr. LAM Tsan & Mr. Peter SUEN # Lecture Hall, Tuen Mun Hospital, New Territories 家務助理陪月服務訓練課程 (TC-PNC-0206) Organised by: College of Nursing, Hong Kong	Ms. Karen CHU Tel: 2527 8898 Fax: 2865 0345 Sugar Tel: 2572 9255 Fax: 2838 6280
7 2:00 pm TUE 8:00 pm	HKMA CME Luncheon Lecture on Comoridity of Anxiety and Depression - New Insight on Diagnosis and Treatment Organised by: The Hong Kong Medical Association Chairman: Dr. T.C. SHIH Speaker: Prof. J ZOHAR # Grand Ballroom, Level 2, Langham Hotel, 8 Peking Road, Tsimshatsui, Kowloon HKMA Newsletter Editorial Meeting Organised by: The Hong Kong Medical Association Chairman: Dr. H.H. TSE # HKMA Headquarter Office, 5/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Miss Nina HUNG Tel: 2861 1979 1 CME Point Ms. Tammy TAM Tel: 2527 8941
8 WED 7:30 am	Hong Kong Neurosurgical Society Monthly Academic Meeting - An Update on Neuroanaesthesia Organised by: Hong Kong Neurosurgical Society Speaker: Dr A O'REGAN Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon	Dr. Y.C. PO Tel: 2990 3788 Fax: 2990 3789 2 CME Points
9 2:00 pm THU (10,11)	HKMA Structured CME Programme with Hong Kong Sanatorium & Hospital Year 2006 (XI) - Review on Treatment of Primary Liver Cancer Organised by: The Hong Kong Medical Association & Hong Kong Sanatorium and Hospital Chairman: Dr. T.C. SHIH Speaker: Dr. W.T. LEUNG # HKMA Dr. Li Shu Pui Professional Education Centre, 2/F, Chinese Club Building, 21-22 Connaught Road Central, Hong Kong HKMA Trailwalker 2006 Organised by: The Hong Kong Medical Association Chairman: Dr. C Yu # MacLehose Trail	Miss Nina HUNG Tel: 2861 1979 (Registration fee is required) 1 CME Point Ms. Dora HO Tel: 2527 8285
2:15 pm - 4:30 pm 2:30 pm 11 SAT (12) 8:30 am - 5:00 pm (12)	Practical Management of Major Sexually Transmitted Infections in Social Hygiene Service Organised by: Social Hygiene Service, CHP, DH Speaker: Various # Fanling Social Hygiene Clinic, 6/F Fanling Integrated Treatment Centre, 2 Pik Fung Road, Fanling, N.T. HKMA Refresher Course for Health Care Providers 2006/2007 (III) - Urinary Incontinence in Females Organised by: The Hong Kong Medical Association & Our Lady of Maryknoll Hospital Chairman: Dr. T.C. SHIH Speaker: Dr. L.K. YEO # Our Lady of Maryknoll Hospital, 118 Shatin Pass Road, Wong Tai Sin, Kowloon, Hong Kong HKMA 8th Beijing- Hong Kong Medical Exchange Organised by: The Hong Kong Medical Association Chairman: Dr. S.W. LI & Dr. T.C. SHIH # Holiday Inn Golden Mile, 50 Nathan Road, Tsim Sha Tsui, Kowloon, Hong Kong HKOA Annual Congress 2006 - Knee Surgery 2006: In Pursuit of Excellence Organised by: Hong Kong Orthopaedic Association Chairman: Dr. Wilson LI & Dr. W.M. TANG Speaker: Various # Cyberport Convention & Exhibition Centre	Ms. CHAN Ming Chu Tel: 2639 1437 / 2639 1438 Fax: 2671 7135 Ms. Clara TSANG Tel: 2354 2440 2 CME Points Ms. Gigi MAK Tel: 2527 8285 Ms. Terry LEUNG Tel: 2632 3482 Fax: 2647 7432 Email: congress@hkoa.org 15 CME Points
12 7:00 pm - 11:00 pm SUN 2:00 pm	The Federation's Soccer Five Tournament 2006 Organised by: The Federation of Medical Societies of Hong Kong & The Hong Kong Association of the Pharmaceutical Industry Chairman: Dr. Godfrey C.F. CHAN # Shek Kip Mei Park Sports Centre, 290 Nam Cheong Street, Shek Kip Mei, Sham Shui Po HKMA Structured CME Programme Year 06/07 (VIII) - Psychiatry Organised by: The Hong Kong Medical Association & Queen Elizabeth Hospital Chairman: Dr. T.C. SHIH Speaker: Various # Queen Elizabeth Hospital, Lecture Theatre, Block M, G/F, Queen Elizabeth Hospital	Ms. Karen CHU Tel: 2821 3515 Fax: 2865 0345 Miss Nina HUNG Tel: 2861 1979 (Registration fee is required) 3 CME Points



