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## The Cover Shot



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# Psychosis, and the Violent Psychiatric Patient

## Dr. Paul Tat-chung LAM

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### Editor

Dr. Paul Tat-chung LAM

In this issue we have 5 articles on various aspects of psychosis. Psychosis is defined as (1) a cerebral dysfunction, (2) resulting in abnormal behavioural symptoms, (3) the patient has gross impairment of reality testing and (4) there is loss of insight. Common symptoms of psychosis include hallucination, delusion, and acute emotional upset. It can be broadly categorised into (1) organic psychosis in which there is evident pathology of the brain as detected by traditional examination and investigation. Examples include drug and alcoholic intoxication, epilepsy, and late stage Alzheimer's disease, and (2) functional psychosis in which there are no obvious pathological changes. Examples are schizophrenia and bipolar disorder. Treatment of psychotic patients forms a great part of the work of psychiatrists, and poses a very heavy burden on hospitals and social personnel and facilities. Recent studies have drawn attention to the mechanism of development of the psychotic brain, and to the importance of early detection and treatment of the condition. It is therefore appropriate for all doctors to have some information about current advances and insight into the illness.

Every now and then, perhaps several times in a year, we come across local news reports of gruesome incidents of violence committed by psychiatric patients. These include murder or serious bodily harm to close relatives or innocent people, or self injury, sometimes in the most grotesque, bizarre and unimaginable manner. The greatest majority of incidents committed by psychiatric patients are carried out by patients with psychosis. Following an incident, there are usually sensational reports in the media, followed by public outcry. All would then die down to await the next incident not too distant in the future. Is this an inevitable path? Even our leaders in the local Health Service had come out to say that such incidents are bound to occur, and there is not a lot that can be done.

However, such an attitude of defeatism is not justified. In Hong Kong we have first class psychiatrists, and well trained paramedical personnel such as community psychiatric nurses and social workers. We have efficacious drugs at our disposal, we also have the hard ware such as clinics and hospitals, but we do not have the will power and the service system in place to tackle this very pressing issue. There is no doubt that the public psychiatric service is grossly overloaded. However there are ways to alleviate the situation. Firstly there are many patients with minor complaints such as mild anxiety who do not need to be kept under the Specialist Psychiatric Clinics. Secondly better utilisation should be made of spare capacities of the well trained and vast experience of specialist psychiatrists in the private sector. Recently the Hospital Authority allows specialist psychiatrists who have left the service to take up part time employment. This is certainly a step in the right direction. With some relief of the work load, greater efforts can be directed specifically and intensively to the group of patients at high risk of violence or suicide, and the occurrence of such can be reduced to a minimum. This is something that can be done, and must be done as an urgency.

In preparing this issue of the Medical Diary, I am most indebted to the advice and assistance of Professor Eric YH Chen, and to the coordination of Dr. Sherry KW Chan of the Dept. of Psychiatry, The University of Hong Kong.



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# Rationale and the Local Development of Early Intervention for Psychosis

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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 31 May 2011.*

## Rationale of Early Intervention for Psychotic Disorders

Psychotic disorders including schizophrenia are severe mental illnesses that constitute a major public health problem. Schizophrenia and schizoaffective disorder together rank as the fifth leading cause of disability by the World Health Organization (WHO)<sup>1</sup>. As psychosis typically occurs in late adolescence or early adulthood, which is the critical developmental life stage in terms of personality, social role, scholastic or vocational achievement, it can therefore cause profound adverse impact on patients' long-term functional capacity. Besides having debilitating symptoms of delusions, hallucinations, loss of volition, social withdrawal and neurocognitive impairment, individuals suffering from psychosis are also prone to other psychiatric morbidities such as depression, substance abuse and suicide. At a societal level, enormous economic costs are incurred by psychotic disorders through direct medical costs, lost employment, increased welfare benefits and diminished productivity of caregivers<sup>2</sup>.

In the last decade, early intervention for psychotic disorders has become a major trend in mental health care development worldwide<sup>3</sup>. This specialised programme comprises two key components: 1) early detection to reduce delay in treatment and 2) phase-specific intervention during the early illness stage. A large number of studies have found that prolonged duration of untreated psychosis (DUP) predicted worse symptomatic and functional outcome, and poorer quality of life in patients with first-episode psychosis<sup>4</sup>. As literature revealed that prolonged delays of up to one to two years before treatment were common in individuals experiencing psychosis<sup>5</sup>, DUP is thus posited as a potentially malleable prognostic factor which may be reduced by early identification and prompt intervention. Research also suggested that the first few years of psychotic disorders after onset is a critical period for determining long-term illness outcome<sup>6</sup>. Provision of focused and phase-specific intervention at this early illness stage may therefore ameliorate, if not prevent, potentially pronounced disability. A growing body of evidence has indicated that, when compared with standard psychiatric service, early intervention programmes are associated with shortened treatment delay, increased symptomatic remission, lower relapse rates, lower use of legal detention, reduced hospital

admissions, improved psychosocial functioning, better service engagement, higher client / carer satisfaction and lower suicide rates<sup>7</sup>. In fact, this phase-specific early intervention model has been endorsed by WHO and the International Early Psychosis Association which jointly issued the "Early Psychosis Declaration" in 2005<sup>8</sup>.

## The Local Development of Early Intervention Service for Psychosis

The Early Assessment Service for Young People with Psychosis (abbreviated as EASY), which has been launched since 2001, is a publicly-funded specialised programme that provides early assessment and phase-specific intervention for all individuals aged 15 to 25 years experiencing their first-episode psychosis<sup>9</sup>. The programme consists of five treatment teams covering the whole territory of Hong Kong. Being one of the first and most comprehensive early intervention programmes in Asia, the EASY programme comprises three main components: 1) to raise public awareness; 2) to create an easily accessible referral system and 3) to provide a phase-specific intervention.

In order to improve the mental health literacy to psychosis in the general public, a series of public education programmes have been organised utilising various means of channels including TV, radio interviews, press release, public talks, school visits, leaflets and exhibitions, to name a few. The EASY programme also introduced a more perceptive Chinese term for psychosis, namely "思覺失調" (literally means dysregulation in thinking and perception) to ameliorate the stigma. Regarding the referral pathway, a broad range of referral mechanisms is implemented to encourage early help-seeking in individuals suffering from first-episode psychosis. These include a hotline direct referral system, referrals from community via emails, walk-ins, school social workers and non-governmental organisations (NGOs), as well as within the public health care system. After receiving a referral, a telephone-based initial screening assessment is carried out by a case manager. An individual who has been identified as a potential client for the programme will then be thoroughly evaluated by a psychiatrist to ascertain the diagnosis and to formulate a management plan within one week after screening.



The programme adopts a case management approach and assertively follows up patients for the first three years after their initial episodes (including follow-up in a transitional step-down clinic in year three). Each individual patient is assigned a case manager. Standardised clinical assessments measuring symptom profiles and psychosocial functioning are performed to each patient. Besides optimal psychopharmacotherapy, the EASY programme also provides a range of protocol-based psychosocial interventions to enhance the patient's psychological adjustment, to minimise secondary psychiatric morbidities, to promote illness recovery and to alleviate the carer's stress. These include psychoeducation groups for patients and families, individual supportive counselling, cognitive behavioural therapy for treatment-resistant psychotic symptoms and family intervention. The programme also has close collaboration with NGOs and local community networks to facilitate rehabilitation process of patients who are clinically stabilised with treatment. Patients will be transferred to a general psychiatric team for continuous follow-up at the end of the three-year EASY service.

In order to evaluate the effectiveness of the local early intervention programme, a large scale three-year follow-up case-control study was carried out comparing the clinical and functional outcome between 700 cases in the EASY programme with 700 historical controls who received standard care prior to the implementation of the programme<sup>10</sup>. Subjects were individually matched for age, sex and diagnosis, and had similar level of positive and negative symptoms at presentation. The results suggested that the early intervention (EI) group had significantly fewer days of hospitalisation, less severe positive and negative symptoms, fewer suicides, reduced service disengagement and higher likelihood of achieving a period of recovery than the control group three years after treatment initiation. Additionally, it has also been shown that EI is cost-neutral with extra personnel costs being offset by reduced inpatient costs<sup>9</sup>. The robust positive findings therefore suggest that key elements of the EASY programme have been effective for the Hong Kong population.

## Conclusion

Schizophrenia and other psychotic disorders have long been regarded as chronic and debilitating illnesses resulting in significant disabilities. The paradigm shift from institutional model of care towards community-based early intervention service delivery changes the long-held pessimism attached to psychotic disorders to an expectation of a much more positive outlook by clinicians, patients and their families. Given that there is considerable evidence supporting the adoption of early intervention for psychosis and the success of the EASY programme, the Government of Hong Kong is going to plan for an extension of this early intervention service to cover a wider age range (above 25 years of age)<sup>11</sup>. It is to hope that patients of all ages can benefit from this high-quality, cost-effective and non-stigmatising phase-specific treatment to facilitate their recovery and pursuit in education and work.

