College of Family Physicians Singapore

The Singapore Family Physician

Permit No. MCI(P):058/12/2012

Vol 39(1) January–March 2013

Schizophrenia

Improving the Mental Health of the Population – an Asian Perspective

A mental health symposium held in conjunction with the WORLD HEALTH SUMMIT REGIONAL MEETING – ASIA, SINGAPORE 2013

Mental disorders are among the most common causes of disability. Poor mental health impedes individuals' capacity to realise their potential, work productively, and make a contribution to their community, while positive mental health is linked to a range of beneficial outcomes and is fundamental to coping with adversity. To improve mental health and lessen the burden of disease, mental health services must be provided in ways which are proactive and can effectively impact on relevant factors at both population and individual levels.

This one-day symposium is focused on innovative and multidisciplinary approaches to improving mental health. Participants will learn about the state of mental health and approaches to improve it from leading mental health professionals and researchers. Break-out sessions focusing on specific areas such as child and geriatric mental health and cost of mental health delivery will be discussed in small groups using case-studies. The venue of the workshop – Singapore's only tertiary psychiatric hospital – offers participants an opportunity to see first-hand, tertiary facilities to support mental health recovery.

Symposium

8 April 2013
9.30am – 4.00pm

Institute of Mental Health, Buangkok Green Medical Park, 10 Buangkok View, Singapore 539747

8.30am	**Registration**
9.30am	**Opening Address** *A/Prof Chua Hong Choon* CEO, Institute of Mental Health, Singapore
9.40am	***Conceptual and Empirical Approaches to Understand Physical and Psychological Well-being of the Caregivers of Children with Developmental Disability and Older Adults with Dementia: A Life Course Perspective to Caregiver Health*** Professor Parminder Raina Raymond and Margaret Labarge Chair in Optimal Aging Department of Clinical Epidemiology & Biostatistics Faculty of Health Sciences, McMaster University Hamilton, Ontario Canada
10.10am	**The Singapore Mental Health Study: Translating Research to Policy** *A/Prof Chong Siow Ann* Vice Chairman Medical Board (Research) Senior Consultant Psychiatrist Institute of Mental Health, Singapore
10.40am	**Tea Break**
11.00am	**Mental Health Literacy and Population Mental Health** *Professor Anthony Francis Jorm* Professorial Fellow ORYGEN Research Centre University of Melbourne, Australia
11.30am	**A City-State of Mind - Facing the Challenge of Mental Health in Singapore** *Dr Alan Ong* Deputy Director (Community Mental Health) Community Mental Health Branch Primary and Community Care Division Ministry of Health, Singapore
12.00pm	**Panel Discussion**
12.30pm	**Lunch & Tour of IMH Facilities**
2.00pm	**Breakout Sessions** **Session 1** REACH: An Evidence-based Delivery System that is Cost Effective for Singapore *REACH Team, IMH* **Session 2** Advancing Psychogeriatric Care: A Multidisciplinary Approach *Geriatric Psychiatry, IMH* **Session 3** Economic Evaluation in Healthcare *Dr. Hristina Petkova* *Researcher, Health Economics* *Centre for the Economics of Mental and Physical Health,* *Institute of Psychiatry, King's College London*
3.30pm	**End**

Transport to Ritz Carlton Hotel for opening of WORLD HEALTH SUMMIT REGIONAL MEETING – ASIA

Symposium fees:
S$100 (excluding 7% GST) per participant

For registration, please visit
www.imh.com.sg

For more information please contact
symposium@imh.com.sg

Organised by

IMH 1928-2013 8 YEARS ADVANCING MENTAL HEALTHCARE

INSTITUTE of MENTAL HEALTH

Loving Hearts, Beautiful Minds

Contents

Permit No. MCI (P) 058/12/2012
Journal of The Singapore Family Physician
Printed by Tri-Art Printers Pte Ltd

College of Family Physicians Singapore
23rd Council (2011-2013)

President	A/Prof Lee Kheng Hock
Vice President	Dr Tan See Leng
Censor-in-Chief	A/Prof Tan Boon Yeow
Honorary Secretary	Dr Pang Sze Kang Jonathan
Honorary Treasurer	Dr Tan Tze Lee
Assistant Honorary Secretary	Dr Leong Choon Kit
Assistant Honorary Treasurer	Dr Rukshini Puvanendran
Honorary Editor	Dr Tan Ngiap Chuan
Council Members	Dr Ang Choon Kiat Alvin
	Dr Eu Tieng Juoh Wilson
	Dr Chng Shih Kiat
	A/Prof Koh Choon Huat Gerald
	Dr Lim Fong Seng
	Dr Siew Chee Weng
	Dr Tham Tat Yean
	Dr Yee Jenn Jet Michael

College Secretariat

Executive Director	Dr Pang Sze Kang Jonathan
Assistant Executive Director	Dr Tan Ban Leong Kenny
Director of Curriculum Development	Dr Tan Lip Pin
Senior Manager	Ms Jennifer Lau
Corporate Communications Executive	Ms Stella Teh
Programmes & Training Executive	Mr Ang Chee Yen
Programmes & Administrative Executive	Ms Ng Sei Li
Programmes and IT Executive	Ms Anica Goh
Administrative Assistant	Ms Briana Ko

SCHIZOPHRENIA AS A CHRONIC DISEASE

A/Prof Goh Lee Gan

SFP2013; 39(1): 4

Schizophrenia is one of the ten conditions under the Ministry of Health's Chronic Disease Management Programme (CDMP). Through CDMP, the Ministry aims to increase the level of care of the ten selected diseases through the promotion of systematic, evidence-based care. The use of Medisave is aimed to reduce out of pocket cash payments for outpatient bills, making these ten conditions more manageable to patients. Reprint of the notes on the administration of the CDMP on schizophrenia from the MOH CDMP Handbook is also included in this issue of the SFP. Thanks are due to the Agency for Integrated Care (AIC), Institute of Mental Health (IMH) and Ministry of Health (MOH) for supporting this Family Practice Skills Course. Thanks are also due to the many colleagues who have contributed to the papers in this issue of the Singapore Family Physician as well as speaking in the seminar and conducting the workshops.

The aim of this issue of the Singapore Family Physician is to provide the reader with an understanding of schizophrenia, its diagnosis, holistic management covering early referral, biological interventions, psychosocial interventions, follow up care, and care that meets and exceeds the clinical indicators of care.

Unit 1 highlights the importance of early diagnosis and intervention in schizophrenia as this gives the patient with such a condition the best outlook possible. The family doctor plays an important role in the early diagnosis and referral of the patient for care, in supporting the family, and holistic management.

Unit 2 describes the Singapore experience of the Early Psychosis Intervention Programme (EPIP) in Singapore. EPIP has shown good outcomes in terms of number of patients accepted into the programme, as well as our clinical service provision. Such outcomes are achieved with our community partners playing an important role. General Practitioners, in particular, are vital not only in the detection, management of such individuals, but also in the re-integration of our patients back to community.

Unit 3 covers the differential diagnoses to be considered and these can include a number of medical and neuropsychiatric illnesses. Substance use, schizoaffective and bipolar affective disorders, delusional and certain personality disorders, metabolic, endocrine and infectious illness can mimic and complicate a diagnosis of schizophrenia. More than 50% of patients with schizophrenia have co-morbid psychiatric or medical conditions including impairment of cognitive function, depression, obsessive-compulsive behavior, substance abuse, and aggressive behavior, and these affect the prognosis of both acute as well chronic schizophrenia.

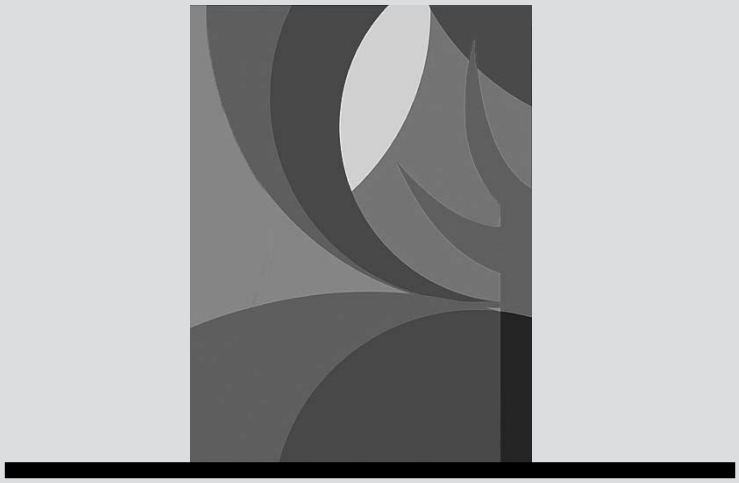
Unit 4 describes the GP Partnership Programme (GPPP), an integrated care programme, and its contributions over a span of ten years, since its implementation in 2003 by the Institute of Mental Health, a tertiary mental health institution in Singapore. The GPPP is a collaboration between the GPs and IMH, for the care and management of stable patients with mental illness in the community and primary care setting. Since 2003, more than 1300 patients have been referred through the GPPP to a team of 51 GP-Partners for continued care within the community.

Unit 5 covers the management of Relapse of psychotic symptoms in Schizophrenia occurs in up to 40% of patients within a year of being hospitalized. It is necessary to implement a proactive approach towards the prevention of relapses by using strategies such as psychoeducation and early identification of relapse signatures. More importantly, it should be emphasised that empowerment of the individuals in understanding and managing their illness is crucial.

Unit 6 is an update on the medications in the management of the different phases of schizophrenia as well as the diagnosis and management of the adverse effects of antipsychotics.

In addition, this first issue of Singapore Family Physician for 2013 presents to our readers an interesting array of original articles: a topic review on managing high altitude sickness and a case study about managing adverse outcomes during a primary care consultation under the PRISM column.