Date / Time	Function	Enquiry / Remarks
12 SUN	2nd Certificate Course in Recent Medical Advances for General Practitioners Jointly organized by the Family Medicine Unit, the University of Hong Kong and the Family Medicine Division, Hong Kong Sanatorium and Hospital Speakers: Various	Hospital Administration Department Tel: 2835 8800 Fax: 2835 8008 E-mail:hospadm@hksh.com, Website: http://www.hksh.com/CME.pdf
13 MON 6:30 pm - 9:30 pm (15,20,22,27,29)	醫療護理常用英語初階 (SUSMH 025 0 B) Organised by: College of Nursing, Hong Kong	Sugar Tel: 2572 9255 Fax: 2838 6280
15 WED 2:00 pm 6:00 pm - 8:30 pm (16,17)	HKMA CME Luncheon Lecture on Medico-legal Seminar Organised by: The Hong Kong Medical Association Chairman: Dr. K. CHOI Speaker: Dr. M.K. TEOH # Crystal Ballroom, Basement 3, Holiday Inn Golden Mile HK, 50 Nathan Road, Tsimshatsui, Kowloon, Hong Kong Clinical Nurse Specialist Group Evening Forum - Topic: Overview of Urinary Incontinence (SCNSG-06-03) Organised by: College of Nursing, Hong Kong Speaker: Mr. LUI Ka Lok 13th Hong Kong International Cancer Congress & 3rd Annual Meeting of Centre for Cancer Research Organised by: The Faculty of Medicine of The University of Hong Kong & The Cancer Centre of Queen Mary Hospital # Cheung Kung Hai Conference Centre, William MW Mong Block Li Ka Shing Faculty of Medicine, The University of Hong Kong, 21 Sassoon Road, Pokfulam Road, Hong Kong	Miss Nina Hung Tel: 2861 1979 1 CME Point Sugar Tel: 2572 9255 Fax: 2838 6280 2 CME Points Congress Secretariat Tel: 2855 4235 / 2818 0232 Fax: 2818 1186 Email: hkjcc06@hku.hk Website: www.hkicc.org
16 THU 6:30 pm - 8:00 pm 6:00 pm - 8:00 pm (23,30)	(1) An Atypical Disease Presenting Atypically (2) An Elderly Gentleman With Lung Infiltrates and Renal Impairment Organised by: Hong Kong Thoracic Society / ACCP (HK & Macau Chapter) Chairman: Dr. W.C. YU & Dr. M.L.WONG Speaker: Dr. Y.C. YEUNG & Dr. C.W. CHOW # LG1, Lecture Room, Ruttonjee Hospital, Wanchai Advanced Wound Care Management (TC-AWCM-0106-CNSG) Organised by: College of Nursing, Hong Kong Speaker: Various	Dr. W.M. CHAN / Dr. C.M. CHU Tel: 2855 5841 / 2855 5824 Fax: 2855 9667 Sugar Tel: 2572 9255 Fax: 2838 6280
18 SAT 9:30 am - 12:30 pm	Research Symposium - Topic: Research Partnership Among Service, Education and Research Sectors Organised by: College of Nursing, Hong Kong Speaker: Various	Sugar Tel: 2572 9255 Fax: 2838 6280 2 CME Points
19 SUN 1:30 pm	HKMA Family Sports Day Organised by: The Hong Kong Medical Association Chairman: Dr. C.F. YEUNG # Stanley Ho Sports Centre, 10 Sha Wan Drive, Pokfulam, Hong Kong	Ms. Dora HO Tel: 2527 8285
24 FRI 2:00 pm	HKMA CME Luncheon Lecture on The Long-term Cardiovascular Safety for a COX-2 Specific Inhibitor, Etoricoxib - The MEDAL Program Organised by: The Hong Kong Medical Association Chairman: Dr. T.C. SHIH Speaker: Prof. S NAVARRA # Grand Ballroom, Level 2, Langham Hotel Hong Kong, 8 Peking Road, Tsimshatsui, Kowloon, Hong Kong	Miss Nina HUNG Tel: 2861 1979 1 CME Point
26 SUN 2:00 pm	HKMA Structured CME Programme Year 06/07 (VIII) - Endocrinology Organised by: The Hong Kong Medical Association and Kwong Wah Hospital Chairman: Dr. T.C. SHIH Speaker: Various # Kwong Wah Hospital, Lecture Theatre, 10/F., Yu Chun Keung Medical Memorial Centre, Kwong Wah Hospital, Kowloon	Miss Nina HUNG Tel: 2861 1979 (Registration fee is required) 3 CME Points
28 TUE 6:30 pm - 8:00pm	Management Interest Group - Seminar on 消除怨氣開開心心工作無煩憂™ (SMIG-04-06) Organised by: College of Nursing, Hong Kong Speaker: Dr. Alex CHEUNG	Sugar Tel: 2572 9255 Fax: 2838 6280 1.5 CME Points