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Please read the article entitled "Rationale and the Local Development of Early Intervention for Psychosis" by Dr. Wing-chung CHANG 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 sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 May 2011. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

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

- 1. Schizophrenia and schizoaffective disorder together rank as the fifth leading cause of disability by World Health Organization.
2. The typical age of onset of psychotic disorders is within 30 to 40 years.
3. Common psychiatric morbidities of schizophrenia include depression and substance abuse.
4. Prolonged duration of untreated psychosis has been shown by numerous studies to be associated with poor clinical outcome.
5. A significant proportion of patients having psychotic disorders had duration of untreated psychosis of up to one to two years prior to implementation of early intervention service.
6. Critical period hypothesis stated that the prodrome of psychotic disorders is the prime interval for intervention.
7. Literature has demonstrated that early intervention programmes improve symptomatic and functional outcome of patients with psychosis when compared with standard psychiatric service.
8. The Early Assessment Service for Young People with Psychosis (EASY) programme targets at individuals aged 15 to 30 years experiencing their first psychotic episodes.
9. Each patient enrolled in the EASY programme is assigned a case manager and is followed up for three years before transfer to general psychiatric service.
10. Case-control study revealed that there was no significant difference between the EASY programme and standard care in terms of length of hospitalisations and suicide rate.

ANSWER SHEET FOR MAY 2011

Please return the completed answer sheet to the Federation Secretariat on or before 31 May 2011 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Rationale and the Local Development of Early Intervention for Psychosis

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Answers to April 2011 Issue

Carbapenem-resistant or Multidrug-resistant Acinetobacter Baumannii - a Clinician's Perspective

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

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References: 1. Cutler A et al. Poster presented at the 161<sup>st</sup> Annual Meeting of the American Psychiatric Association, May 3-8, 2008, Washington, DC, USA. 2. Suppes T et al. J Affect Disord 2010;121:106-115. 3. Seroquel XR Package Insert Version: March 2010.

#### Abbreviated Prescribing Information:

**Presentations:** Quetiapine fumarate extended-release tablet. **Indications:** Treatment of Schizophrenia & preventing relapse in stable patients on Seroquel XR. Treatment of manic episodes and major depressive episodes associated with bipolar disorder. For preventing recurrence in bipolar disorder in patient whose manic, mixed or depressive episode has responded to quetiapine treatment. **Dosage:** Adults **Schizophrenia:** Once-daily, without food (at least one hr before meal. Starting daily dose is: 300 mg (Day 1) & 600 mg (Day 2). Recommended daily dose is 600 mg. Range 400-800 mg/day depending on clinical response & tolerability of patient. Same dosage is used for maintenance therapy. **Manic episodes associated with bipolar disorder:** Starting daily dose is: 300 mg (Day 1) & 600 mg (after Day 2). Range 400-800 mg/day depending on clinical response & tolerability of patient. **Major depressive episodes associated with bipolar disorder:** Once-daily at bedtime. Starting dose is 50mg (Day 1) & 100 mg (Day 2) & 200 mg (Day 3) & 300 mg (Day 4). Recommended daily dose is 300 mg. Individual patients may benefit from a 600 mg dose. **Preventing bipolar disorder recurrence:** Use same dose as active treatment for prevention of manic, depressive or mixed episodes in bipolar disorder. Range of 300-800 mg/day depending on clinical response & tolerability of patient. **Switching from Seroquel XR:** Switch at equivalent total daily dose. Individual adjustments may be necessary. Elderly or hepatic impairment patients: Initially 50 mg/day increased in increments of 50 mg/day to an effective dose. **Renal impaired patients:** No dosage adjustment needed. **Contraindications:** Hypersensitive to the active substance or excipients of this product. Concomitant administration of cytochrome P450 3A4 inhibitors, such as HIV-protease inhibitors, azole-antifungal agents, erythromycin, clarithromycin and nefazodone is contraindicated. **Precautions:** Not recommended for below 18y old; increased suicide-related events; somnolence; severe neutropenia/increase in cardiovascular & cerebrovascular disease; Conditions predisposing to hypotension; orthostatic hypotension; extrapyramidal symptoms; seizures; tardive dyskinesia; neuroleptic malignant syndrome; not approved in elderly patients with dementia-related psychosis; jaundice development; venous thromboembolism; galactose intolerance. **Interactions:** Centrally acting drugs; alcohol; thioridazine; carbamazepine; phenytoin; ketoconazole. **Undesirable effects:** Dry mouth; withdrawal symptoms; elevations in serum triglyceride levels; elevations in total cholesterol; decrease in HDL cholesterol; dizziness; somnolence; headache; leukopenia; tachycardia; vision blurred; constipation; dyspepsia; mild asthenia; peripheral edema; irritability; weight gain; hyperprolactinaemia; increased appetite; extrapyramidal symptoms; Dysarthria; elevations in serum transaminases (ALT, AST); decreased neutrophil count; blood glucose increased to hyperglycaemic level; syncope; rhinitis; abnormal dreams & nightmares and orthostatic hypotension. **Full local prescribing information is available upon request.**  
APIJK-SXR.0310

# Relapse in Schizophrenia

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## Introduction

Schizophrenia is characterised not only by its florid and extraordinary positive symptoms, but also negative and disorganisation symptoms; these symptoms affect almost all aspects of mental function in emotion, language, motor, as well as perception and reasoning. Clinical observations have suggested that there are a great variety of courses and outcome in schizophrenia. The premorbid and prodromal phase refers to the period prior to illness onset in which vulnerability traits or subclinical symptoms are expressed, respectively. First-episode psychosis refers to the period when a patient presents with a diagnosable psychotic disorder for the first time, usually characterised by frank psychotic symptoms of hallucinations, delusions and behavioural disturbances.<sup>1</sup>

Outcome is often conceptualised in terms of remission, recovery and relapse. Remission is a state when these psychotic symptoms subside. Recovery is remission from psychotic symptoms, as well as attaining adequate social and occupational functioning where some patients can achieve. Relapse is usually defined as the re-emergence of psychotic symptoms. A 20-year follow-up of the Madras study showed that about 40% of patients relapsed with complete remission in between, 44% relapsed with partial remission in between; and only 8% had complete remission.<sup>2</sup> Importantly, this long-term follow-up study indicated that the level of disability incurred is high and relapse is the typical pattern. This article will first introduce the concept of relapse and its associated costs, followed by investigating both naturalistic and controlled studies on the risk of relapse. It will end with a brief discussion on the important clinical decision concerning medication discontinuation and relapse.

## Defining Relapse

Relapse can be defined more broadly or more narrowly. Narrow definition of relapse involves the definite re-emergence of psychotic symptoms associated with significant disturbance in functioning and social behaviour.<sup>3</sup> According to Johnstone, relapse could also be defined as Type I, the reappearance of schizophrenic symptoms in a patient who has been free of them following the initial episode, and Type II, the exacerbation of persistent positive symptoms.<sup>4</sup> Clinical instruments such as the Positive and Negative Syndrome Scale (PANSS), Clinical Global Impressions (CGI) and the Brief Psychiatric Rating Scale (BPRS) are often used for operationally defining relapse.

In response to these diverse approaches in measuring symptoms, some researchers adopt a broader definition of relapse, such as 'rehospitalisation' being a proxy for relapse.<sup>5-8</sup> However, rehospitalisation can result from a much wider range of other clinical scenarios such as suicidal attempt, violence, medication side effects, and thus relapse is only one of the many possible causes for rehospitalisation. In reality, rehospitalisation is usually the most expensive part in the mental health cost for psychotic patients, the measurement of rehospitalisation would be most relevant in health economics considerations.<sup>9</sup>

## Relapse Costs

Consequence of relapse can be enormous. Medical costs, non-medical costs and productivity losses associated with relapses are enormous from the economic perspective.<sup>10-11</sup> Studies have found that patients have a poorer response to treatment in subsequent relapse episodes, as well as a longer time to remission with each subsequent episode.<sup>12-14</sup> To the patients, a relapse with re-emergence of psychotic symptoms may imply the necessity of staying on medication for a considerably longer period of time or even on a long-term basis. This fact could be particularly devastating to a young patient who has been making an otherwise smooth recovery from his or her first-episode illness.<sup>15</sup>

## Relapse Rates: Naturalistic and Controlled Studies

Relapse rates in schizophrenia have been studied extensively in both naturalistic and controlled studies. Despite the fact that studies varied in relapse definitions and duration of follow-up, the risk of relapse is still high. Naturalistic studies have found that the cumulative relapse rate was 70%-82% up to 5 years following the first admission or episode.<sup>16-17</sup> In Hong Kong, a naturalistic longitudinal follow-up study of 93 first-episode psychosis patients found that relapse rates were 21%, 33%, and 40% in the first, second and third year respectively.<sup>18</sup> Conclusions drawn from naturalistic studies, however, failed to exclude the fact that the high relapse rate is a result of medication discontinuation where it is not uncommon in patients with psychotic disorders.<sup>19-20</sup>

In contrast, double-blind randomised placebo-controlled trials where discontinuation was controlled,



have shown that early discontinuation of antipsychotics therapy results in more relapses at 1 year: 63% vs 38%,<sup>21</sup> 61% vs 27%;<sup>22</sup> 41% vs 0%.<sup>23</sup> In Hong Kong, relapse was studied in a randomised controlled trial on remitted first-episode psychosis patients who have been on maintenance medication for at least 1 year. It was found that relapse rates for those discontinuing medication was 79% while continuing medication was 41%.<sup>24</sup> These findings all point to the importance of continuing medication in preventing relapse.