GOH LEE GAN, Professorial Fellow, Division of Family Medicine, University Medicine Cluster, National University Health System, Director, Institute of Family Medicine, College of Family Physicians Singapore



Distance Learning Course on "Schizophrenia"

- Overview of "Schizophrenia" Family Practice Skills Course
- Unit 1 : An Overview of Schizophrenia
- Unit 2 : Outcomes of the Early Psychosis Intervention Programme (EPIP), Singapore
- Unit 3 : Differential Diagnosis of Schizophrenia & Co-morbid Psychiatric Conditions in Schizophrenia and their Management
- Unit 4 : Ten Years of Successful Collaboration between Psychiatrists, a Mental Health Institution and General Practitioners in Primary Care
- Unit 5 : Management of Relapse in Schizophrenia
- Unit 6 : Update on Medications in Schizophrenia

OVERVIEW OF "SCHIZOPHRENIA" FAMILY PRACTICE SKILLS COURSE

A/Prof Goh Lee Gan

SFP2013; 39(1): 6-7

INTRODUCTION

Schizophrenia is one of the ten conditions under the Ministry of Health's Chronic Disease Management Programme (CDMP). Through CDMP, the Ministry aims to increase the level of care of the ten selected diseases through the promotion of systematic, evidence-based care. The use of Medisave is aimed to reduce out of pocket cash payments for outpatient bills, making these ten conditions more manageable to patients. Early diagnosis and intervention in schizophrenia gives the patient with such a condition the best outlook possible. The aim of this Family Practice Skills Course is to provide the reader with an understanding of schizophrenia, its diagnosis, holistic management covering early referral, biological interventions, psychosocial interventions, follow up care, and care that meets and exceeds the clinical indicators of care. The family doctor plays an important role in the early diagnosis and referral of the patient for care, in supporting the family, and holistic management. This course has been developed with the family doctor in mind. Thanks are due to the Agency for Integrated Care (AIC), Institute of Mental Health (IMH) and Ministry of Health (MOH) for supporting this Family Practice Skills Course. Thanks are also due to the many colleagues who have contributed to the papers in this issue of the Singapore Family Physician as well as speaking in the seminar and conducting the workshops

COURSE OUTLINE AND CME POINTS

This Family Practice Skills Course is made up of the following components. You can choose to participate in one or more parts of it. The CME points that will be awarded are also indicated below.

Components and CME Points

- Distance Learning Course – 6 units (6 Core FM CME points upon attaining a minimum pass grade of 60% in Distance Learning Online MCQ Assessment)
- 2 Seminars (2 Core FM CME points per seminar)
- 2 Workshops (1 Core FM CME point per workshop)
- 10 Readings – read 5 out of 10 recommended journals (maximum of 5 CME points for the whole CME year)

Distance Learning Course

Unit 1 : An Overview of Schizophrenia
A/Prof Chong Siow Ann

Unit 2 : Outcomes of the Early Psychosis Intervention Programme (EPIP), Singapore
Poon Lye Yin, A/Prof Swapna Verma, A/Prof Chong Siow Ann

Unit 3 : Differential Diagnosis of Schizophrenia & Co-morbid Psychiatric Conditions in Schizophrenia and their Management
Dr Sutapa Basu

Unit 4 : Ten Years of Successful Collaboration between Psychiatrists, a Mental Health Institution and General Practitioners in Primary Care
Dr Lum Wai Mun Alvin, Christine Tan, Joshua Wee

Unit 5 : Management of Relapse in Schizophrenia
Assistant Prof Sujatha Rao

Unit 6 : Update on Medications in Schizophrenia
Dr Roger Ho Chun Man

COURSE TOPIC DETAILS

Unit 1: An Overview of Schizophrenia

- Clinical Features
- Aetiological basis of schizophrenia
- Natural history and course

Unit 2: Outcomes of the Early Psychosis Intervention Programme (EPIP), Singapore

- Introduction
- Method
- Results
- Discussion
- Conclusion

Unit 3: Differential Diagnosis of Schizophrenia & Co-morbid Psychiatric Conditions in Schizophrenia and their Management

- Introduction
- Differential Diagnoses
- Co morbidities and their Management in Schizophrenia

GOH LEE GAN, Professorial Fellow, Division of Family Medicine, University Medicine Cluster, National University Health System, Director, Institute of Family Medicine, College of Family Physicians Singapore

Unit 4: Ten Years of Successful Collaboration between Psychiatrists, a Mental Health Institution and General Practitioners in Primary Care

- Introduction
- GP-Partnership Programme
- Programme to date
- A Matured Programme Focusing on Sustained Care
- Conclusions

Unit 5: Management of Relapse in Schizophrenia

- Introduction
- Risk Factors for Relapse and Management
- Management of Residual Psychopathlogy
- Management of Poor Compliance and Poor Insight
- Management of Stress
- Management of Poor Social Support
- Management of Substance Misuse, Smoking and Other Medication
- Management of High Expressed Emotion
- Conclusion

Unit 6: Update on Medications in Schizophrenia

- Introduction
- Changes in treatment goals for schizophrenia
- Dopaminergic receptor blocking in the major dopamine pathways
- Typical antipsychotics
- Atypical antipsychotics
- Are SGAs more effective than FGAs?
- Adverse effects of antipsychotic medications
- Antipsychotic induced weight gain
- Recommendations on the use of medications in the different phases of the disease

FACE-TO-FACE SESSIONS

Seminar 1: 23 Feb 2013, 2.00pm – 4.00pm

Unit 1 : An Overview of Schizophrenia
A/Prof Chong Siow Ann

Unit 2 : Outcomes of the Early Psychosis Intervention Programme (EPIP), Singapore
A/Prof Swapna Verma

Unit 3 : Differential Diagnosis of Schizophrenia & Co-morbid Psychiatric Conditions in Schizophrenia and their Management
Dr Sutapa Basu

Workshop 1: 23 Feb 2013, 4.30pm – 6.00pm

Case Studies/ Role Play

- Interviewing Skills
- Early Detection of Schizophrenia
- Assessment of Co-morbidities

A/Prof Swapna Verma, Dr Ashwin Chee, Helen Lee, Christopher Loh

Seminar 2: 24 Feb 2013, 2.00pm – 4.00pm

Unit 4 : Ten Years of Successful Collaboration between Psychiatrists, a Mental Health Institution and General Practitioners in Primary Care
Dr Lum Wai Mun Alvin

Unit 5 : Management of Relapse in Schizophrenia
Assistant Prof Sujatha Rao

Unit 6: Update on Medications in Schizophrenia
Dr Roger Ho Chun Man

Workshop 2: 24 Feb 2013, 4.00pm – 6.00pm

Case Studies/ Role Play

- Relapse & Emergencies
- Risk Assessment

Dr Alvin Lum, K Pushpa, Jagan s/o Rama

UNIT NO. 1

AN OVERVIEW OF SCHIZOPHRENIA

A/Prof Chong Siow Ann

ABSTRACT

Schizophrenia is characterised by multiplicity of symptoms affecting cognition, emotion and perception. The early age of onset, varying degree of intellectual and psychosocial impairment and possibility of long-term disability makes it a severe and devastating mental illness. Symptoms of schizophrenia are divided into four categories: positive, negative, disorganised and cognitive symptoms. Various combinations of severity of these four categories are found in patients. They may also experience symptoms of other mental disorders, including depression, obsessive and compulsive symptoms, somatic concerns, and mood or anxiety symptoms. More than 80% of patients with schizophrenia have parents who do not have the disorder. The risk of having schizophrenia is greater in persons whose parents have the disorder. The peak incidence of schizophrenia is at 21 years. The onset is earlier for men (between ages 15 and 25 years) and later in women (between ages 25 and 35 years). Childhood onset schizophrenia is rare. The first psychotic episode is often preceded by a prodromal phrase lasting weeks or even years. The psychotic phase progresses through an acute phase, a recovery or stabilisation phase, and a stable phase. Early detection and treatment results in a better outcome. Management of schizophrenia is holistic and multidisciplinary. Family physicians play an important role in the early detection of those who are psychotic; managing patients who are stabilised and require maintenance pharmacotherapy; and the detection of physical illnesses of cardiovascular diseases, obesity and diabetes which have a higher prevalence among patients with schizophrenia as compared to the general population.

Keywords: Cognition, emotion, perception, symptoms, early detection, physical illnesses, role of family physicians

SFP2013; 39(1): 8-9

CLINICAL FEATURES

Schizophrenia is a mental illness characterised by a multiplicity of symptoms affecting the fundamental human attributes: cognition, emotion and perception. The early age of onset, varying degree of intellectual and psychosocial impairment and possibility of long-term disability makes schizophrenia one of the most severe and devastating mental illnesses. Persons with schizophrenia also suffer disproportionately from an increased incidence of general medical illness, and increased mortality, especially from suicide, which occurs in up to 10% of patients[1].

No single symptom is pathognomonic of schizophrenia. Symptoms of schizophrenia are divided into four categories: positive, negative, disorganised and cognitive symptoms. Various combinations of severity in these four categories are found in patients.

Positive symptoms are those that appear to reflect the presence of mental features that should not normally be present. These include delusions and hallucinations.

Negative symptoms are those that appear to reflect a diminution or loss of normal emotional and psychological function. These include affective flattening (difficulty in expressing emotions), alogia (limited speech with consequent difficulty in maintaining a continuous conversation or saying anything new), avolition (extreme apathy with lack of initiation, drive and energy which result in academic, vocational and social deterioration), anhedonia (lack of pleasure or interest in life) and asociality (social withdrawal and few social contacts). These Negative symptoms are less obvious and often persist even after the resolution of positive symptoms.

Cognitive symptoms include impairment in attention, reasoning and judgment, and difficulty in processing information.

Disorganised symptoms refer to disturbances in thinking, speech, behaviour and incongruous affect.

These psychological and behavioral disturbances are associated with a variety of impairments in occupational or social functioning. Although there can be marked deterioration with impairments in multiple domains of functioning (e.g. learning, self-care, working, interpersonal relationships, and living skills), the manifestation of the disorder can vary across persons and within persons over time.

Individuals with schizophrenia may also experience symptoms of other mental disorders, including depression, obsessive and compulsive symptoms, somatic concerns, and other mood or anxiety symptoms.

AETIOLOGICAL BASIS Y OF SCHIZOPHRENIA

Schizophrenia is a complex disorder and arises from a combination of risk factors including genetic vulnerability. Although more than 80% of patients with schizophrenia have parents who do not have the disorder, the risk of having schizophrenia is greater in persons whose parents have the disorder; the lifetime risk is 13% for a child with one parent with schizophrenia and 35-40% for a child with two affected parents and about 50% concordance rate among monozygotic twins[2].

The genetic vulnerability arises from a complex combination of multiple genes of small effect. Environmental risk factors are also necessary and some operate early in life[3].

NATURAL HISTORY AND COURSE

The peak incidence of schizophrenia is at 21 years[4]. The onset is earlier for men (between ages 15 and 25 years) and later in women

CHONG SIOW ANN, Vice Chairman, Medical Board (Research) and Senior Consultant, Institute of Mental Health

(between ages 25 and 35 years). Childhood onset schizophrenia is rare and that psychotic symptoms in this age group may not always be indicative of schizophrenia[5-7].

The first psychotic episode is often preceded by a prodromal phrase. The prodromal phase involves a change from premorbid functioning and extends up to the time of the onset of frank psychotic symptoms. It may last weeks or even years. During the prodromal phase the person experiences substantial functional impairment and nonspecific symptoms such as sleep disturbance, anxiety, irritability, depressed mood, poor concentration, fatigue, and behavioral deficits such as deterioration in role functioning and social withdrawal. Perceptual abnormalities and suspiciousness may emerge later in the prodromal phase[8,9].