Calendar of Events

Meetings

1-3/12/2006	9th International Symposium on Thrombolysis and Acute Stroke Therapy (TAST 2006) & 19th Annual Scientific Meeting of The Hong Kong Neurological Society Organised by: The Hong Kong Neurological Society, Chinese Society of Neurology & The Hong Kong Polytechnic University (Rehabilitation Science Department) Speaker: Various # Jockey Club Auditorium, The Hong Kong Polytechnic University Enquiry: Conference Secretariat Email: tast2006@icc.com.hk Website: www.tast2006.com
9-10/12/2006	Hong Kong Ophthalmological Symposium 2006 - Theme: Glaucoma Organised by: College of Ophthalmologists of Hong Kong, Euro Asia Congress Chairman: Prof. Clement C.Y. THAM Speaker: Prof. Robert STEGMANN # Hong Kong Convention & Exhibition Centre, Wanchai Enquiry: Ms. Vicki WONG Tel: 2761 9128 Fax:2715 0089
13/1/2006	G B Ong Lecture: Live Surgery - A New Specialty Organised by: The American College of Surgeons, Hong Kong Chapter & Department of Surgery, Li Ka Shing Faculty of Medicine, The University of Hong Kong Speaker: Prof. Henri BISMUTH # Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam Road, Hong Kong Enquiry: Forum Secretary Tel: 2855 4885/2855 4886 Fax: 2819 3416 Email: hksk@hkucc.hku.hk Website: http://www.hku.hk/surgery
25-27/01/2007	International Colorectal Disease Symposium (ICDS) 2007 Organised by: Hong Kong Society for Coloproctology & Pamela Youde Nethersole Eastern Hospital (Department of Surgery) Chairman: Mr. Michael K.W. LI Speaker: Various # 2/F New Wing, Hong Kong Convention & Exhibition Centre, Wanchai Enquiry: Ms. Olivia HO Tel: 2595 6362 Fax: 2515 3195
2-4/02/2007	Cardio Rhythm 2007 Organised by: Hong Kong College of Cardiology & Chinese Society of Pacing and Electrophysiology # Hong Kong Convention & Exhibition Centre, Wanchai Enquiry: Secretariat, CMP Medica Pacific Limited Tel: 2559 5888 Fax: 2559 6910 Email: info@cardiorhythm.com Website: www.cardiorhythm.com



Meetings

10-11/02/2007	Cancer Imaging 2007 - Joint Meeting of the International Cancer Imaging Society & Hong Kong College of Radiologists Organised by: International Cancer Imaging Society & Hong Kong College of Radiologists Chairman: Ms. Lilian LEONG Speaker: Various # Hong Kong Academy of Medicine Jockey Club Building Enquiry: Mrs. Maureen WATTS Tel: 44 (0) 208 661 3420 Fax: 44 (0) 208 661 3901 E-mail: Maureen.Watts@icr.ac.uk or Ms. Diane LEE Tel: 2871 8788 Fax: 2554 0739 E-mail: enquiries@hkcr.org
13-17/06/2007	The 21st Congress of International Association of Paediatric Dentistry IAPD Organised by: Hong Kong Society of Paediatric Dentistry # Hong Kong Convention & Exhibition Centre, Wanchai Enquiry: Mr. Daniel CHOK Tel: 2871 8896 Fax: 2871 8898 Email: info@iapd2007.com Website: http://www.iapd2007.com