## Consideration of Medication Discontinuation

Discontinuing medication is tempting and seems logical to many patients when their psychotic symptoms have subsided, and is consistent to our usual conceptualisation of recovery. Although antipsychotic maintenance treatment seems to be effective in preventing relapse,<sup>25-26</sup> controlled studies suggested that the subsequent rate of relapse could be substantial even on maintenance medication.<sup>21-24</sup> Long-term maintenance therapy is also increasingly recognised as a costly option, as it could lead to substantial long term metabolic or neurological side-effects, as well as psychological and economic consequences.<sup>27</sup> The clinical decision on whether to continue the medication is hence complex. To patients and their families, the uncertainty and psychological burdens surrounding potentially lifelong continuation of medication may also be substantial. In brief, medication discontinuation should be a joint and planned decision involving the patients, the carers and the clinicians. The clinicians should discuss openly with the patients all the possible options and consequences, and also look beyond the short-term risk and focus on the long-term health risks and benefits for the patient. After all, there is a small proportion of patients who could potentially remain relapse free even without maintenance medication.

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## Psychosis High Risk Research – Local Scene

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### Rationale for Early Intervention for People with High Risk of Developing Psychosis

Psychotic disorders (including schizophrenia and its related disorders) involve complex neurobehaviour dysfunction, influenced by genetic and environmental factors affecting up to 3% of the population<sup>17</sup>. They constitute one of the highest disease burden globally and locally. Schizophrenia and its related psychotic disorders ranked globally amongst the top ten leading causes of disability-adjusted life years (DALYS)(WHO 2001). The conditions inflict devastating consequences for youths and adults at the most productive years in their lives. It is estimated that each year 1000- 2000 individuals in Hong Kong develop a psychotic disorder for the first time in their lives. Despite progress in the development of medications with fewer side effects, the treatment often cannot alleviate the disability associated with this chronic form of illness. Deficit symptoms and cognitive impairment, which appear to be the greatest determinants of disability, remain largely beyond the reach of current forms of treatment. The treatment outcome is often poor and associated with extensive cost, burden, morbidity and mortality. Identification and treatment of psychotic disorders is a priority for most public health services worldwide.

Emerging evidence suggests that much of the disability associated with psychotic illnesses, particularly schizophrenia, develops long before the onset of frank psychosis. This pre-onset or prodromal period is characterised by non-specific symptoms such as depressed mood and anxiety as well as sub-threshold symptoms<sup>5,23</sup>. Cortical changes during this period are associated with cognitive, social and motivational dysfunctions<sup>10</sup>, and are difficult to reverse even if the first psychotic episode is successfully treated<sup>8,10</sup>. The prodromal period is therefore potentially important for early intervention and the possible prevention of the development of the psychotic disorders.

However, a major challenge has been to prospectively identifying the prodromal phase, particularly given the non-specific nature of prodromal symptoms<sup>21</sup>. Subjective cognitive impairment disturbances known as “basic symptoms” have been described by the German Early Detection Team and found to be good predictors for onset of psychosis<sup>4,16</sup>. McGorry et al. introduced the term “At Risk Mental State”, implying that the sub-threshold syndrome can be regarded as a risk factor for the subsequent development of psychosis, but that the onset

of psychosis is not inevitable<sup>21,22</sup>. The operationalised “at risk mental state” described 3 subgroups: (1) genetic risk in combination of functioning decline, (2) Attenuated positive psychotic symptoms, and (3) Transient psychotic episode. Several studies conducted internationally in recent years using the criteria yielded an average 1 year conversion rate of 36.7% in high risk subjects who did not receive antipsychotic treatment<sup>15</sup>.

Several clinical trials have been conducted to evaluate the efficacy of interventions in reducing the transition rate to psychosis over the recent few years. The interventions used included the combined cognitive behavioural therapy and antipsychotic medication<sup>11</sup>, antipsychotic medication alone<sup>9</sup>, cognitive behaviour therapy alone<sup>14</sup> and essential fatty acids<sup>1</sup>. These studies demonstrated that psychiatric symptoms and psychosis onset can be delayed by specific intervention. Several clinical trials on the high risk samples have been initiated recently. The intervention agents use of these ongoing studies include antidepressants, mood stabilisers, methylglycine Ethyl-EPA, case management, cognitive training and cognitive behavioural therapy<sup>3</sup>.

Increasing evidence has demonstrated high rates of psychotic like experiences exist in community cohorts<sup>18</sup> and reduction in the transition rate to psychosis internationally<sup>23</sup>. These findings and consequently higher false positive rates mean that safer and more benign interventions must be offered as the first line treatment to these high risk people.

### Local Scene-Clinical Aspects

Early Assessment Service for Young People with Psychosis (EASY) was established in Hong Kong in 2001. It is a population wide early intervention service with an annual average of 600 new cases targeted at age 15-25<sup>2</sup>. The referrals are open and direct, derived from educational settings, youth services, adolescent medical centres, primary care, general health services, mental health professionals and hotlines. Among the EASY referrals, those with first episode psychosis will receive phase specific intensive comprehensive treatment; those who are not frankly psychotic, but are judged to be “high risk” by the assessing psychiatrist will receive non-specific need based treatment while being monitored regularly. Up until this stage, the EASY does not have an operationalised inclusion criteria for the “high risk” cases. The defined “high risk” cases are based on clinical assessment by the individual psychiatrist in the EASY team.

## Local Scene-Research Aspects

A naturalistic prospective study was conducted in 2002 in one of the EASY centre (EASY-KCH Clinic) with the aim to assess the rate of transition to psychosis in a high risk group. Between 1<sup>st</sup> June 2002 and 30<sup>th</sup> April 2003, there were a total of 256 referrals made to the EASY-KCH Clinic, among which 153 were psychotic and they were treated accordingly. With the remaining 103 subjects, 67 met the operationalised CAARMS "At risk Mental State"<sup>21,22</sup> criteria, and 62 of them consented to participate in the project. Over a 6 month follow up period, 18 subjects (29%) met the criteria for a psychotic disorder. In addition, significant differences were found in the intake symptomatology and functioning scores between the group that ultimately became psychotic and the group that did not<sup>6</sup>. At two-year follow up, 45% of the group made transition to psychosis.

The study results indicate that it is possible to identify a sub-sample of the Hong Kong population with a high rate of transition to psychosis (29%) within 6 months and 45% of the identified high-risk subjects developed psychosis within two years. The identified high risk subjects had moderate levels of functional decline and psychopathology at the study intake. A lengthy delay was found between the onset of symptoms and the study intake from 11 days to 6.6 years<sup>6</sup>.

## Challenges and Ethical Issues on Pre-psychotic Intervention

With the worldwide vast growing enthusiasm in pre-psychotic identification and intervention over the past decade, people working in the field need to be aware of the obstacles and ethical issues surrounding this area<sup>5</sup>. Many of these arise from the genuine problems associated with defining the onset in psychiatric disorders. The lack of a clear boundary between normality and psychotic disorders<sup>18</sup> is especially relevant during onset as syndromes emerge and progress from origins which are indistinguishable from normal experiences<sup>13</sup>.

Misunderstanding the implications of a positive diagnostic test may lead to negative outcomes including inappropriate stigmatisation, discrimination in employment, and difficulties in obtaining life insurance<sup>24</sup>. Communicating one's risk status to others can deprive social and occupational opportunities in several ways including overt discrimination; self stigma presents another potential hazard to the subjects' psychological and social development<sup>24</sup>. Self stigma was seen related to low self esteem, diminished self-efficacy and abandonment of developmental challenges and occupational goals. In addition, growing concerns regarding long term and short term consequences of exposing a developing brain to drugs need to be considered<sup>25</sup>. The problems raised by false negatives are less frequently mentioned<sup>9,25</sup>. However, being wrongly reassured may also be a harmful consequence of early detection.