The psychotic phase progresses through an acute phase, a recovery or stabilisation phase, and a stable phase. The acute phase refers to the presence of florid psychotic features such as delusions, hallucinations, formal thought disorder, and disorganised thinking. The stabilisation (recovery) phase refers to a period after acute treatment. During the stable phase, negative and residual positive symptoms that may be present are relatively consistent in magnitude and usually less severe than in the acute phase. Some patients may be asymptomatic whereas others experience nonpsychotic symptoms such as tension, anxiety, depression, or insomnia.

The longitudinal course of schizophrenia is variable. Complete remission with a full return to a premorbid level of functioning is not common although some individuals are free from further episodes. The outcome following first admission and first diagnosis of schizophrenia with follow-up time of more than 1 year suggests that less than 50% of patients have a poor outcome and with good outcome in less than 50% – this is thought to be due to unexplained heterogeneity rather than uniform poor outcome.[3] A small proportion (10%-15%) will remain chronically and severely psychotic. Early detection and treatment, however, would lead to a better outcome[10].

The management of schizophrenia should take a holistic and multidisciplinary approach. The type and range of intervention is to a large extent specific to the different phases of the illness. In the acute phase of the illness, the patient requires specialised psychiatric care.

Family physicians play an important role in the early detection of those who are psychotic. They are also important in managing patients who are stabilised and require maintenance pharmacotherapy. Most of these stabilised patients are best managed in the community. Further, as the rate of physical illnesses like cardiovascular diseases, obesity and diabetes are higher among patients with schizophrenia as compared to the general population, family physicians would be able to screen and treat these illnesses[11].

REFERENCES

1. McGrath J, Saha S, Chant D, Welham J. Schizophrenia: a concise overview of incidence, prevalence, and mortality. Epidemiol Rev. 2008;30:67-76. doi: 10.1093/epirev/mxn001

2. Nasrallah HAS, D. J. The patient with schizophrenia. Pennsylvania: Handbooks in Health Care Co; 2003.

3. van Os J, Kapur S. Schizophrenia. Lancet. 2009 Aug 22;374(9690):635-45. doi:10.1016/S0140-6736(09)60995-8

4. Psychosocial disorders in young people. Chichester: Wiley; 1995.

5. American Academy of Child and Adolescent Psychiatry. Practice parameter for the assessment and treatment of children and adolescents with schizophrenia. J Am Acad Child Adolesc Psychiatry. 2001 Jul;40(7 Suppl):4S-23S.

6. Asarnow JR, Tompson MC, McGrath EP. Annotation: childhood-onset schizophrenia: clinical and treatment issues. J Child Psychol Psychiatry. 2004 Feb;45(2):180-94. DOI: 10.1111/j.1469-7610.2004.00213.x

7. McClellan J, Werry J. Practice parameters for the assessment and treatment of children and adolescents with schizophrenia. American Academy of Child and Adolescent Psychiatry. J Am Acad Child Adolesc Psychiatry. 1997 Oct;36(10 Suppl):177S-93S.

8. Yung AR, McGorry PD. The prodromal phase of first-episode psychosis: past and current conceptualizations. Schizophr Bull. 1996;22(2):353-70. doi: 10.1093/schbul/22.2.353

9. McGorry PD, Yung AR, Phillips LJ. The "close-in" or ultra high-risk model: a safe and effective strategy for research and clinical intervention in prepsychotic mental disorder. Schizophr Bull. 2003;29(4):771-90. doi: 10.1093/oxfordjournals.schbul.a007046

10. Marshall M, Rathbone J. Early intervention for psychosis. Cochrane Database Syst Rev. 2006(4):CD004718.

11. Leucht S, Burkard T, Henderson J, Maj M, Sartorius N. Physical illness and schizophrenia: a review of the literature. Acta Psychiatr Scand. 2007 Nov;116(5):317-33. DOI: 10.1111/j.1600-0447.2007.01095.x

LEARNING POINTS

- **Schizophrenia is characterised by multiplicity of symptoms affecting cognition, emotion and perception.**
- **Symptoms of schizophrenia are divided into four categories: positive, negative, disorganised and cognitive symptoms. Various combinations of severity of these four categories are found in patients.**
- **The peak incidence of schizophrenia is at 21 years. The onset is earlier for men (between ages 15 and 25 years) and later in women (between ages 25 and 35 years).**
- **Early detection and treatment results in a better outcome.**
- **Family physicians play an important role in the early detection of those who are psychotic; managing patients who are stabilised and require maintenance pharmacotherapy; and the detection of physical illnesses of cardiovascular diseases, obesity and diabetes which have a higher prevalence among patients with schizophrenia as compared to the general population.**

UNIT NO. 2

OUTCOMES OF THE EARLY PSYCHOSIS INTERVENTION PROGRAMME (EPIP), SINGAPORE

Poon Lye Yin, A/Prof Swapna Verma, A/Prof Chong Siow Ann

ABSTRACT

Psychoses are serious and potentially chronic mental disorders with a profound impact, in terms of economic cost and human suffering, on patients, their families and society. Early detection and treatment, through reducing the duration of untreated psychosis, however, could lead to a better outcome. In 2001, the Early Psychosis Intervention Programme (EPIP), Singapore was started with the following key strategies: (1) early detection of psychosis through outreach to and network with the community and our partners; (2) provision of clinical treatment that is evidence-based; and (3) conducting clinically relevant research to evaluate our service to be accountable to the stake-holders and to ensure cost-effectiveness. A myriad of structure, process and outcome measures offering a multi-dimensional evaluation were chosen to make us accountable to a broad range of stakeholders, from our funders, other service providers, to our patients and their families. EPIP has shown good outcomes in terms of number of patients accepted into the programme, as well as our clinical service provision. Such outcomes are achieved with our community partners playing an important role. General Practitioners, in particular, are vital not only in the detection, management of such individuals, but also in the re-integration of our patients back to community.

Keywords: First episode psychosis; Singapore; Outcomes; Clinical response; Remission; Functioning; General practitioners; Stakeholders

SFP2013; 39(1): 10-13

INTRODUCTION

What is psychosis?

Psychosis is a condition that causes disturbances in the brain and people suffering from psychosis lose touch with reality. It affects their way of thinking, perceiving and/or behaving. The symptoms are broadly categorised into hallucinations, delusions and disorganised thinking and behaviour.

Hallucinations are sensory experiences (whether through sound, touch, sight, taste or smell) in the absence of the external stimuli. Delusions are beliefs that are firmly held and unshakeable, such as thinking that someone has hatched a plot to harm the individual. Disorganised thinking could take the form of circumstantiality or tangentiality. Age of onset is typically in the late adolescence and early adulthood and affects both males and females equally.

Burden of psychosis

Worldwide, psychosis is ranked third amongst the most disabling condition, following quadriplegia and dementia and ranking higher than blindness and paraplegia (NHS Executive, 1996). The illness generates an enormous burden in both economic cost and human suffering. The British National Health System (NHS) conducted a study on the financial impact of chronic diseases[1] and found that psychosis was the most costly illness to treat.

In Singapore, our Ministry of Health conducted a study in 2004 to find out the leading causes of disability: schizophrenia, a form of psychosis, was ranked top three in the leading causes of disability-adjusted life year (DALY) for Singaporeans aged between 15-44 years old[2]. According to the World Health Organisation (WHO), DALYs is defined as the sum of years of potential life lost due to premature mortality and the years of productive life lost due to disability.

Early intervention of psychosis

In view of the high costs to treat psychosis, as well as the extensive disability associated with it, a movement for early intervention of psychosis started in the late 1980s with the Early Psychosis Prevention and Intervention Centre (EPPIC) from Melbourne, Australia led by Prof Patrick McGorry. The premise behind the provision of such a clinical service is to reduce the duration of untreated psychosis (DUP). DUP is defined as the time between the onset of the first psychotic symptoms and the first adequate treatment. A recent meta-analysis[3] showed that a shorter DUP is related to a greater response to treatment and functional outcomes.

The concept of early intervention for psychosis garnered much support from the international community as provision of such a service could improve the outcomes for someone who suffers from psychosis. Buoyed by the potential to intervene early for better outcomes in psychosis as well as findings from the research studies, the notion of early intervention for psychosis quickly gained momentum. Many early intervention sites began

POON LYE YIN, Assistant Manager, Early Psychosis Intervention Programme (EPIP), Institute of Mental Health

SWAPNA VERMA, Senior Consultant and Chief, Early Psychosis Intervention Programme (EPIP), Institute of Mental Health

CHONG SIOW ANN, Vice Chairman, Medical Board (Research) and Senior Consultant, Institute of Mental Health

to develop worldwide: in the UK [Lambeth Early Onset (LEO) Service, London; REDIRECT, Birmingham], Norway (TIPS), Canada [The Prevention and Early Intervention Program for Psychoses (PEPP), Ontario; Early Psychosis Program, Calgary], Hong Kong (Early Assessment Service for Young People with Early Psychosis Programme) and Japan (Early Intervention Centre Tokyo Youth Club).

Early Psychosis Intervention Programme (EPIP), Singapore

In 2001, the Early Psychosis Intervention Programme (EPIP) was started as a Health Service Development Programme (HSDP) under the auspices of the Ministry of Health (MOH), Singapore. Based in the Institute of Mental Health, EPIP is a comprehensive, integrated, and patient centred programme led by a multidisciplinary team of psychiatrists, psychologists, case managers, social workers, nurses and occupational therapists. It is one of the first few programmes in Asia to introduce an early intervention service, and a pioneer in the use of case management in a psychiatric setting. Details of our service provision have been described elsewhere[4].

EPIP's aims are to:

- raise awareness of and reduce stigma associated with psychosis;
- establish links with primary health care providers and collaborate in the detection, referral, and management of those with psychosis; and
- improve the outcome of our patients and reduce the burden of care for their families.

In order to improve the outcomes of individuals with psychosis, it is important to focus not only on the timing of intervention but also its quality. Our key strategies are to:

- outreach to and network with the community and our partners, thus focusing on early detection of psychosis;
- provide clinical treatment that is evidence-based; and
- conduct clinically relevant research as well as evaluate our service to be accountable to the stake-holders and to ensure cost-effectiveness.

In April 2007, EPIP came under the National Mental Health Blueprint. Drawn by MOH together with stakeholders, the Blueprint aims to promote mental health and where possible, prevent the development of mental health disorders as well as reduce the impact of mental disorders. The Blueprint has four main thrusts: mental health promotion, integrated mental health care, developing manpower and, research and evaluation. All programmes under the Blueprint are evaluated regularly on performance indicators established a priori so as to be accountable to our stakeholders, as well as for the monitoring and evaluation of these initiatives. These indicators are mutually set by the individual programme directors and MOH and incorporated a myriad of structure, process and outcome measures to offer a multi-dimensional evaluation of the programmes.

METHOD

Patients accepted to EPIP since April 2007 were included in this analysis. EPIP's inclusion criteria are: age between 16 and 40 years, first episode psychotic disorder, and psychosis was not secondary to substance abuse or medical problems. Patients accepted into EPIP are followed up for a period of two years before being discharged to downstream services.