Courses

1,6,8,13,15,20,22,27,29/12/2006 3,5,10,12,17,19,24,26,31/01/2007 2,7,9,14,16,28/02/2007 2,7,9,14,16,21,23,28,30/03/2007	健康服務助理員訓練課程 (TC-HCA-0306) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
1,8,15,29/12/2006	Certificate Course on Quality Management (TC-CQM-0106) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
4,6,11,13/12/2006	醫療護理常用英語初階 (SUSMH 025 0 B) Organised by: College of Nursing, Hong Kong Sugar Tel: 2572 9255 Fax: 2838 6280
4,7,11,14/12/2006	家務助理陪月服務訓練課程 (TC-PNC-0206) Organised by: College of Nursing, Hong Kong Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
7/12/2007	Advanced Wound Care Management (TC-AWCM-0106-CNSG) Organised by: College of Nursing, Hong Kong Speaker: Various Enquiry: Sugar Tel: 2572 9255 Fax: 2838 6280
10&17/12/2006	Pre-hospital Trauma Life Support (PHTLS) Provider Course Organised by: Department of Surgery, University of Hong Kong and Hong Kong Chapter of the American College of Surgeons Enquiry: Course Secretariat, Department of Surgery, University of Hong Kong Medical Centre Tel: 2530 8016
17/12/2006 21/1/2007, 11/2/2007 18/3/2007, 22/4/2007 20/5/2007, 17/6/2007	2nd Certificate Course in Recent Medical Advances for General Practitioners Jointly organized by the Family Medicine Unit, the University of Hong Kong and the Family Medicine Division, Hong Kong Sanatorium and Hospital Speakers: Various, Enquiry: Hospital Administration Department Tel: 2835 8800, Fax: 2835 8008, E-mail:hospadm@hksh.com, Website: http://www.hksh.com/CME.pdf
18,20,27/12/2006 3,8,10,15,17,22,24/1/2007	醫療護理常用英語初階 (SUSMH 026 0 B) Organised by: College of Nursing, Hong Kong Sugar Tel: 2572 9255 Fax: 2838 6280

Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

Date	Course No	Course Name	Co-organiser	Target Participants
6 Nov 06 - 11 Dec 06 (Mon)	C106	Certificate Course on Sleep Health & Disorders	Hong Kong Society of Sleep Medicine	Public
6 Nov 06 - 27 Nov 06	C113	Certificate Course on Drugs Dispensing in Office Clinic		Medical & health professionals
8 Nov 06 - 13 Dec 06 (Wed)	C98	Certificate Course on Diagnosis, Prevention and Management of Thalassaemia	Hong Kong Society for the Study of Thalassaemia	Medical & health professionals
17 Nov 06 - 29 Dec 06 (Fri) (except 22 Dec 06)	C103	Certificate Course on Wilderness Medicine for Healthcare Professionals	Hong Kong Society for Emergency Medicine & Surgery	Health care professionals
3 Jan 07 - 7 Feb 07 (Wed)	C111	Certificate course on Medical Genetics		Medical & health professionals
9 & 16 Jan 07 (Tue)	C112	Certificate Course on Drugs Safety in Old Aged Home		Medical & health professionals

CERTIFICATE COURSE FOR MEDICAL AND HEALTH PROFESSIONALS

Certificate Course on Medical Genetics

醫學遺傳學證書課程

(Course no. C111)

Jointly organised by



The Federation of Medical Societies of Hong Kong
香港醫學組織聯會



Hong Kong Society of Medical Genetics
香港醫學遺傳學會

Objective: The field of medical genetics has seen rapid advances in the last ten to twenty years, especially so with the knowledge brought about by the Human Genome Project. This course aims to provide the participants an overview and update in this field, so that they can appreciate how the practice of medicine is changing with the genetic advances.

Date	Topic	Lecturer
3 January 2007	Medical Genetics in Hong Kong - An Overview 醫學遺傳學在香港的概覽	Dr. Stephen Lam 林德深醫生
10 January 2007	Genetic Counseling 遺傳輔導	Dr. Ivan Lo 盧輝文醫生
17 January 2007	Chromosomal Disorders in Hong Kong 香港的染色體疾病	Mr. Chan Wing-kwong 陳永光高級化驗師
24 January 2007	Application of Molecular Genetics in Patient Care 分子遺傳學的臨床應用	Dr. Brian Chung 鍾侃言醫生
31 January 2007	Prenatal Diagnosis & Therapy 產前診斷及治療	Dr. Leung Kwok-yin 梁國賢醫生
7 February 2007	Treatment Strategies in Genetic Diseases 遺傳病的療法	Dr. Larry Baum 包立怡博士 Dr. Richard Choy 蔡光偉博士

Date : 3 January 2007 to 7 February 2007 (Every Wednesday)

Time : 7:00 p.m. - 8:30 p.m.