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- Rapid pain relief, with significant effects from **Day 2**<sup>7</sup>
- Significantly improves pain-related sleep interference<sup>8</sup>

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**LYRICA ABBREVIATED PACKAGE INSERT 1. TRADE NAME:** LYRICA. **2. PRESENTATION:** Each Lyrica hard capsule contains 25mg, 50 mg, 75 mg, 150 mg, 225mg or 300 mg of pregabalin. (not all strengths may be marketed). **3. INDICATIONS:** Treatment of peripheral and central neuropathic pain in adults: As adjunctive therapy in adults with partial seizures (epilepsy) with or without secondary generalization. Treatment of Generalized Anxiety Disorder (GAD) in adults. For the management of fibromyalgia. **4. DOSAGE:** 150 to 600 mg/day to be taken in two or three divided doses with or without food. For neuropathic pain: start at 150 mg/day, increase to 300 mg/day after 3 to 7 days. If needed, then to a maximum of 600 mg/day after an additional 1-day interval. For epilepsy: start with 150 mg/day, increase to 300 mg/day after 1 week if needed, then to a maximum of 600 mg/day after an additional week. For GAD: start with 150 mg/day, increase to 300 mg/day after 1 week if needed, then increase to 450mg/day following an additional week if needed, then to a maximum of 600 mg/day after an additional week. For fibromyalgia, recommended dose is 300 to 450 mg/day; dosing should begin at 75 mg BID (150mg/day) and may be increased to 150mg BID (300 mg/day) within one week based on efficacy and tolerability. Patients who do not experience sufficient benefit with 300 mg/day may be further increased to 225 mg BID (450 mg/day). Renal impairment: daily dose should be adjusted based on renal function. Elderly may require a dose reduction. Discontinuation of pregabalin should be done gradually over a minimum of 1 week independent of indication. **5. CONTRAINDICATIONS:** Hypersensitivity to the pregabalin or to any of the excipients. **6. WARNINGS & PRECAUTIONS:** Avoid in patients with galactose intolerance, the Lapp lactase deficiency or glucose-galactose maldigestion. Adjust hypoglycaemic medications if weight gain occurs in diabetic patients. Use with caution in patients with severe congestive heart failure. Withdrawal symptoms may occur after discontinuation of short-term and long-term treatment. May cause dizziness and somnolence, which could increase the occurrence of accidental injury (falls) in the elderly population and influence the ability to drive or use machinery. The incidence of adverse events especially somnolence may be increased in the treatment of central neuropathic pain due to spinal cord injury which may be attributed to the additive effect from concomitant medication for the condition. **7. INTERACTIONS:** Oxycodone, ethanol and lorazepam. **8. PREGNANCY AND LACTATION:** Should not be used during pregnancy unless in the opinion of the physician, the potential benefit outweighs the potential risk. Effective contraception must be used in women of child bearing potential. Breast-feeding is not recommended. **9. SIDE EFFECTS:** Dizziness, somnolence, appetite increased, euphoric mood, confusion, libido decreased, instability, ataxia, disturbance in attention, coordination abnormal, memory impairment, tremor, dysarthria, paraesthesia, vision blurred, diplopia, vertigo, dry mouth, constipation, vomiting, fatigue, erectile dysfunction, fatigue, oedema peripheral, feeling drunk, oedema, gait abnormal, weight increased, disorientation, insomnia, balance disorder, amnesia, sedation, lethargy, adominal distention, feeling abnormal. Reference: HK PI (Mar 2008) Date of preparation: May 2010 Identifier number: LYR0510 FULL PRESCRIBING INFORMATION IS AVAILABLE UPON REQUEST.



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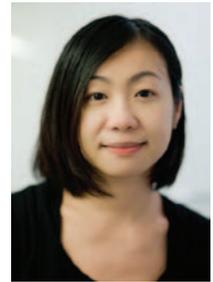
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# Early Symptomatology of Schizophrenia

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## Introduction

The management of schizophrenia and its related disorders has advanced substantially in the past decades, with the use of better tolerated antipsychotics and the introduction of specialised intervention programmes in many parts of the world. Patients' outcome can be particularly improved when treated early within the critical period.<sup>1,2</sup>

Early identification of schizophrenia is thus crucial. In countries with low to medium level of resources, the World Health Organization (WHO) and International Early Psychosis Association (IEPA) recommend surveying high-risk population groups or instituting surveillance for early psychosis in the community.<sup>3</sup> It is now recognised that in the majority (68%) of cases, the index psychotic episode is preceded by a prodromal stage.<sup>4</sup> During this stage, subthreshold psychotic symptoms and other nonspecific early signs may be observed. These early signs and symptoms may serve as flags for identifying at-risk individuals clinically.

## Subthreshold Psychotic Symptoms

Sometimes referred to as attenuated psychotic symptoms or brief limited intermittent psychotic symptoms (BLIPS), these are mental problems that occur close to the onset of a full-blown disease, either with a lower intensity or of a shorter duration (resolving without antipsychotic medication) than those seen in frank psychosis.

According to the Comprehensive Assessment of At-Risk Mental States (CAARMS),<sup>5</sup> these symptoms can be grouped under four dimensions as listed in the Table. Attenuated psychotic symptoms are defined as those experienced occasionally at a moderate to severe (but not psychotic) intensity. When these are experienced at a severe to psychotic intensity but remitted spontaneously within 1 week, BLIPS is said to be present.

**Table. Symptom dimensions in the CAARMS criteria for attenuated psychotic symptoms or BLIPS.<sup>5</sup>**

Dimensions	Symptoms
Unusual thought content	Delusional mood and perplexity, ideas of reference, bizarre ideas (e.g. passivity, thought insertion, withdrawal, broadcasting, or mind reading)
Non-bizarre ideas	Suspiciousness or persecutory, grandiose, somatic, guilt, nihilistic, jealous, religious, and erotomantic ideas
Perceptual abnormalities	Visual, auditory, olfactory, gustatory, tactile, and somatic changes
Disorganised speech	Subjective changes (e.g. difficulty with speech, trouble finding words, not getting to the point, difficulty in understanding, repeating words of others, staying silent) and objective changes (e.g., incorrect words, circumstantial, tangential, vague, overly abstract or concrete, use of strange words)

## Nonspecific Early Signs

Sometimes referred to as "basic symptoms", these are subtle and often subjective changes in cognition, affects, drive, stress tolerance, sleep, speech, perception, and motor actions, which are believed to be early expressions of the underlying physiological disturbances for later development of psychosis.

A wide range of early signs has been proposed, including for example coenaesthetic symptoms and cognitive abnormalities,<sup>6</sup> changes in the sense of self and the world,<sup>7</sup> disorder of selective attention,<sup>8</sup> affective-dynamic disturbances (e.g. impaired tolerance to certain stressors or novel demands), and body perception disturbances (e.g. numbness, bodily sensations migrating through the body),<sup>9</sup> to name a few.

Researchers have been trying to narrow down the list by identifying those most frequently precede onset of psychosis. Current data from prospective and retrospective studies<sup>4,10,11</sup> suggest the following: reduced concentration and attention; reduced motivation and anergia; depression; slowness; sleep disturbances; anxiety and worrying; social withdrawal; lack of self-confidence; suspiciousness; deterioration in role functioning; irritability and restlessness; thought interferences, preservation, pressure, or blockages; disturbances of receptive language; decreased ability to discriminate between ideas and perception and between phantasy and true memory; derealisation; unstable ideas of reference; and visual and acoustic perception disturbances.

## Discussion

While diagnosis of frank psychosis may be less problematic, early signs and symptoms suggestive of later psychosis are comparatively elusive. The nonspecificity of many of these features means possible overlaps with normal adjustment problems or other psychiatric conditions (e.g. depression).<sup>4</sup> At present, a set of early signs and symptoms that are invariably followed by psychosis onset is yet to be identified.

Despite these problems, early detection and monitoring of help-seeking individuals presenting with risk features remains an important strategy to ensure timely intervention should they become ill. This is especially true when considered together with other risk factors (e.g. family history, age) and traits (e.g. schizotypy).



While routine screening of risk features may not be feasible, a number of self-assessment tools have been made available. Some of these, including the Psychosis Screening Questionnaire (PSQ)<sup>12</sup> and Prodromal Questionnaire, Brief Version (PQ-B),<sup>13</sup> have been translated and adapted for use by local organisations and early psychosis intervention projects, and can be accessed via the websites [www3.ha.org.hk/easy](http://www3.ha.org.hk/easy), [www.episo.org](http://www.episo.org) and [www.jcep.hk](http://www.jcep.hk). Suspected psychosis entails a more thorough mental state assessment.

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## Dermatological Quiz



## Dermatological Quiz

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Fig 2: Skin lesion at (a) upper back and (b) right upper arm

A 50-year-old woman complained of one year's history of insidious onset of this mildly itchy skin rash around her upper back (Fig. 2a), proximal limbs (Fig. 2b) and her face extensively. The skin rash was associated with weight loss. Complete blood picture, liver and renal function tests were normal except a raised ESR of 70mm/hr. Skin biopsy at the papular lesion showed increased mucin deposition within the dermis with no epidermal change. There was an increase in irregularly arranged spindle cells in the dermis identified as dermal fibroblasts with intervening dermal fibrosis.

### Questions:

1. What is your provisional diagnosis or differential diagnoses?
2. What other important specific tests you would like to order for investigating her weight loss?
3. How will you manage this patient?