EPIP has built in an evaluation component to our clinical programme by administering clinical assessments at regular intervals as well as generating operational statistics from our hospital's data systems. In our discussions with MOH, the following a priori indicators were agreed upon and the targets were set based on the experience of first five years of our service, as well as the outcomes recommended within the international consensus statement on early psychosis[5]:

Outreach and network

- Number of patients screened and accepted into EPIP.

Clinical treatment

- Average Length of stay in the hospital.
- Proportion of patients with an improvement in their symptomatology at the end of 2 years.
- Proportion of patients with an improvement in their level of functioning at the end of 2 years.
- Levels of satisfaction with the EPIP service by patients.
- Proportion of patients who remained engaged with EPIP and did not default.
- Suicide rate within first 2 years of diagnosis.

Data such as the number of patients screened and accepted, and length of stay in the hospital was obtained by the hospital's data systems. The other clinical data was obtained through the systematic assessments by the EPIP team (psychiatrists and case managers): on first presentation (baseline), 3 months, 6 months, 1 year and 2 years later. Severity of psychopathology was assessed by Positive and Negative Scale for Schizophrenia (PANSS)[6]; a higher score indicates more severe symptoms. Clinical response was defined as at least 20% reduction in their PANSS total score from baseline to 1 year and at the end of 2 years[7]. The Global Assessment of Functioning (GAF) was used to assess level of functioning[8]; a higher score indicates higher level of functioning. Recovery was defined as a score of 60 or more on the GAF Disability subscale, which indicates some difficulty in social, occupation or school functioning but generally functioning well, with some meaningful interpersonal relationships. The case managers also used a semi-structured socio-demographic questionnaire to assess if our patients were employed or engaged in age-appropriate roles (for example, student or homemaker).

Patients rated their satisfaction with the service provided by EPIP on the Client Satisfaction Questionnaire 8 (CSQ-8)[9]. Engagement with EPIP was rated by the case managers using a semi-structured scale (1= not a defaulter, 2 = telephone contact with patient + / - family, 3 = telephone contact with family only, 4 = no contact). Engagement was defined as face-to-face or phone contact with the patients, or phone contact with their families. Suicide rate was established when the team was notified of patients' suicides through their caregivers or through police investigations.

Proportions of patients who achieved clinical response, recovery and remained engaged with EPIP's services were calculated as total number of patients meeting the criteria over total number of available data sets.

RESULTS

Between April 2007 to March 2011, EPIP has screened 1293 individuals and accepted 815 into our programme. Data was available for 803 patients for our current analysis; as 12 (1.5%) of them had missing data. The sample comprised of 388 females (48.7%) and 408 males (50.8%) with a mean age of 27 years (± 6.5 years) and ranged between 15 to 41 years. The socio-demographic data for this sample is presented in Table 1.

Table 1: Socio-demographic characteristics of sample (n = 803)

Variable		N (%)
Gender	Male	411 (51.2)
	Female	392 (48.8)
Race	Chinese	592 (75.1)
	Malay	109 (13.8)
	Indian	62 (7.9)
	Others	25 (3.2)
Highest educational level	No education	9 (1.2)
	Primary	87 (11.2)
	Secondary and Pre-University	316 (40.6)
	Vocational	99 (12.7)
	Tertiary	262 (33.6)
	Others	6 (0.8)
Referral source	Relatives, Friends or Self	369 (47.3)
	Hospital	110 (14.1)
	General Practice or Polyclinic	103 (13.2)
	Police or Court	98 (12.6)
	Counsellor from welfare organisation or school	28 (3.6)
	Private Psychiatrist	8 (1.0)
	Others (MINDEF, MCYS, school staff, religious organisations)	64 (8.2)
First presentation status	Inpatient	448 (55.8)
	Outpatient	355 (44.2)

Mean length of stay per admission in the hospital, calculated as number of days of hospitalisations divided by number of admissions), was 16.6 days (2693/378). 86.1% (198/230) had at least 20% reduction in their PANSS total score from baseline to 2 years. At the end of 2 years, 84.2% (197/234) of our patients scored 60 or more on the GAF Disability. 76.4% (230/301) of them have returned to performing age appropriate roles (back to school or gainfully employed). The baseline and 2 year symptomatology and functional data is shown in Table 2.

Table 2: Clinical characteristics of sample (n = 803)

Variable	Baseline Mean (SD)	2 years Mean (SD)
PANSS Total	66.7	39.0
	N (%)	**N (%)**
GAF Disability score ≥60	75 (9.5)	197 (84.2)
In age-appropriate roles	193 (54.4)	230 (76.4)

At the end of 2 years, 94.9% (187/197) of our patients who completed the CSQ-8 rated our service as "good" or better. 93.4% (281/301) remained engaged with EPIP services (outpatient attendances and/or maintaining phone contact). To our knowledge, we had 8 patients who committed suicide within 2 years of diagnosis – giving the suicide rate of 0.89% (8/898).

DISCUSSION

Through our active outreach and networking, there was a steady increase of the number of patients seen by our service. We have also provided quality clinical service as shown by our clinical outcomes in terms of response and recovery, as well as the high level of service satisfaction, and high proportion of patients who did not default. We have kept the length of stay per admission in the hospital at 16.6 days and none of the patients to date has subsequently been transferred to the chronic wards of Woodbridge Hospital. The suicide rate is also lower than the 1% target contained in the international consensus statement on early psychosis[5].

A limitation of this analysis is the missing data from patients who have completely defaulted their contact with EPIP or have chosen not to fill up some of the self-rated questionnaires. Also, we did not have adequate data to conduct a cost effectiveness analysis.

Importance of role of General Practitioners

Before the start of EPIP, around two-thirds of patients with first episode psychosis had sought the help in the primary health care sector[10]. As shown in Table 1, 13.2% of our patients continued to be referred from general practice and polyclinics even after the establishment of EPIP, thus reinforcing primary care as an important source of referrals to our service. One of EPIP's foci is to equip primary healthcare providers with the knowledge to detect psychosis, to inform of EPIP as a specialised resource and to provide assistance in the referral process.

To make the treatment continuous and seamless, it is vital for GPs to be engaged not just in detecting unwell

individuals early, but also to collaborate in the management of these patients. EPIP's recognition for the need to move towards community management of psychosis is in line with the MOH's recent initiative to manage more chronic illnesses using community primary health services. In recent years, the IMH-GP Partnership Programme (which was first initiated as part of the EPIP) has been implemented to involve GPs in the care and management of stable individuals and right-site the care within the community. A select group of GPs have already been trained by us. This is an ongoing collaboration with the specialists in the hospital and the GPs in the community.

Thus, in addition to being an important source of referral, general practitioners also play an important role in the re-integration of our EPIP patients back to society. Such collaboration allows our patients to resume their previous social roles and still access the appropriate medical care they require.

New services

Having established EPIP as a leader in the detection and treatment of early psychosis in Singapore and Asia, we have pushed the envelope further with an initiative for indicated prevention by focusing on individuals with at-risk mental state (ARMS), that is, where there are some features present which place this person at high risk for the development of psychosis or other mental disorders. By providing treatment to such individuals, we can minimise the disability of a possible mental illness, prevent or delay the onset of mental illness, and rapid detection and timely commencement of treatment if needed. This service which is the Support of Wellness Achievement Programme (SWAP) was launched in March 2008 to focus on individuals between the ages of 16 to 30.

CONCLUSION

EPIP has articulated a range of process and outcome indicators which evaluate the various aspects of our service such as service delivery and patient and caregiver outcomes. This makes the service accountable to stakeholders which include not only our funders, other service providers but also our patients and their families.