Venue : Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong

Course Fee : HK\$960 (6 Sessions)

Language : English

Certificate : Awarded to participants with a minimum attendance of 70%

Enquiry : The Secretariat of the Federation of Medical Societies of Hong Kong

Tel. : 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

CME/CPE Accreditation applied for

For downloading the application form, please refer to our website:
<http://www.fmshk.org>



THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG
香港醫學組織聯會

Certificate Course on Drugs Safety in Old Aged Home

(Course No. C112)

Objective: To enhance safety of drugs handling in old aged home

9 January 2007

Common Drugs Used in Elderly Homes 安老院舍常見藥物

Mr. Henry Chan 陳智傑
香港註冊藥劑師及香港藥學會幹事

16 January 2007

Management of Drugs 處理藥物的原則

1. 妥善儲存藥物
2. 正確派發藥物
3. 促使跟醫囑服藥

Ms. Rebecca Po-wah Poon

Date : 9 & 16 January 2007
Time : 7:00 p.m. - 8:30 p.m.
Venue : Lecture Hall, 4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Hong Kong
Course Fee : HK\$350 (2 Sessions)
Language : Cantonese (Supplemented with English)
Certificate : Awarded to participants with a minimum attendance of 70%
Enquiry : The Secretariat of the Federation of Medical Societies of Hong Kong
Tel. : 2527 8898 Fax: 2865 0345 Email: info@fmshk.org

CME/CPE Accreditation applied for
For downloading the application form, please refer to our website:
<http://www.fmshk.org>



THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG
香港醫學組織聯會

Certificate Course on Drug Dispensing in Office Clinics
診所藥物處理及配藥基本課程
(Course No. C113)

Objective: To enhance safety and efficacy of clinic assistants in drug dispensing in office clinics



2006年11月6日

Drug Classification in Hong Kong - A Simple Approach Common Drugs Identifications in Clinic

香港藥物分類簡介及診所藥物識別

Mr. Peter Suen 孫耀燦先生
天一醫務所總藥劑師

2006年11月13日

Clinic Dispensing Management

診所配藥管理

Mr. Peter Suen 孫耀燦先生
天一醫務所總藥劑師

2006年11月20日

Good Dispensing Guidelines

良好配藥守則

Dr. Lam Tsan 林璨醫生
家庭醫學顧問醫生



2006年11月27日

Drugs Stock Keeping and Recording

診所藥品庫存及記錄

Mr. Peter Suen 孫耀燦先生
天一醫務所總藥劑師

日期：2006年11月6日至2006年11月27日
時間：下午2時至3時30分
地點：屯門醫院演講廳，新界屯門青松觀道
收費：每位港幣\$500元(4堂)
語言：粵語
備註：如出席率達70%，可獲發證書

此課程將於2007年1月份在沙田醫院及醫學組織聯會會址舉行，詳情於稍後公佈。

索取報名表格及查詢，請與香港醫學組織聯會秘書處聯絡

香港灣仔軒尼詩道十五號溫莎公爵社會服務大廈四樓

電話：2527 8898 傳真：2865 0345 電郵：info@fmshk.org

或瀏覽網址：www.fmshk.org 下載報名表格



THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG

香港醫學組織聯會

A Go Go to Count Down

The Federation's 2006 Annual Dinner

7:00 pm, 31st December, 2006 (Sunday)

Run Run Shaw Hall

The Hong Kong Academy of Medicine Jockey Club Building

99 Wong Chuk Hang Road, Aberdeen, Hong Kong

Registration Form

Please reserve _____ table(s)* / seat(s) for me at the Federation Annual Dinner 2006. A cheque for the amount of HK\$ _____ (HK\$900 per person) in favour of "The Federation of Medical Societies of Hong Kong" is enclosed.

* Each table will seat 10 to 12 people.

From: Surname: _____ First name: _____
(Please use block letter)

Position _____

Society / Association _____

Address _____

Tel No. _____ Fax No. _____

Signature _____ Date: _____

**Kindly return this form on or before December 10, 2006
to the Secretariat at Fax 2865 0345.**

醫聯成員一家親，市民健康齊關心

4/F, Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong • Tel: (852) 2527 8898 • Fax: (852) 2865 0345
Homepage: www.fmskh.org • E-mail: info@fmskh.org

A Go Go to Count Down

The Federation's 2006 Annual Dinner
31st December 2006

Come and take a walk down memory lane and revisit the 60's

Drive your oldest car to the venue to join the vintage car competition

Dress up in the 60's style for the best-dressed men and ladies competition

Tickets on sale from 1st October 2006 (HK\$900 per person)



Venue

Run Run Shaw Hall

The Hong Kong Academy of Medicine Jockey Club Building

99 Wong Chuk Hang Road, Aberdeen, Hong Kong

For further information and assistance, please contact our secretariat Ms Karen Chu
on 2821 3515 or email: karen.chu@fmshk.org



The Federation of Medical Societies of Hong Kong

香港醫學組織聯會

Homepage: www.fmshk.org