(See P. 25 for answers)

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# Pharmacological Models of Psychosis – Amphetamine and Ketamine

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## Introduction

Although substance abuse disorder is a common comorbidity of mental illness, it is particularly prevalent in patients with schizophrenia<sup>1</sup>. One of the most widely held explanations for this phenomenon is the self-medication hypothesis<sup>2,3</sup> which is based on the negative reinforcement theory; that is the behaviour is reinforced by the purposeful removal of aversive experience, which could be disease symptoms and/or side effects of the medication. However recent studies on the neuropathology of schizophrenia and addiction behaviour have provided an alternative hypothesis. It has been suggested that there is a common neuropathological substrate independently causing the manifestation of symptoms of schizophrenia and addiction disorder. There are substantial literature suggesting that the mesolimbic dopamine (DA) system is a major substrate for reinforcing effects of substance and involving in mediating drug craving. The mesolimbic DA system is also an important system involved in the neuropathology of schizophrenia<sup>4</sup>. In fact, studies of pharmacological models of psychosis using different psychoactive substances have provided further evidence on this hypothesis and also improve our understanding of the biological basis of psychotic symptoms and the disorder as a whole. This article aims at providing further understanding of the dopamine hypothesis of schizophrenia through brief discussions on two commonly studied pharmacological models of psychosis – Amphetamine and Ketamine.

## Dopamine Hypothesis of Psychosis – Amphetamine Model of Psychosis

It was first proposed that the hyperactivity of dopamine transmission is responsible for the psychotic symptoms<sup>5</sup>. This was supported by the correlation of the clinical dose of antipsychotic drugs and their potency in blocking the dopamine D2 receptors<sup>6,7</sup> mainly in the subcortical regions. Further evidence has been accumulated using amphetamine challenge. Amphetamine is an indirect-acting dopamine agonist which increases dopamine levels in the synaptic cleft by inhibiting the action of the dopamine transporter<sup>8</sup>. High dose repeated administrations of amphetamine to normal volunteers result in paranoid symptoms and formal thought disorders<sup>9</sup>. More recently, studies using imaging techniques such as PET and Single Photon Emission Computed Tomography (SPECT) during amphetamine challenge have shown that there is an elevation in the binding of dopamine at the D2 receptors

after amphetamine challenge in schizophrenic patients compared to age-matched controls, and the elevation is associated with positive psychotic symptoms<sup>10-12</sup>.

However, there is little indication that amphetamine psychosis provides a model of negative symptoms. Some studies have shown a decreased dopamine turnover<sup>13,14</sup> and hence raised a possibility of hypoactive dopamine system involvement. This has led to the revision of the classical hypothesis of schizophrenia. The hyperactive subcortical mesolimbic dopamine projection (hyperstimulation of the D2 receptors) is associated with positive psychotic symptoms; while hypoactive mesocortical dopamine projection (hypostimulation of D1 receptors) is associated with negative and cognitive symptoms<sup>15,16</sup>. Consistent with this, pre-clinical studies have demonstrated that a deficit of dopamine transmission at the D1 receptors in the prefrontal cortex might be implicated in cognitive impairments and negative symptoms of schizophrenia<sup>17</sup>.

The possibility of coexistence of both hypodopaminergic and hyperdopaminergic states in the same condition has raised the possibility of involvement of other neurotransmitters as modulators. Consistent with this is the observation that in addition to amphetamine, many other psychoactive agents can produce similar disturbances in thought process and perception, including PCP/Ketamine.

## Dopamine and Glutamate - Ketamine Model of Psychosis

Ketamine is a structural analogue of phencyclidine (PCP). Both PCP and ketamine are dissociative anaesthetic agents and are non-competitive antagonists of the N-methyl-D-aspartic acid (NMDA) subtype of glutamate receptors. It was observed that a subanaesthetic dose of PCP (0.1 mg/kg) could induce a schizophrenic-like psychotic state in healthy human subjects<sup>18</sup>. The symptoms include positive psychotic symptoms (such as hallucinations, delusions and thought disorder), negative symptoms (such as apathy), and cognitive symptoms (such as inability to maintain cognitive sets, planning deficits and concrete ideation).

PCP non-competitively blocks the ion flow through the NMDA-sensitive glutamate receptor ionophore<sup>19</sup>. Because of the neurotoxic effects of PCP determined by studies in rodents<sup>20,21</sup>, the use of PCP in studies in humans is considered unethical. The structural analogue of PCP, ketamine, provides an alternative model of



psychosis for use in human subjects. Further studies have been carried out in recent years both in healthy volunteers and schizophrenic patients to examine this model of psychosis. In schizophrenic patients, ketamine briefly exacerbated existing symptoms that patients had experienced before and some of them had delayed or prolonged effects; patients did not experience new symptoms that they had not previously encountered as part of their illness<sup>22-24</sup>.

In healthy volunteers, ketamine transiently produces a range of dose-related psychotomimetic and cognitive effects that include positive symptoms, negative symptoms, mood changes and thought disorders<sup>22, 24-29</sup>. Dissociative symptoms are prominent and these may be important early features of the illness. Cognitive dysfunction, consistent with the impairments seen in patients with schizophrenia, are also evident in healthy subjects following exposure to ketamine, including impairment in attention, memory, abstract thinking, planning and judgement<sup>24, 25, 27, 30-39</sup>.

The NMDA receptor is one of the receptors present on the GABAergic interneurons which modulate the excitatory pathways. The antagonistic effect of ketamine on these NMDA receptors reduces the GABAergic inhibitory action and hence disinhibits the excitatory pathways, including dopamine, glutamatergic, serotonin and norepinephrine, and cholinergic systems<sup>40</sup>. The understanding of the psychogenic effects of ketamine and neuropathological process supports the hypothesis that endogenous hypo-function of the NMDA receptor may be a key component of the pathophysiology of psychosis<sup>40-43</sup>.

This hypothesis has received further supports from the preclinical studies. It was shown that acute administration of NMDA receptor antagonists increased the release of dopamine in striatum and nucleus accumbens<sup>43-45</sup>. PET imaging of <sup>11</sup>C-raclorpiride binding in human subjects showed ketamine increased striatal dopamine release<sup>46</sup> and the magnitude of its increase correlated with ketamine induced psychosis<sup>47,48</sup>. Preclinical studies also showed acute administration of NMDA antagonists increased dopamine transmission in the prefrontal cortex<sup>13,43,49,50</sup>. It was found that ketamine increased cortical dopamine levels particularly in the posterior cingular and dorsolateral prefrontal cortex in human subjects<sup>51</sup>.

The above evidence supports the idea that changes in dopaminergic function are closely associated with changes of the glutamate system, particularly via the NMDA receptors: this is a dynamic and reciprocal relationship, with evidence of glutamatergic modulation of dopamine, as described above, but equally, dopaminergic influences on glutamate: D2 receptor stimulation inhibits NMDA-mediated glutamate transmission whereas D1 receptor stimulation facilitates it<sup>52, 53</sup>.

## Conclusion

The study of the amphetamine model of psychosis supports the role of dopamine in the neuropathological process of psychosis. Studies of ketamine model of

psychosis further suggest the modulatory role of glutamate in this process. It is clear that studying the psychogenic effects of different substances and their associated neuropathological changes, the pharmacological models of psychosis, provides us with a window to further explore the complex neuropathological process of psychosis. One of the other pharmacological models being studied actively is the delta-9-tetrahydrocannabinol (THC) model, which is a major component of cannabis. These different models have provided us with more detailed insight into the interaction of other neural substrates with dopamine and the relationship with the symptom formation. This would be an important tool to enhance our understanding of the neuropathological process of psychosis.

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## THE SOCIETY OF PHYSICIANS OF HONG KONG

PRESIDENT: DR. LAM TAT CHUNG PAUL  
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CME FOR MEDICAL DOCTORS  
SUNDAY SYMPOSIUM

June 12, 2011

June 26, 2011

July 10, 2011

The Langham Hotel, Peking Road, TST.

Further details can be seen on  
[www.SOPHYSICIANSHK.org](http://www.SOPHYSICIANSHK.org)



# The 5<sup>th</sup> Annual Scientific Meeting – Hong Kong Society of Biological Psychiatry (19-20 March 2011)

**Prof. Siu-wa TANG**

*President, Hong Kong Society of Biological Psychiatry*

Psychiatry is medicine of the brain. The human brain is the most complex organ in the human body and we are far from understanding many of its functions. Because of this, clinical psychiatry has generally concerned itself with the most serious brain disorders which led to major and observable disturbances in human behaviour, such as schizophrenia and dementia. Terms such as “crazy”, “retarded” or “mental disorders” were often used by non-clinicians to describe unfortunate patients suffering from these serious disorders. Treating “crazy behaviour” was perceived as equivalent to what psychiatry was about. This biased and ignorant perception of psychiatry has resulted in the prejudiced attitude towards psychiatry for many years. As a result, the brain was an “untouchable” organ. The brain could never go wrong. Although the brain is a vital organ, brain examination has never been part of a general routine physical examination.

Advances in neurosciences and brain medicine have now begun to change the scope of psychiatry. Treatment of major depression, anxiety disorders, psychosomatic disorders, ADHD and many behavioural problems related to disorders of brain function have rapidly

expanded the field of clinical psychiatry. One of the most significant changes in psychiatry in the last decade has been in the field of social psychiatry. Social psychiatry used to be in the backwater of medicine. Though important to the understanding of abnormal human behaviour and a very interesting subject in itself, it was difficult to associate social psychiatry with the biology of the brain. It was difficult to relate the knowledge of brain medicine, e.g. neurobiochemistry, neuro-psychopharmacology, neurophysiology to the subject matters of social psychiatry.