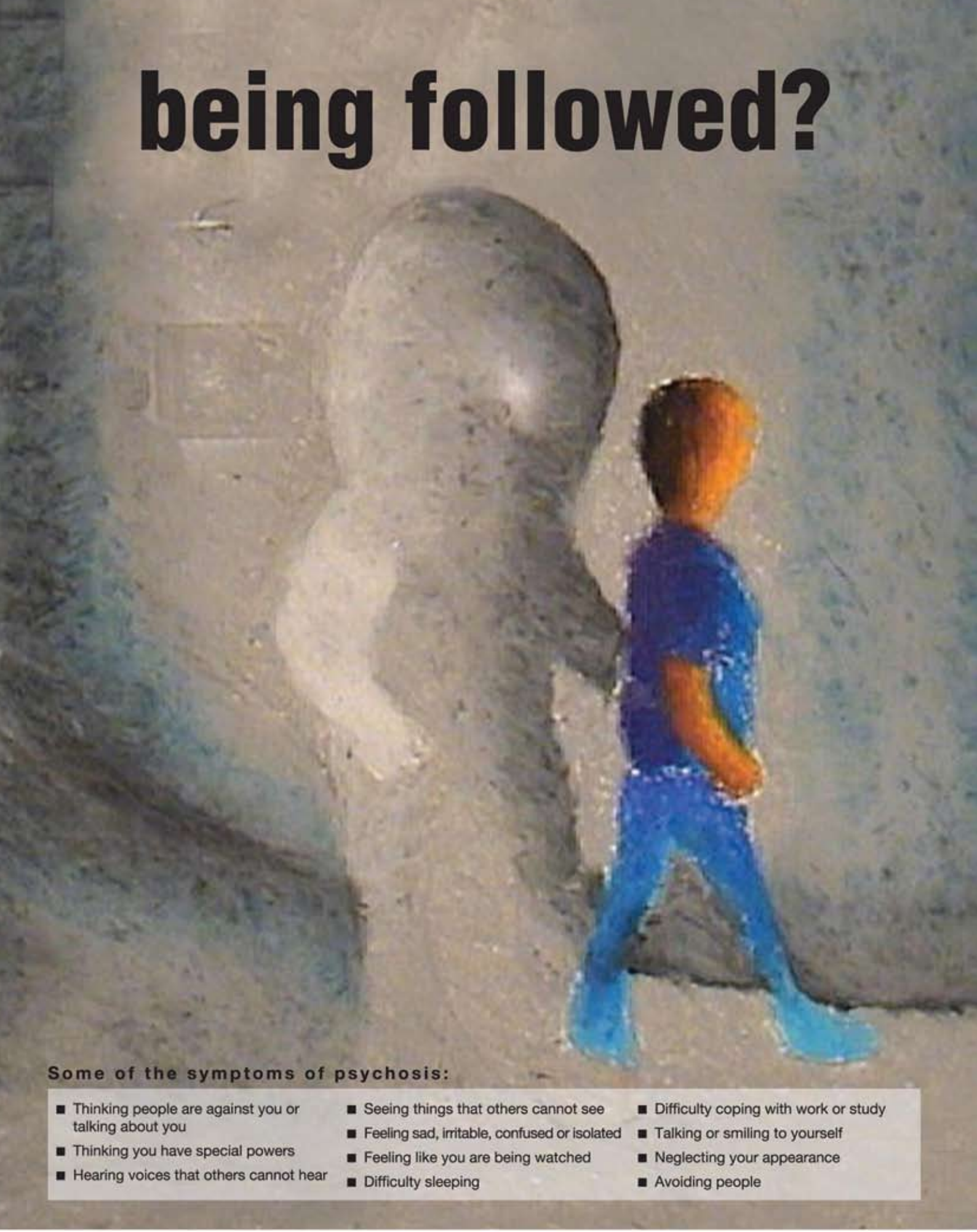
REFERENCES

1. Burdens of disease: a discussion document. NHS Executive, Department of Health (United Kingdom); 1996.
2. Burden of Disease Study. Ministry of Health, Singapore; 2004.
3. Perkins DO, Gu H, Boteva K, et al. Relationship between duration of untreated psychosis and outcome in first-episode schizophrenia: a critical review and meta-analysis. Am J Psychiatry, 2005;162:1785-804. doi: 10.1176/appi.ajp.162.10.1785
4. Chong SA, Lee C, Bird L, et al. A risk reduction approach for schizophrenia: the early psychosis intervention programme. Ann Acad Med Singapore, 2004;33:630-5.
5. Bertolote J, McGorry P. Early intervention and recovery for young people with early psychosis: consensus statement. Br J Psychiatry, 2005;187(suppl 48):s116-s119. doi: 10.1192/bjp.187.48.s116
6. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull, 1987;13:261-276.
7. Andreason NC, Carpenter WT Jr, Kane JM, et al. Remission in schizophrenia: proposed criteria and rationale for consensus. Am J Psychiatry, 2005;162:441-9. doi: 10.1176/appi.ajp.162.3.441
8. Piersma H, Boes J. The GAF and psychiatric outcome: a descriptive report. Community Ment Health J, 1997;33:35-41.
9. Attkisson CC, Zwick R. The client satisfaction questionnaire: Psychometric properties and correlations with service utilisation and psychotherapy outcome. Eval Program Plann, 1982;5:233-7.
10. Chong SA, S Mythily, Verma S. Reducing the duration of untreated psychosis and changing help-seeking behaviour in Singapore. Soc Psychiatry Psychiatr Epidemiol, doi: 2005;40(8):619-21. 10.1007/s00127-005-0948-4.

LEARNING POINTS

- **The Early Psychosis Intervention Programme (EPIP), Singapore was started in 2001 with the following key strategies: (1) early detection of psychosis through outreach to and network with the community and our partners; (2) provision of clinical treatment that is evidence-based; and (3) conducting clinically relevant research to evaluate our service to be accountable to the stake-holders and to ensure cost-effectiveness.**
- **EPIP has shown good outcomes in terms of number of patients accepted into the programme, as well as our clinical service provision; such outcomes are achieved with our community partners playing an important role.**
- **General Practitioners, in particular, are vital not only in the detection, management of such individuals, but also in the re-integration of our patients back to community.**

being followed?



Some of the symptoms of psychosis:

- Thinking people are against you or talking about you
- Thinking you have special powers
- Hearing voices that others cannot hear
- Seeing things that others cannot see
- Feeling sad, irritable, confused or isolated
- Feeling like you are being watched
- Difficulty sleeping
- Difficulty coping with work or study
- Talking or smiling to yourself
- Neglecting your appearance
- Avoiding people

The earlier psychosis is treated the better the recovery
Seek help early. Speak to your doctor or counselor.

Or contact our hotline at **6389 2972** or **9017 8212**
Monday-Friday, 8am - 5pm. **www.epip.org.sg**

epip early psychosis intervention programme

UNIT NO. 3

DIFFERENTIAL DIAGNOSIS OF SCHIZOPHRENIA & CO-MORBID PSYCHIATRIC CONDITIONS IN SCHIZOPHRENIA AND THEIR MANAGEMENT

Dr Sutapa Basu

ABSTRACT

Schizophrenia is a complex, heterogeneous, and disabling psychiatric disorder that impairs cognitive, perceptual, emotional, and behavioral functioning. It has a worldwide prevalence rate of about 1%. There are a number of physical and mental illnesses which are co-morbid with schizophrenia and this article will include a brief description and management of some of the commoner ones. Similarly, it can be mimicked by several mental and physical illnesses and accurate diagnosis is important to reduce the disability associated with the illness. Morbidity and mortality is elevated in patients in Schizophrenia as compared to the general population. More than 50% of patients with schizophrenia have co-morbid psychiatric or medical conditions including impairment of cognitive function, depression, obsessive-compulsive behavior, substance abuse, and aggressive behavior, and these reflect on prognosis of both acute as well chronic schizophrenia.

Keywords: Differential diagnosis, co morbidity, schizophrenia, schizoaffective disorder

SFP2013; 39(1): 15-18

INTRODUCTION

In an ideal world, each disorder will be in its own neat slot and it will be easy to diagnose a patient and treat an illness according to what is written in the text books. The clinical reality is that patients often do not present with "pure" diagnoses but rather with multiple coexisting psychiatric and medical conditions. Differential diagnoses need to be considered and these can include a number of medical and neuropsychiatric illnesses. Substance use, schizoaffective and bipolar affective disorders, delusional and certain personality disorders, metabolic, endocrine and infectious illness can mimic and complicate a diagnosis of schizophrenia.

DIFFERENTIAL DIAGNOSES

Differential diagnoses that need to be considered are as follows:

- Bipolar I Disorder with psychotic features
- Delusional Disorders
- Schizoaffective Disorder
- Brief Psychotic Disorder
- Psychosis NOS
- Certain personality disorders
- Drug and medication induced psychosis
- Psychosis secondary to organic causes
- Psychotic Depression

1) Bipolar disorder with psychotic features

Bipolar disorder with psychotic features are often misdiagnosed as schizophrenia. The two disorders have certain features in common.

a) The positive symptoms of schizophrenia can resemble the symptoms in manic episodes, especially those with psychotic features. (These can include delusions of grandeur, hallucinations, disorganised speech, paranoia, etc).
b) They share medications as some of the current atypical antipsychotics originally approved to treat schizophrenia are now also approved as treatment for acute mania.
c) The negative symptoms of schizophrenia can closely resemble the symptoms of a depressive episode (these include apathy, extreme emotional withdrawal, lack of affect, low energy, social isolation, etc).
d) The two disorders share abnormalities in some of the same neurotransmitter systems. For example, both depressive episode symptoms and the negative symptoms of schizophrenia are at least partially mediated by serotonin. Likewise, the positive symptoms of schizophrenia and the symptoms of mania are mediated in some way by excesses of dopamine. The atypical antipsychotics approved for both these disorders work on both the serotonin and the dopamine systems[2].

Some **key differences** are visible at the initial onset of symptoms. According to a Depression and Bipolar Support Alliance survey (formally the National Manic-Depression Association), 33% of people diagnosed with bipolar disorder remember depression as being their initial symptom experiences, and 32% recall mania at their first onset. Only 9% of survey respondents experienced psychotic symptoms first. This shows that even though these symptoms can appear in people with either disorder, certain types of symptoms may be more likely to appear at the onset of one disease than the other. Similarly, the classic onset of schizophrenia symptoms will be more likely to include delusions that are odd or bizarre, not so much delusions of religious grandiosity, which are more often seen in bipolar disorder. Rapid onset and family history of affective disorder is common in bipolar disorder and a more insidious onset and positive family history of schizophrenia will also help to differentiate the two.

2) Delusional disorder

In delusional disorder the person has a variety of paranoid beliefs, but these beliefs are usually not bizarre and are not accompanied by any other symptoms of schizophrenia. For example, a person who is functioning well at work but becomes

SUTAPA BASU, Associate Consultant, Early Psychosis Intervention Programme (EPIP), Institute of Mental Health, Singapore

unreasonably convinced that his or her spouse is having an affair has a delusional disorder rather than schizophrenia.

3) Schizoaffective disorders

Schizoaffective disorders are characterised by recurring episodes of mood/affective symptoms and psychotic symptoms.

Mood symptoms maybe manic, depressive or both manic and depressive.

Psychotic symptoms may occur before, during or after their depressive, mixed or manic episodes. The illness tends to be difficult to diagnose since the symptoms are similar to other disorders with prominent mood and psychotic symptoms like bipolar disorder with psychotic features, depression with psychotic features and schizophrenia.

The main similarity between schizoaffective disorder, bipolar disorder with psychotic features, and major depressive disorder with psychotic features, is that in all three disorders psychosis occurs during the mood episodes.

By contrast, in schizoaffective disorder psychosis must also occur during periods without mood symptoms.

4) Brief Psychotic Disorders

In brief psychotic disorder, there is presence of one or more of the following symptoms: Delusions, Hallucinations, Disorganised speech (e.g., frequent derailment or incoherence), grossly disorganised or catatonic behavior similar to schizophrenia. However, the duration of an episode is at least 1 day but less than 1 month and with eventual full return to premorbid level of functioning.

5) Psychoses NOS (Not Otherwise Specified)

Here the patient has psychotic symptoms but does not qualify for any of the other categories.

6) Personality disorders

There are three personality disorder s that need to be considered in the differential diagnosis.

(a) Schizotypal personality disorder is characterised by a pervasive pattern of discomfort in close relationships with others, along with the presence of odd thoughts and behaviors. The oddness in this disorder is not as extreme as that observed in schizophrenia.

(b) Schizoid personality disorder, the person has difficulty and lack of interest in forming close relationships with others and prefers solitary activities. No other symptoms of schizophrenia are present.

(c) Paranoid personality disorder, the person is distrustful and suspicious of others. No actual delusions or other symptoms of schizophrenia are present.

7) Substance abuse

Substance abuse (eg, abuse of alcohol, cocaine, opiates, psycho stimulants, or hallucinogens) often leads to disturbed perceptions, thought, mood, and behavior. The anabolic steroids used by body builders and athletes can lead to psychotic symptoms[3]. Anticholinergic medications can lead to delirium, especially if abused.

Many prescribed medications have been associated with mental status changes, especially the following:

Corticosteroids (psychosis or mania)
Levodopa (hallucinations or insomnia)
Antidepressants (mania)
Beta blockers (depression)
Sibutramine, an anti obesity medication, (contained in many slimming products) is often used by patients to lose weight. A history of use of slimming pills should always be enquired into, to rule out psychoses secondary to it.

8) Psychoses secondary to organic causes

There are several psychoses that may are secondary to organic causes.

(a) Metabolic illnesses

(i) Wilson disease, (hepatolenticular degeneration), an autosomal recessive illness is a disorder of the metabolism of copper. The first symptoms are often vague changes in behavior during adolescence, which are followed by the appearance of odd movements.

The diagnosis can be indicated by increased urinary levels of copper, low serum levels of copper and ceruloplasmin or by the detection of Kayser-Fleischer rings (copper deposits around the cornea) with or without a slit-lamp examination. The diagnosis is usually confirmed by finding increased hepatic copper at biopsy. As adolescence is often the period when psychotic symptoms may appear in a patient with schizophrenia, diagnosis could be confused.

(ii) Porphyria is a disorder of heme biosynthesis that can present as psychiatric symptoms. The psychiatric symptoms may be associated with electrolyte changes, peripheral neuropathy, and episodic severe abdominal pain. Abnormally high levels of porphyrins in a 24-hour urine collection confirm the diagnosis.

(iii) Hypoxemia or electrolyte disturbances may present with confusion and psychotic symptoms.

(iv) Hypoglycemia can produce confusion and irritability and may be mistaken for psychosis.

(b) Delirium from whatever cause (eg, metabolic or endocrine disorders) is an important condition to consider, especially in the elderly or hospitalised patient. Although patients with delirium may have a wide range of neuropsychiatric abnormalities, the clinical hallmarks are decreased attention span and a waxing-and-waning type of confusion.

(c) Endocrine disorders

Infrequently, **thyroid illness** may be confused with schizophrenia. Severe hypothyroidism or hyperthyroidism can be associated with psychotic symptoms. Hypothyroidism is usually associated with depression, which if severe may be accompanied by psychotic symptoms. A hyperthyroid person is typically anxious, and irritable.

Both **adrenocortical insufficiency (Addison disease) and hypercortisolism (Cushing syndrome)** may result in mental status changes. However, both disorders also produce physical signs and symptoms that can suggest the diagnosis. In addition, most patients with Cushing syndrome will have a history of long-term steroid therapy for a medical illness.

Hypoparathyroidism or hyperparathyroidism can on occasion be associated with vague mental status changes. These are related to abnormalities in serum calcium concentrations.

(d) Infectious illnesses

Many **infectious illnesses**, such as influenza, Lyme disease, hepatitis C, and any of the encephalitides including the Anti-NMDA (N-methyl D-aspartate) receptor encephalitis can cause mental status changes such as depression, anxiety, irritability, or psychosis. Elderly people with pneumonias or urinary tract infections may become confused or frankly psychotic.

The infectious illnesses of particular interest are the following: Neurosyphilis, HIV infection, Cerebral abscess, Creutzfeldt-Jakob disease (CJD).

The Venereal Disease Research Laboratory (VDRL) and rapid plasma reagin (RPR) tests are nontreponemal tests that use antigens to detect antibodies to Treponema pallidum.

Patients with **systemic lupus erythematosus**, typically young women, may present with psychiatric symptoms, such as psychosis or cognitive deficit, in association with of malar flush and the laboratory findings of anemia, renal dysfunction, elevated erythrocyte sedimentation rate (ESR), and, most specifically, elevated antinuclear antibody.

(e) Heavy metal toxicity may cause changes in personality, thinking, or mood. Occupational exposure is the usual source of heavy metal toxicity, but cases have also resulted from ingestion of herbal medications contaminated with heavy metals. So, a detailed occupational history and history of consumption of over the counter herbal medications should be obtained.

9) Psychotic Depression

People with psychotic depression have symptoms of depression and psychosis. The symptoms of low mood are prominent and it may be associated with mood congruent depression delusions and hallucinations. For example, some patients may hear voices criticising them, or telling them that they don't deserve to live. The person may develop false beliefs about their body, for example that they have cancer.

CO MORBIDITIES AND THEIR MANAGEMENT IN SCHIZOPHRENIA

The commoner co morbidities and their management are as follows:

Schizophrenia with Substance Use Disorders

The most commonly abused drugs include alcohol, cannabis, and cocaine, and the use of these substances markedly worsens the course of illness. In addition, between 50% and 90% of schizophrenic patients smoke cigarettes, contributing to increased mortality from medical illness. Smoking also decreases the effectiveness of some antipsychotics. Co morbid substance use disorder in schizophrenia is associated with greater deterioration of function, higher rates of psychotic relapse, and increased social dysfunction. Furthermore, the dual diagnosis is associated with increased suicidal ideation and victimisation[4-6]. The use of longer-acting oral medications and depot injections have also been shown to help, owing to poor treatment adherence in patients with dual diagnoses[7]. Clozapine treatment seems to be most effective in reducing alcohol and substance abuse in schizophrenia[8,9]. The increased potential for adverse effects from mixing prescribed medications with abused substances should also be considered in dual-diagnosis patients. Sibutramine, an anti obesity medication is often used by patients to lose weight.

Depression in Schizophrenia

The prevalence of depression in schizophrenia is 25% - 81%[10]. The presence of depressive symptoms in schizophrenic patients worsens quality of life[11] and increases the risk for danger to self and others (including suicide), psychotic relapse, substance-related problems, and psychiatric hospitalization[12-15]. In conclusion, concurrent depressive symptoms in schizophrenia are common and are associated with significantly poorer long-term functional outcome. Active treatment of depression targeting specific symptoms should be a standard of care.

OCD in Schizophrenia

The common themes are of contamination, sexual, somatic, religious, aggressive, and somatic, with or without accompanying compulsions[16,17]. These manifestations overlap with the underlying psychosis, demonstrating overvalued ideations and delusional manifestations[18]. Recent evidence suggests a poorer clinical course and long-term outcome, as well as greater neuropsychological dysfunction[19-22].

The syndrome may manifest during the prodromal phase or during active psychotic illness, as obsessive ruminations during recovery or the remission phase, as a de novo OC syndrome associated with treatment with Atypical Antipsychotics, or as a concurrent independent OC disorder[23,24]. Treatment is use of adjunctive anti-OC pharmacotherapy with antipsychotics like haloperidol. Cognitive Behaviour Therapy could also be used.

Eating Disorder in Schizophrenia

An eating disorder is often difficult to distinguish from psychotic phenomena, as the patient may not eat due to delusions. Case reports and open-label trials have investigated informal use of second-generation antipsychotics with potent metabolic side effect profiles in the treatment of anorexia, both by itself and as a co-morbidity with schizophrenia[25-27].

Schizophrenia and Persistent Aggressive Behavior

It is important to manage aggressive behavior in schizophrenia. Epidemiology revealed that co-occurring substance abuse and intoxication increase the risk of violence in patients with schizophrenia. Some studies have reported that ten percent of patients attack others within 24 hours after their admission in hospitals. Transient violence is associated with environmental factors and positive symptoms of psychosis.

Several medication strategies are considered for treatment of persistently aggressive psychotic patients, including conventional neuroleptics, atypical neuroleptics, and mood stabilisers like sodium Valproate and occasionally lithium carbonate. A recent study[28] revealed the effectiveness of clozapine on violence in patients with schizophrenia.

REFERENCES

1. Medscape Education Psychiatry & Mental Health. Management of Schizophrenia With Comorbid Neuropsychiatric Disorders. Henry A. Nasrallah, MD; Michael Y. Hwang, MD.
2. Scizophrenia.com
3. Pope HG Jr, Katz DL. Psychiatric and medical effects of anabolic-androgenic steroid use. A controlled study of 160 athletes. Arch Gen Psychiatry. May 1994;51(5):375-82.
4. Choulijan TL, Shumway M, Balancio E, Dwyer EV, Surber R, Jacobs M. Substance use among schizophrenia outpatients: prevalence, course, and relation to financial status. Ann Clin Psychiatry. 1995;7:19-24.
5. Mason P, Harrison G, Glazebrook C, Medley I, Croudace T. The course of schizophrenia over 13 years. A report from the International Study on Schizophrenia (ISoS) coordinated by the World Health Organization. Br J Psychiatry. 1996;169:580-586. doi: 10.1192/bjp.169.5.580
6. Cuffel BJ. Violent and destructive behavior among the severely mentally ill in rural areas: evidence from Arkansas' community mental health system. Community Ment Health J. 1994;30:495-504. 10.1007/BF02189065
7. Kane JM. Improving treatment adherence in patients with schizophrenia. J Clin Psychiatry. 2011;72:e28. doi:10.4088/JCP.9101tx2c
8. Drake RE, Xie H, McHugo GI, Green AI. The effects of clozapine on alcohol and drug use disorder among patients with schizophrenia. Schizophr Bull. 2000;26:441-449. Abstract. doi: 10.1093/oxfordjournals.schbul.a033464
9. Green AI, Burgess ES, Dawson R, Zimmet SV, Strous RD. Alcohol and cannabis use in schizophrenia: effects of clozapine vs. risperidone. Schizophr Res. 2003;60:81-85. Abstract. doi: 10.1016/S0920-9964(02)00231-1.
10. Siris SG, Addington D, Azorin JM, Falloon IR, Gerlach J, Hirsch SR. Depression in schizophrenia: recognition and management in the USA. Schizophr Res. 2001;47:185-197. Abstract. doi: 10.1016/S0920-9964(00)00135-3.
11. Reine G, Lancon C, Di Tucci S, Sapin C, Auquier P. Depression and subjective quality of life in chronic phase schizophrenic patients. Acta Psychiatr Scand. 2003;108:297-303. Abstract. doi: 10.1034/j.1600-0447.2003.00132.x
12. Reine G, Lancon C, Di Tucci S, Sapin C, Auquier P. Depression and subjective quality of life in chronic phase schizophrenic patients. Acta Psychiatr Scand. 2003;108:297-303. Abstract. doi: 10.1034/j.1600-0447.2003.00132.x
13. Siris SG. Suicide and schizophrenia. J Psychopharmacol. 2001;15:127-135. Abstract. doi: 10.1177/026988110101500209
14. Tollefson GD, Andersen SW, Tran PV. The course of depressive symptoms in predicting relapse in schizophrenia: a double-blind, randomized comparison of olanzapine and risperidone. Biol Psychiatry. 1999;46:365-373. Abstract. doi: 10.1016/S0006-3223(99)00049-9.
15. Conley RR, Ascher-Svanum H, Zhu B, Faries DE, Kinon BJ. The burden of depressive symptoms in the long-term treatment of patients with schizophrenia. Schizophr Res. 2007;90:186-197. Abstract. doi: 10.1016/j.schres.2006.09.027
16. Hwang MY, Bermanzohn PC, Opler LA. Obsessive-compulsive symptoms in patients with schizophrenia. In: Hwang MY, Bermanzohn PC, eds. Schizophrenia and Comorbid Conditions. Washington, DC: American Psychiatry Press; 2001:57-78.
17. Poyurovsky M, Koran LM. Obsessive-compulsive disorder (OCD) with schizotypy vs. schizophrenia with OCD: diagnostic dilemmas and therapeutic implications. J Psychiatr Res. 2005;39:399-408. Abstract. doi: 10.1016/j.jpsychires.2004.09.004
18. Insel TR, Akiskal HS. Obsessive-compulsive disorder with psychotic features: a phenomenological analysis. Am J Psychiatry. 1986;143:1527-1533. Abstract.
19. Buckley PF, Miller BJ, Lehrer DS, et Castle DJ. Psychiatric comorbidities and schizophrenia. Schizophr Bull. 2009;35:383-402. Abstract. doi: 10.1093/schbul/sbn135
20. Hwang MY, Morgan JE, Losonczy MF. Clinical and neuropsychological profiles of OC schizophrenia. J Neuropsychiatr Clin Neurosci. 2000;12:91-4.
21. Borkowska A, Pilaczyñska E, Rybakowski JK. The frontal lobe neuropsychological tests in patients with schizophrenia and/or obsessive-compulsive disorder. J Neuropsychiatry Clin Neurosci. 2003;15:359-362. Abstract. doi: 10.1176/appi.neuropsych.15.3.359
22. Whitney KA, Fastenau PS, Evans JD, Lysaker PH. Comparative neuropsychological function in obsessive-compulsive disorder and schizophrenia with and without obsessive-compulsive symptoms. Schizophr Res. 2004;69:75-83. Abstract. doi: 10.1016/j.schres.2003.08.013.
23. Bottas A, Cooke RG, Richter MA. Comorbidity and pathophysiology of obsessive-compulsive disorder in schizophrenia: is there evidence for a schizo-obsessive subtype of schizophrenia? J Psychiatry Neurosci. 2005;30:187-93.
24. Hwang MY, Kim SW, Yum SY, Opler LA. Management of schizophrenia with obsessive-compulsive features. Psychiatr Clin North Am. 2009;32:4:835-851. doi: 10.1016/j.psc.2009.08.002
25. Dadić-Hero E, Ružić K, Grahovac T, Valković T, Petranović D. Treatment strategy in schizophrenia combined with eating disorder. Psychiatr Danub. 2011;23:95-97. Abstract.
26. Powers PS, Bannon Y, Eubanks R, McCormick T. Quetiapine in anorexia nervosa patients: an open label outpatient pilot study. Int J Eat Disord. 2007;40:21-26. Abstract. doi: 10.1002/eat.20325
27. Powers PS, Santana CA, Bannon YS. Olanzapine in the treatment of anorexia nervosa: an open label trial. Int J Eat Disord. 2002;32:146-154. Abstract. doi: 10.1002/eat.10084.
28. Wilson WH, Claussen AM. 18-month outcome of clozapine treatment for 100 patients in a state psychiatric hospital. Psychiatr Serv. 1995;46(4):386-9.