Research using new biological tools in the past decade has revolutionised the understanding of normal and abnormal human social behaviour. Presentations by Professors Carter, Porges, Yamawaki and Leonard and other local researchers in this symposium of the Hong Kong Biological Psychiatry represent some of the most important works enabling us to understand human social interaction such as love, attachments, bonding and stress in biological terms. Together, the rapidly accumulating volume of work in this field has created an international impetus towards an emerging field of medicine, which I call “Biological Social Psychiatry”.

## Stress, Inflammation and Mental Illness

**Prof. Brian LEONARD**

PhD

*Pharmacology Department, The National University of Ireland, Galway  
Department of Psychiatry and Psychotherapy, Ludwig Maximilian University, Munich, Germany*

Stress causes maladaptive changes in the neurotransmitter, immune and endocrine systems which play a major role in initiating ill-health and major psychiatric disorders. In recent years there has been a paradigm shift in our understanding of the inter-relationship between the hypothalamic-pituitary-adrenal [HPA] and the immune axes. Thus activation, rather than suppression, of important aspects of the immune system occurs following chronic stress. One of the reasons for this is ascribed to the glucocorticoids induced apoptosis of hippocampal neurons that occurs as a consequence of the desensitisation of central and peripheral glucocorticoids receptors. Thus chronic low grade

inflammation, which results from the stress induced activation of peripheral and central inflammatory pathways, is central to the pathogenesis of depression and schizophrenia and linked to diabetes, cancer, asthma, arthritis and cardiovascular disease that are frequently co-morbid with these disorders.

Evidence in support of the inflammation hypothesis of major psychiatric disorders was first provided by Smith [Med.Hypoth. 35,298-306, 1991] who suggested that the symptoms of psychiatric disorders arise from the stress and genetically programmed activation of peripheral [macrophages/monocytes] and central [microglia,



astrocytes and oligodendroglia] macrophages that result in the elevation of pro-inflammatory cytokines and other inflammatory mediators, such as prostaglandin E<sub>2</sub>, in the blood and cerebrospinal fluid. Thus there is an imbalance between the pro- and anti-inflammatory arms of the immune system which characterises most major psychiatric disorders, changes that are largely attenuated following effective treatment.

The rise in glucocorticoids and pro-inflammatory cytokines also results in the activation of the tryptophan-kynurenine pathway whereby tryptophan is shunted away from serotonin synthesis to the formation of kynurenine and its end-products following the activation of indoleamine 2, 3-dioxygenase, by pro-inflammatory cytokines, and tryptophan dioxygenase, by glucocorticoids, respectively. These changes link stress and inflammation with the formation of the neurotoxic metabolites of the tryptophan-kynurenine pathway [3-hydroxykynurenine and quinolinic acid]. Further, in the brain the pro-inflammatory cytokines activate cyclo-oxygenase and nitric oxide synthase thereby increasing the PGE<sub>2</sub> and NO concentrations in the brain. These add to the inflammatory stress within the brain [Leonard and Myint, Neurotox.Res. 10,149-160,2006].

Tis in chronic depression and schizophrenia the inflammatory changes, coupled with stress-induced hypercortisolaemia which blocks the synthesis of neurotrophic factors that normally repair damaged neurons, the neurodegenerative pathways predominate over the neuroprotective pathways, Thus it is hypothesised that chronic stress and inflammation are causally associated with the pathology of major psychiatric disorders such as depression and schizophrenia.

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*Better Healthcare by  
Good Management*



Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
<ul style="list-style-type: none"> <li>★ HKCC 19th Annual Scientific Congress</li> <li>★ HKMA Dragon Boat Team Practice Session</li> </ul> <p><b>1</b></p>	<ul style="list-style-type: none"> <li>★ Learning Experience from UK – FRCS (Urol) Revision Course</li> <li>★ HKMA Choir Rehearsal</li> </ul> <p><b>2</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Tai Po Community Network - Puberty &amp; Pubertal Disorders in Children</li> <li>★ FMSHK Officers' Meeting</li> <li>★ Council Meeting</li> </ul> <p><b>3</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) - Session 1</li> </ul> <p><b>4</b></p>	<ul style="list-style-type: none"> <li>★ HKMA NTW Community Network - New Advances in Anticholinergic Therapy</li> <li>★ HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2011 – Refractive and Presbyopia Treatment</li> <li>★ HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2011 – Refractive and Presbyopia Treatment</li> <li>★ 18th Asian Congress of Surgery &amp; 37th Philippine College of Surgeons Mid-Year Convention</li> <li>★ 第18屆世界美容醫學大會</li> </ul> <p><b>5</b></p>	<ul style="list-style-type: none"> <li>★ Joint Surgical Symposium - Management of Benign and Malignant Anorectal Diseases</li> </ul> <p><b>6</b></p>	<ul style="list-style-type: none"> <li>★ 18th Asian Congress of Surgery &amp; 37th Philippine College of Surgeons Mid-year Convention</li> <li>★ 第18屆世界美容醫學大會</li> <li>★ Refresher Course for Health Care Providers 2010/2011</li> </ul> <p><b>7</b></p>
<ul style="list-style-type: none"> <li>★ HKMACF Charity Concert</li> <li>★ HKMA Dragon Boat Team Practice Session</li> </ul> <p><b>8</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Choir Rehearsal</li> </ul> <p><b>9</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Kin West Community Network – Lecture Series on Urology (Series 2)</li> <li>★ FMSHK Executive Committee Meeting and Council Meeting</li> </ul> <p><b>10</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) - Session 2</li> </ul> <p><b>11</b></p>	<ul style="list-style-type: none"> <li>★ HKMA NTW Community Network - Treatment Option for Major Depressive Disorder</li> <li>★ HKMA Yau Tsim Mong Community Network - Quadrivalent HPV Prevention - More than Cervical Cancer Prevention</li> <li>★ (1) A Sleepless Night (2) Bad News!? Black News!</li> </ul> <p><b>12</b></p>	<ul style="list-style-type: none"> <li>★ 18th Asian Congress of Surgery &amp; 37th Philippine College of Surgeons Mid-Year Convention</li> <li>★ 第18屆世界美容醫學大會</li> </ul> <p><b>13</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Shatin Doctors Network - Osteo-arthritis Current Treatment and Beyond</li> <li>★ HKMA – KLN East Community Network; HA – UCH; HKCFP - CME Course for Health Personnel 2011</li> <li>★ 12th Regional Osteoporosis Conference 2011</li> </ul> <p><b>14</b></p>
<ul style="list-style-type: none"> <li>★ 第18屆世界美容醫學大會</li> <li>★ HKMA Dragon Boat Team Practice Session</li> <li>★ HKMA Certificate Course on Family Medicine 2011</li> <li>★ HKMA Squash Tournament</li> </ul> <p><b>15</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Choir Rehearsal</li> </ul> <p><b>16</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Tai Po Community Network – "Treatment Strategies in Type 2 Diabetic Patient to Avoid Hypoglycemia"</li> </ul> <p><b>17</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) - Session 3</li> </ul> <p><b>18</b></p>	<ul style="list-style-type: none"> <li>★ HKMA NTW Community Network - Treatment Option for Major Depressive Disorder</li> <li>★ HKMA Yau Tsim Mong Community Network - Quadrivalent HPV Prevention - More than Cervical Cancer Prevention</li> </ul> <p><b>19</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Shatin Doctors Network - Osteo-arthritis Current Treatment and Beyond</li> </ul> <p><b>20</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Yau Tsim Mong Community Network &amp; Kowloon Central Cluster - Certificate Course Bringing Better Health to the Community (Lecture 1)</li> <li>★ HKMA Youth Committee Career Seminar</li> </ul> <p><b>21</b></p>
<ul style="list-style-type: none"> <li>★ HKMA Dragon Boat Team Practice Session</li> <li>★ 12th Regional Osteoporosis Conference 2011</li> <li>★ 2011 Paediatric Update No. 1 Seminar on Infant and Young Child Feeding</li> </ul> <p><b>22</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Choir Rehearsal</li> </ul> <p><b>23</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Tai Po Community Network – "Treatment Strategies in Type 2 Diabetic Patient to Avoid Hypoglycemia"</li> </ul> <p><b>24</b></p>	<ul style="list-style-type: none"> <li>★ Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) - Session 2</li> </ul> <p><b>25</b></p>	<ul style="list-style-type: none"> <li>★ HKMA NTW Community Network - Treatment Option for Major Depressive Disorder</li> <li>★ HKMA Yau Tsim Mong Community Network - Quadrivalent HPV Prevention - More than Cervical Cancer Prevention</li> </ul> <p><b>26</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Shatin Doctors Network - Osteo-arthritis Current Treatment and Beyond</li> </ul> <p><b>27</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Yau Tsim Mong Community Network &amp; Kowloon Central Cluster - Certificate Course Bringing Better Health to the Community (Lecture 1)</li> <li>★ HKMA Youth Committee Career Seminar</li> </ul> <p><b>28</b></p>
<ul style="list-style-type: none"> <li>★ HKMA Dragon Boat Team Practice Session</li> <li>★ Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) - Session 4</li> <li>★ HKMA/APS 2nd Photo Competition &amp; Sharing Session 2011</li> </ul> <p><b>29</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Choir Rehearsal</li> <li>★ HK International Dragon Boat Race Local Team Manager Meeting</li> </ul> <p><b>30</b></p>	<ul style="list-style-type: none"> <li>★ HKMA Kin West Community Network – Lecture Series on Urology (Series 3)</li> </ul> <p><b>31</b></p>				