LEARNING POINTS

- **Schizophrenia is a complex, heterogeneous, and disabling psychiatric disorder that impairs cognitive, perceptual, emotional, and behavioral functioning.**
- **The differential diagnoses are: Bipolar I Disorder with psychotic features; Delusional Disorders; Schizoaffective Disorder; Brief Psychotic Disorder; Psychosis NOS; Certain personality disorders; Drug and medication induced psychosis; and Psychosis secondary to organic causes; Psychotic Depression.**
- **Schizophrenia can be mimicked by several mental and physical illnesses and accurate diagnosis is important to reduce the disability associated with the illness.**
- **More than 50% of patients with schizophrenia have co-morbid psychiatric or medical conditions including impairment of cognitive function, depression, obsessive-compulsive behavior, substance abuse, and aggressive behavior, and these reflect on prognosis of both acute as well chronic schizophrenia.**

UNIT NO. 4

TEN YEARS OF SUCCESSFUL COLLABORATION BETWEEN PSYCHIATRISTS, A MENTAL HEALTH INSTITUTION AND GENERAL PRACTITIONERS IN PRIMARY CARE

Dr Lum Wai Mun Alvin, Christine Tan, Joshua Wee

ABSTRACT

This paper gives an overview of what the GP Partnership Programme (GPPP), an integrated care programme, has achieved over a span of ten years, since its implementation in 2003 by the Institute of Mental Health, a tertiary mental health institution in Singapore. The GPPP is a collaboration between the GPs and IMH, for the care and management of stable patients with mental illness in the community and primary care setting. Since 2003, more than 1300 patients have been referred through the GPPP to a team of 51 GP-Partners for continued care within the community.

Keywords: general practice, GP, primary care, mental health, collaboration, community engagement

SFP2013; 39(1): 19-21

INTRODUCTION

Following the recent surge in global attention given to mental healthcare over the last decade, one of the main initiatives was an attempt to alleviate the strain and burden that treatment of mental disorders put on a country's tertiary and specialised health services[1]. To achieve this, the idea of community-based health care and the integration of mental healthcare with primary healthcare was mooted[2]. Likewise in Singapore, this initiative was quickly adopted as it complemented the healthcare landscape. General practitioners (GPs) are multiskilled primary care providers supporting 83% of all primary medical care in Singapore[3], and are often the first point of contact for a patient with mental illness[4]. This placed the GPs at a crucial role in detecting, treating and/or referring a patient presenting with a mental illness. In addition, services provided by GPs for patients with mental illnesses were deemed to be more accessible, convenient, and less costly, as compared to specialised care[5]. The ease of access as well as the less stigmatising environment at the primary care level provided for a platform for regular follow-ups and co-management of other physical health conditions. One of these initiatives of collaboration with GPs, implemented by the Institute of Mental Health (IMH) since 2003, is known as the GP-Partnership Programme (GPPP). The GPPP is an integrated mental health service aimed at engaging GPs in the detection and management of mental illnesses[5]. This paper serves to give a brief history to the establishing of the GPPP as well as to give an update of what has been achieved over the past ten years.

LUM WAI MUN ALVIN, Resident Physician, Shenton Family Medical Clinic and Deputy Director, GP Partnership Programme, Institute of Mental Health

CHRISTINE TAN, Deputy Director, Education Office, Institute of Mental Health

JOSHUA WEE, Executive, GP Partnership Programme, Institute of Mental Health

GP-PARTNERSHIP PROGRAMME

In 2003, the GP-Partnership Programme was formed with four pioneer GPs. The programme began with the initial intent of getting GPs involved with the care and management of stable patients experiencing early psychosis. Following the formulation of the National Mental Health Blueprint (NMHB) in 2007, which stated that Singapore's health care was moving towards a policy of right-siting, the GP Partnership Programme was formally announced as one of its Integrated Mental Health programmes. The strategy of the programme was dual-pronged. It aimed to provide a value-added, decentralised and high quality of service to patients suffering from psychiatric disorders that would be affordable, de-stigmatised and convenient, through the right-siting of care within the GP community. In addition, the programme also aimed to have in place an integrated network of collaboration between mental health workers and GPs for the management of patients with chronic major psychiatric disorders as well as individuals with minor psychiatric disorders.

To prepare the GPs involved, a detailed training programme was formulated. This provided the GPs with additional skills and theoretical knowledge crucial in caring and managing patients with mental illness. The training programme included an induction course and was followed by regular refresher workshops and dialogue sessions which provided the GPs with up-to-date information on various aspects of mental healthcare. The GPs were also given the opportunity to meet IMH's psychiatrists with whom they attended ward rounds and were also attached to specialists' clinics. Given the importance of early detection and management of certain mental illnesses[6], and acknowledging that GPs may possibly be the first point of contact with mentally ill patients, lectures were given to the GPs to provide them with relevant clinical skills such as mental state examination, pharmacological treatment of mental illness and management of psychiatric emergencies.

Under the GPPP, patients identified by psychiatrists as suitable and fulfilling the agreed upon referral criteria by both the specialist team and the GP partners, were referred to the GPs with initial support from case managers when required.

PROGRAMME TO DATE

As of 2013, the programme has successfully grown its pool of GP-partners to 51 and has referred more than 1300 patients to their care since the inception of the programme in 2003 (see Figure 1). Since 2007 a total of 18 trainings have been conducted for the GPs, including Introductory Training (for new GP Partners) and Refresher Courses (for existing GP Partners). As the programme has progressed through the years, there has been a need to refine various aspects of the GPPP to ensure continued improvement. One of which was a further tightening of the referral criteria (see Figure 2) in 2009 which excluded most patients who were on benzodiapines. While this may have contributed to a sizeable reduction of suitable patients for the programme, it also lowered the possibility of default thus increasing the chance of each new referral remaining longer in the GP's care and within the community. In line with continued improvement, the GP Partnership Programme has conducted annual "GP Satisfaction" and "Patient Satisfaction" surveys (see Figure 3). As compared to our previous update in 2010[7], our latest survey for (GPs FY/2011) continued to show high levels of satisfaction with the programme (82.1%). In addition more than three quarters of GPs agreed (78.6%), with none disagreeing, that they would recommend this programme to their GP colleagues. As a result of these annual surveys, several new initiatives have been launched. Some of these initiatives include visits to GP clinics to update GPs, streamlining of the referral process, increasing training activities for GPs and improving of process for requisition of drugs from IMH Pharmacy.

A MATURED PROGRAMME FOCUSING ON SUSTAINED CARE

The GP-Partnership has matured with most of the first-tier immediately-suitable patients from IMH's existing pool already right-sited, the programme's on-going screening efforts for identifying suitable patients for right-siting has shifted to either existing patients who have stabilised enough to be eligible or first-time patients who already fulfil the criteria. A significant portion of its current workload now focuses on providing sustained care to the existing pool of patients in the programme. Case-tracking has become increasingly crucial as a portion of these patients have been in the community for two years or more, thus the programme has had to manage more complex problems from this group of patients. This has also lead to a need for more support to be given to the programme's GP-partners. More effort is now focused towards addressing their concerns, troubleshooting any problems that arise, as well as to coordinate and ensure that all of them are updated on new policies. In addition the GP Partnership Programme will be looking towards further collaboration with other departments in IMH, as well as with partners in other hospitals, polyclinics and mental healthcare providers.