Date / Time	Function	Enquiry / Remarks
<b>1</b> SUN 8:00 am (8,15,22,29)	<b>HKCC 19th Annual Scientific Congress</b> Chairman: Dr. CS CHIANG, Venue: Sheraton Hotel & Towers, Kowloon  <b>HKMA Dragon Boat Team Practice Session</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. CY YAM & Dr. PY CHENG, Venue: Stanley Main Beach or Sai Kung	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285  Miss Alice TANG / Miss Sharon HUNG Tel: 2527 8285
<b>3</b> TUE 1:45 pm 8:00 pm – 10:00 pm 9:00 pm	<b>HKMA Tai Po Community Network - Puberty &amp; Pubertal Disorders in Children</b> Organiser: HKMA Tai Po Community Network, Chairman: Dr. SH CHIU, Speaker: Dr. Chak-man YU, Venue: Tai Po  <b>FMSHK Officers' Meeting</b> Organiser: The Federation of Medical Societies of Hong Kong, Venue: Gallop, 2/F., Hong Kong Jockey Club Club House, Shan Kwong Road, Happy Valley, Hong Kong  <b>Council Meeting</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. CHOI Kin, Venue: Wanchai	Miss Sophia LAU Tel: 2527 8285 1 CME Point  Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345  Ms. Christine WONG Tel: 2527 8285
<b>4</b> WED 12:45 pm (11,18,29)	<b>Certificate Course on Management of Drug Abuse Patients for Family Doctors (HK Island) - Session 1 to Session 4</b> Organisers: HKMA Beat Drugs Action Committee; HKMA CW&SCN and HKMA HKCCN, Speakers: Various, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central	Miss Carman WONG & Miss Candice TONG Tel: 2527 8285
<b>6</b> FRI 8:00 am - 9:00 am	<b>Joint Surgical Symposium - Management of Benign and Malignant Anorectal Diseases</b> Organisers: Department of Surgery, The University of Hong Kong & Hong Kong Sanatorium & Hospital, Chairman: Dr. Angus CW CHAN, Speakers: Dr. Jensen POON & Dr. Siu-Hung LO, Venue: Hong Kong Sanatorium & Hospital	Department of Surgery, Hong Kong Sanatorium & Hospital Tel: 2835 8698 Fax: 2892 7511 1 CME Point (Active)
<b>8</b> SUN 8:00 pm	<b>HKMACF Charity Concert</b> Organiser: HKMA Charitable Foundation, Venue: City Hall	Ms. Candy YUEN Tel: 2527 8285
<b>9</b> MON 7:30 – 8:30 pm 8:00 pm (16,23,30)	<b>Learning Experience from UK – FRCS (Urol) Revision Course</b> Organiser: Hong Kong Urological Association, Chairman: Dr. Chi-wai FAN, Speakers: Dr. Vera CHUNG; Dr. Thomas LAM & Dr. Stanley KAN, Venue: Seminar Room, G/F, Block A, Queen Elizabeth Hospital, Kowloon  <b>HKMA Choir Rehearsal</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. YS CHAN & Dr. YM NG, Venue: GP1, HKCC	Dr. Hing-hoi HUNG / Ms. Tammy HUNG Tel: 2958 6006 / 9609 6064 Fax: 2958 6076 / 8344 5115 1 CME Point (The College of Surgeons of Hong Kong)  Ms. Candy YUEN Tel: 2527 8285
<b>11</b> WED 7:30 am	<b>Hong Kong Neurosurgical Society Monthly Academic Meeting –Anticoagulation and Antiplatelet Therapy in Intracranial Stenting : Update and Consensus</b> Organiser: Hong Kong Neurosurgical Society, Chairman: Dr. Peter PANG, Speaker: Dr. Calvin MAK, Venue : Seminar Room, Ground Floor, Block A, Queen Elizabeth Hospital	Dr. Gilberto LEUNG Tel: 2255 3368 Fax: 2818 4350 1.5 points (College of Surgeons of Hong Kong)
<b>12</b> THU 1:00 pm 2:00 pm (13,14) (13,14,15)	<b>HKMA NTW Community Network – New Advances in Anticholinergic Therapy</b> Organiser: HKMA NTW Community Network, Chairman: Dr. Ivan CHUNG, Speaker: Dr. Thomas Joo-shium LEE, Venue: Plentiful Delight Banquet, 1/F., Ho Shun Tai Building, 10 Sai Ching Street, Yuen Long, N.T.  <b>HKMA Structured CME Programme with Hong Kong Sanatorium &amp; Hospital Year 2011 – Refractive and Presbyopia Treatment</b> Organiser: The Hong Kong Medical Association, Chairmen: Dr. CM CHENG; Dr. HK HO & Dr. BL WONG, Speaker: Dr. John S. CHANG Jr., Venue: Central  <b>18th Asian Congress of Surgery &amp; 37th Philippine College of Surgeons Mid-year Convention</b> Organiser: Asian Surgical Association, Venue: Waterfront Cebu City Hotel & Casino, Lahug, Cebu City, Philippines  <b>第18屆世界美容醫學大會</b> Organiser: Union International de Medicine Esthetique (UIME), Chairman: 劉洪臣先生, Venue: 中國北京市朝陽區北辰東路8號中國北京國際會議中心	Miss. Carman WONG Tel: 2527 8285 1.5 CME Points  Miss Sophia LAU Tel: 2527 8285 1 CME Point  Congress Secretariat Tel: (632) 9274973-74; (632) 9281083; (632) 9292359 Fax: (632) 9292297 E-mail: secretariat@acs2011.org Website: www.acs2011.org  Ms. Echo LEUNG Tel: 3575 8600 Fax: 2301 2414 Email: aiam_hk@yahoo.com Website: http://www.wcam2011.org
<b>14</b> SAT 2:30 pm	<b>Refresher Course for Health Care Providers 2010/2011</b> Chairmen: Dr. CM CHENG; Dr. HK HO & Dr. BL WONG, Speaker: Ka-chung WONG, Venue: OLMH	Miss Sophia LAU Tel: 2527 8285 2 CME Points
<b>15</b> SUN 2:00 pm 2:00 pm	<b>HKMA Certificate Course on Family Medicine 2011</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. CM CHENG; Dr. HK HO & Dr. BL WONG, Speakers: Dr. Alvin Yee-shing CHAN & Dr. Ka-yeung FONG, Venue: Queen Elizabeth Hospital, Kowloon  <b>HKMA Squash Tournament</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. TY CHAN Venue: Kowloon Cricket Club	Miss Sophia LAU Tel: 2527 8285 3 CME Points  Miss Alice TANG / Miss Sharon HUNG Tel: 2527 8285
<b>17</b> TUE 1:00 pm (31) 8:00 pm – 10:00 pm	<b>HKMA Kin West Community Network – Lecture Series on Urology (Series 2 &amp; 3)</b> Organiser: HKMA Kin West Community Network, Chairmen: Dr. WH WONG & Dr. CP CHAN, Speakers: Dr. Pak-ling LIU & Dr. Ming-kwong YIU, Venue: Panda Hotel, Tsuen Wan  <b>FMSHK Executive Committee Meeting and Council Meeting</b> Organiser: The Federation of Medical Societies of Hong Kong, Venue: Council Chambers, 4/F., Duke of Windsor Social Service Building, 15 Hennessy Road, Wanchai, Hong Kong	Miss Candice TONG Tel: 2527 8285 1 CME Point  Ms. Sonia CHEUNG Tel: 2527 8898 Fax: 2865 0345
<b>20</b> FRI 1:00 pm	<b>HKMA Shatin Doctors Network - Osteo-arthritis Current Treatment and Beyond</b> Organiser: HKMA Shatin Doctors Network, Chairman: Dr. Wing-kin MAK, Speaker: Dr. Ming-yan LUI, Venue: Royal Park Hotel, Shatin	Miss Candice TONG Tel: 2527 8285



Date / Time	Function	Enquiry / Remarks
<b>21 SAT</b> 1:30 pm (22)	<b>HKMA – KLN East Community Network; HA – UCH; HKCFP - CME Course for Health Personnel 2011</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. Man-fuk LEUNG, Speaker: Dr. Kwok-fai HUI, Venue: Lecture Theatre, G/F., Block F, United Christian Hospital, Kowloon <b>12th Regional Osteoporosis Conference 2011</b> Organiser: Osteoporosis Society of Hong Kong & Hong Kong Society of Rheumatology, Speakers: Various, Venue: Hong Kong Convention and Exhibition Centre	Ms. Gary WONG Tel: 3513 4821 1.5 CME Points  Conference Secretariat Tel: 2559 9973 Fax: 2547 9528 Email: roc2011@icc.com.hk
<b>22 SUN</b>	<b>2011 Paediatric Update No. 1 Seminar on Infant and Young Child Feeding</b> Organiser: Hong Kong College of Paediatricians, Chairman: Dr. Sik-nin WONG & Dr. Shirley LEUNG, Speakers: Various, Venue: Lecture Theatre, Hospital Authority Head Office, M Floor	Ms. Vanessa WONG Tel: 2871 8773 Fax: 2785 1850 3 CME (Category A)
<b>24 TUE</b> 1:00 pm	<b>HKMA Tai Po Community – “Treatment Strategies in Type 2 Diabetic Patient to Avoid Hypoglycemia”</b> Organiser: HKMA Tai Po Community Network, Chairman: Dr. SH CHIU, Speaker: Dr. Alice Pik-shan KONG, Venue: Tai Po	Miss Sophia LAU Tel: 2527 8285 1 CME Point
<b>26 THU</b> 1:00 pm	<b>HKMA NTW Community Network – Treatment Option for Major Depressive Disorder</b> Organiser: HKMA NTW Community Network, Chairman: Dr. Lambert Lam-fung CHAN, Speaker: Dr. Ka-lik KWAN, Venue: Pleasant Delight Banquet, 1/F., Ho Shun Tai Building, 10 Sai Ching Street, Yuen Long, N.T.	Miss Carman WONG Tel: 2527 8285
<b>26 THU</b> 1:00 pm	<b>HKMA Yau Tsim Mong Community Network - Quadrivalent HPV Prevention - More than Cervical Cancer Prevention</b> Organiser: HKMA Yau Tsim Mong Community Network, Speaker: Dr. Kar-fai TAM, Venue: Eaton Hotel	Miss Candice TONG Tel: 2527 8285 1 CME Point
<b>26 THU</b> 6:30 pm – 8:00 pm	<b>(1)A Sleepless Night (2) Bad News!? Black News!</b> Organiser: Hong Kong Thoracic Society/American College of Chest Physicians (HK & Macau Chapter), Chairpersons: Dr. Jamie LAM & Dr. Chi-fong WONG, Venue: LG1, Lecture Room, Ruttonjee Hospital, Hong Kong	Dr. Fanny Wai-san KO / Dr. Arthur Chun-wing LAU Tel: 2632 2785 Fax: 2637 5396 1.5 – 2 CME Points
<b>28 SAT</b> 1:00 pm	<b>HKMA Yau Tsim Mong Community Network &amp; Kowloon Central Cluster - Certificate Course Bringing Better Health to the Community (Lecture 1)</b> Organiser: HKMA Yau Tsim Mong Community Network & Kowloon Central Cluster, Chairman: Dr. CP HO, Speakers: Dr. Gia Hung NGUYEN & Dr. Chun LAM, Venue: Queen Elizabeth Hospital	Miss Candice TONG Tel: 2527 8285
<b>28 SAT</b> 3:00 pm	<b>HKMA Youth Committee Career Seminar</b> Organiser: HKMA Youth Committee, Chairmen: Dr. CF PONG & Dr. PY SIN, Venue: The Hong Kong Medical Association Central Premises, Dr. Li Shu Pui Professional Education Centre, 2/F., Chinese Club Building, 21-22 Connaught Road Central, Hong Kong	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
<b>29 SUN</b> 2:00 pm	<b>HKMAPS 2nd Photo Competition &amp; Sharing Session 2011</b> Organiser: The Hong Kong Medical Association, Chairman: Dr. A PANG, Venue: Wanchai	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285
<b>30 MON</b>	<b>HK International Dragon Boat Race Local Team Manager Meeting</b> Chairman: Dr. CY YAM & Dr. PY CHENG	Miss Alice TANG & Miss Sharon HUNG Tel: 2527 8285

## Course / Meeting

16/7/2011	<b>Hong Kong Surgical Forum – Summer 2011</b> Organiser: Department of Surgery, The University of Hong Kong; Queen Mary Hospital & Hong Kong Chapter of American College of Surgeons, Venue: Underground Lecture Theatre, New Clinical Building, Queen Mary Hospital, Pokfulam, Hong Kong. Enquiry: Forum Secretary, Hong Kong Surgical Forum, Tel: 2255 4882 / 2255 4886, Fax: 2819 3416, Email: hksf@hku.hk, Website: <a href="http://www3.hku.hk/surgery/forum.php">http://www3.hku.hk/surgery/forum.php</a>
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## Upcoming Certificate Courses of the Federation of Medical Societies of Hong Kong

Date	Course No	Course Name	Target Participants	CME/CNE
5/5/2011 - 9/6/2011	C172	Certificate Course on Current Management of Common Head & Neck Cancers	Medical, Health Professionals and General Public	9 CNE Points; CME/CPD Accreditation in application
12/7/2011 - 16/8/2011	C178	Certificate Course on Occupational Hygiene Practice	Healthcare Workers	9 CNE Points; CME/CPD Accreditation in application



## Answer to Dermatological Quiz

- This middle aged woman presented with this quite asymptomatic extensive multiple shiny waxy a few millimetre small discrete whitish to skin-coloured papules which coalesced into larger papules/ small plaques affecting her face, upper back and limbs. The clinical differential diagnoses should include various forms of cutaneous mucinosis, lichen amyloidosis, scleredema of Buschke, scleroderma, eruptive xanthoma, eruptive syringoma and generalised myxoedema. Coupled with the history of systemic upset and histology showing increased dermal mucin deposition and fibroblast proliferation, the clinicopathological diagnosis of scleromyxoedema, which is a generalised form of cutaneous mucinosis, can be made.

Primary cutaneous mucinosis is a heterogenous group of disorders in which an abnormal amount of mucin accumulates in the skin with unknown pathophysiology. The widespread distribution form, as demonstrated in this patient, is known as scleromyxoedema. It presents with generalised shiny waxy small discrete whitish to skin-coloured papular eruptions with or without sclerodermoid features. Histologically, this rare disease is characterised by a triad of a) diffuse deposits of mucin in the dermis b) an increase in collagen deposition c) a marked proliferation of dermal fibroblasts arranged irregularly.

- Scleromyxoedema is almost always associated with paraproteinaemia. The monoclonal gammopathy is usually Ig G with gamma light chains. Less than 10% of scleromyxoedematous patients progress to multiple myeloma. As a result, a malignancy screening especially with immunoglobulin level and serum protein electrophoresis confirmed the presence of monoclonal gammopathy in this patient. Bone marrow aspiration did not show any myeloma changes.
- There is no well proven effective treatment for scleromyxoedema because of the rarity of the disease. The commonly used approach is to treat the underlying paraproteinaemia or haematological malignancies which may alleviate the cutaneous mucinosis. In patients with confirmed myeloma, monthly melphalan combined with various drugs such as thalidomide, systemic steroids, and/or autologous haematopoietic stem cell transplantation are employed. A similar strategy has begun to be adopted for treating scleromyxoedema. However, the risks of marrow suppression and sepsis should be carefully weighed against the benefits. Other modalities which have been reported effective anecdotally include topical and intralesional hyaluronidase, PUVA, UVA1, systemic retinoids, electron-beam radiation, IVIg, plasmapheresis, extracorporeal photochemotherapy, cyclosporine, and granulocytes colony-stimulating factor.

**Dr. Ka-ho LAU**

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Annual Scientific Meeting 2011

# The Era of the Superbugs

18 June 2011



- **Control of MRSA in the Hospital - An Old Problem with New Challenges**  
Dr. Vincent CHENG  
Infection Control Officer, Queen Mary Hospital
- **The Emergence of Ultimate Superbug - Carbapenem-resistant Enterobacteriaceae**  
Dr. KY TSANG  
Associate Consultant, Division of Infectious Disease, Princess Margaret Hospital
- **The Emergence of Multidrug and Extensively Drug-resistant Tuberculosis in Hong Kong**  
Dr. KC CHANG  
Senior Medical Officer, Tuberculous & Chest Unit, Department of Health
- **Multiple Drug-resistant Gram-negative Organisms - from ESBL to Carbapenem-resistant Acinetobacter Species**  
Dr. TC WU  
Associate Consultant, Division of Infectious Disease, Queen Elizabeth Hospital
- **An Update on Pandemic Influenza (H1N1)**  
Dr. Kelvin TO  
Clinical Assistant Professor, Department of Microbiology, The University of Hong Kong

**Date:** 18 June 2011

**Time:** 2:00pm – 5:30pm

**Venue:** M/F, Lecture Theatre, Hospital Authority Building, 147B Argyle Street, Kowloon

**Registration Fee:** HK\$100 for Member of Member Societies  
HK\$200 for Non-member

**Enquiry:** 2527 8898

**Registration:** Application form can be downloaded from website <http://www.fmskh.org>



**CME/CPD Accreditation in application. A total of 2.5 CNE points for the whole meeting.**



THE FEDERATION OF MEDICAL SOCIETIES OF HONG KONG

香港醫學組織聯會