Figure 1: Yearly Patient Referral into GPPP

S/N	FY	Total Patients Referred	Remarks
1	2003-06	164	Prior to NMHB
2	2007	241	
3	2008	181	
4	2009	187	
5	2010	251	
6	2011	196	
7	2012	140	Latest data until Dec 2012
Total:		1360	

Figure 2: Referral Criteria

Inclusion Criteria

a. Patients who are stabilised and requiring just maintenance medication, i.e. under the same medications for the past 3 months with preferably minimum or no dosage adjustments
b. Patients not hospitalised within the past 6 months
c. Patients who are employed, hence requiring flexibility of timing
d. Patients who are prepared to pay the slight price difference for continuation of treatment at GPs

Exclusion Criteria

a. Substance use and/or forensic history
b. Disruptive personality disorder
c. Suicide and aggression risk
d. Clozapine prescription
e. Formal psychotherapy
f. Financial assistance
g. Benzodiazepine-only prescriptions (added in 2009)

Figure 3: Continued Improvement Surveys

1. GP Satisfaction Survey

The GP Satisfaction Survey designed to gather feedback on five main aspects of programme.	(1) Programme Objective (2) Coordination of Care (3) Level of Support from IMH (4) Overall Satisfaction (5) Willingness to Recommend	GPs were asked to rate each aspect as (a) Strongly Agree, (b) Agree, (c) Neutral, (d) Disagree, or (e) Strong Disagree

2. Patient Satisfaction Survey

The Patient Satisfaction Survey aim to gather feedback on three main aspects.	(1) Knowledge and Skills of GP (2) Coordination of Care (3) Willingness to Recommend	Patients were asked to rate each aspect as (a) Strongly Agree, (b) Agree, (c) Neutral, (d) Disagree, or (e) Strong Disagree

CONCLUSIONS

As the GPPP marks ten years of collaboration, the potential and benefits of community engagement and collaboration is evident. Hence, despite having already referred more than 1300 patients through its programme and building up its current team of GP partners to a healthy size of 51, the GPPP will continue

to identify suitable patients for right-siting as well as recruit more GP-partners. However, with a matured programme, there is also a need to focus intently on providing sustained care to existing right-sited patients and continued support to the GPs managing their care. Case-tracking has become increasingly crucial and it has also become more labour intensive. Moving forward, there will be a need to explore the possibility of tapping into technology to aid the GPPP in managing the ever increasing data. This is imperative as patients in the programme are expected to grow yearly.

REFERENCES

1. Medscape Education Psychiatry & Mental Health. Management of . Investing in Mental Health. Department of Mental Health and Substance Dependence, Noncommunicable Diseases and Mental Health. Geneva, Switzerland. World Health Organisation, 2003.

2. WHO/Wonca: Joint report: Integrating mental health into primary care – a global perspective. Geneva, Switzerland: WHO publication data; 2008.

3. Emmanuel SC, Phua HP, Cheong PY. 2001 survey on primary medical care in Singapore. Singapore Med J 2004;45:199-213.

4. Ng TP, Fones CS, Kua EH. Preference, need and utilization of mental health services, Singapore National Mental Health Survey. Aust N Z J Psychiatry 2003;37:613-9.

5. Lum WMA, Kwok KW, Chong SA. Providing integrated mental health services in the Singapore primary care setting – the general practitioner psychiatric programme experience. Ann Acad Med Singapore. 2008;37(2):128-31.

6. Chong SA, Mythily, Lum A, Chan YH, McGorry P. Determinants of duration of untreated psychosis and the pathway to care in Singapore. Int J Soc Psychiatry. 2005 Mar;51(1):55-62. doi: 10.1177/0020764005053278

7. Lum WMA, Chew J, Lim BL. The successful collaboration between psychiatrists, a mental health instituition and general practitioners in primary care. The Singapore Family Physician Vol 36(4) Oct-Dec 2010: 19-24.

LEARNING POINTS

- **The GP Partnership Programme (GPPP) is an integrated care programme implemented since 2003 by the Institute of Mental Health, a tertiary mental health institution in Singapore.**
- **The GPPP is a collaboration between the GPs and IMH, for the care and management of stable patients with mental illness in the community and primary care setting.**
- **Since 2003, more than 1300 patients have been referred through the GPPP to a team of 51 GP-Partners for continued care within the community.**
- **Case-tracking has become increasingly crucial and it has also become more labour intensive.**
- **Moving forward, there will be a need to explore the possibility of tapping into technology to aid the GPPP in managing the ever increasing data.**

UNIT NO. 5

MANAGEMENT OF RELAPSE IN SCHIZOPHRENIA

Assistant Prof Sujatha Rao

ABSTRACT

Relapse of psychotic symptoms in Schizophrenia occurs in up to 40% of patients within a year of being hospitalised. A relapse may be secondary to any individual factor or several factors acting concomitantly. Risk factors that can precipitate a relapse in Schizophrenia are: significant residual psychopathology, poor compliance to medication, poor insight, substance misuse, interactions with other medication, poor social support, increased stress and caregivers with high expressed emotions. A thorough history and assessment should be conducted to elicit all contributory factors and appropriate interventions undertaken to address them in order to prevent the onset of a full blown relapse or to help the individual to achieve remission of symptoms. It is necessary to implement a proactive approach towards the prevention of relapses by using strategies such as psychoeducation and early identification of relapse signatures. More importantly, it should be emphasised that empowerment of the individuals in understanding and managing their illness is crucial.

Keywords: Residual psychopathology, poor compliance to medication, poor insight, substance misuse, poor social support, high expressed emotions

SFP2013; 39(1): 22-25

INTRODUCTION

Schizophrenia is a complex mental disorder, which commonly presents with a relapsing and remitting course. Relapse of psychotic symptoms in Schizophrenia occurs in up to 40% of patients within a year of being hospitalized[1,2]. These episodes of relapse have significant implications both in terms of the cost of health care and economic burden as well as the personal implications of loss of functioning and demoralization for the individual. It has been shown that the recurrent relapses have consequences on the long term prognosis of the Schizophrenia. Recurrent relapses may lead to progressive worsening of psychotic symptoms, increasing neurobiological damage, longer duration to achieve remission, longer hospitalisations and progressive cognitive and psychosocial decline. This may lead to psychological consequences for the individual such as poor self esteem, hopelessness and thus increased suicide risk. Therefore it is important to recognise the detrimental effects of relapses and thus the long term management of Schizophrenia should encompass both the prevention and management of relapses.

SUJATHA RAO, Consultant Psychiatrist, Early Psychosis Intervention Programme (EPIP), Institute of Mental Health, Singapore

RISK FACTORS FOR RELAPSE AND MANAGEMENT

There are a multitude of risk factors that can precipitate a relapse in Schizophrenia which include significant residual psychopathology, poor compliance to medication, poor insight, substance misuse, interactions with other medication, poor social support, increased stress and caregivers with high expressed emotions[3]. Although it is important to treat the symptoms of relapse when it occurs, this approach alone may not suffice and the management of relapses in Schizophrenia has to be targeted towards managing and minimising these risk factors. It is necessary to implement a proactive approach towards the prevention of relapses by using strategies such as psychoeducation and early identification of relapse signatures. More importantly, it should be emphasised that empowerment of the individuals in understanding and managing their illness is crucial. Strategies for prevention and management of the individual factors that may precipitate a relapse will be explained further.

MANAGEMENT OF RESIDUAL PSYCHOPATHOLOGY

In individuals with residual psychopathology or inadequate response to a medication, relapses or worsening of their symptoms may occur despite compliance to the medication. This can occur due to the natural remitting and relapsing course of the illness or in relation to stressful life events. Therefore it is beneficial to optimise treatment with a view to achieving remission of any residual psychopathology, if at all possible. Although in many individuals, this remains a challenging task. The National Institute for Health and Clinical Excellence (NICE)[4] had recommended that individuals experiencing adverse effects or unsatisfactory response on typical antipsychotic medication should be switched to atypical antipsychotics. NICE has also recommended Clozapine for individuals with treatment resistant Schizophrenia, which has been defined as little or no symptomatic response to multiple (at least 2) antipsychotic trials of an adequate duration (at least 6 weeks) and at a therapeutic dose range[5].

Psychological therapies including cognitive behavioral therapy, family interventions, compliance therapy as well as social interventions such as cognitive remediation and social skills training should be used to target any residual symptoms alongside antipsychotics as this has shown to reduce relapse rates. Therefore optimising treatment of residual psychopathology encompasses a holistic approach and includes biopsychosocial interventions.

MANAGEMENT OF POOR COMPLIANCE AND POOR INSIGHT

Non compliance or partial compliance to medication remains a significant problem amongst individuals suffering from Schizophrenia. Weiden et al[6] found that 40% of relapses were secondary to poor treatment adherence. They estimated the rate of outpatient non adherence to antipsychotic treatment to be 50% within 1 year of discharge and 75% within 2 years. Robinson et al[7] reported that individuals who discontinued antipsychotic medication after their first episode of schizophrenia multiplied their risk of relapse by almost five times. The NICE guidelines recommend continuous therapy with antipsychotic medication in the long term management of individuals with Schizophrenia.

Adherence to treatment is influenced by various factors which include adverse effects, limited efficacy, complicated dosing schedules, impaired insight into illness or the importance of medication, cognitive impairment and poor therapeutic relationship with the clinician. Therefore management of poor compliance involves understanding and addressing the cause and concerns of the patient. Certain factors can be managed through a change in medication and simplifying dosing regimes. Blister packs and dosing boxes can be used for patients on several medications or for those with cognitive impairment. Caregivers can also be involved in supervising the medication. However, poor insight can be a challenging factor to overcome in improving adherence to treatment. Psychoeducation, allowing the patient time for acceptance of the illness and contact with a peer support worker or peer support group may enhance the patient's insight into his illness and thereby improve compliance.

Providing psychoeducation on Schizophrenia, the prognosis, the role of medication and the risk of relapse is essential for all patients suffering from this illness. Essentially, this information should be provided to all caregivers as studies have shown that family psychoeducation reduces relapse rates in Schizophrenia[8].

A crucial strategy in relapse prevention lies in identification of the early relapse signs. As relapses often develop gradually, being able to identify the triggers or early signs of relapse may help to prevent the relapse or at least in reducing the severity of the episode. Early recognition of an impending relapse is beneficial as treatment and support can be sought early and hospitalisation may be avoided. In addition to this, the individual would suffer from less disruption to his social and occupational functioning as well as have a quicker recovery. Early relapse signs are subtle warning signs that the patient or caregivers notice before a full relapse of the illness is imminent. They may be symptoms such as poor sleep, feeling confused or nervous, being more isolative or difficulty concentrating. Early relapse signs are unique to the individual. Clinicians should help patients along with their caregivers to identify their individual early warning signs. In Singapore, Relapse Prevention Cards are used in the Department of Early Psychosis Intervention at the Institute of Mental Health. This empowers the individual to take responsibility of his illness and through identifying the early warning signs; the individual, caregiver and clinician can work collaboratively to draw up a relapse prevention plan. This plan may include actions that the individual would take such as promptly contacting the clinician, closer monitoring of symptoms, ensuring compliance, increasing the dosage of medication or alleviating any stress. It has been shown that a full blown relapse in schizophrenia can be avoided if early intervention is provided[9].

However, in patients who continue to have poor insight despite the above interventions or in individuals who default treatment repeatedly, it may be necessary to consider long-acting intramuscular antipsychotic injections rather than oral antipsychotic medication. Long-acting intramuscular antipsychotic injections have been found to lower relapse rates by about 15% when compared to oral antipsychotic medications[10]. The benefit of these long acting antipsychotic injections is that it enables clinicians to detect non adherence which would enable them to monitor the individual for early signs of relapse and early intervention. This is helpful for individuals who have poor social support with a lack of resources for daily supervision of medication, in patients who are resistive to being supervised by caregivers and in patients who are suspected of being partially compliant.

MANAGEMENT OF STRESS

The Stress-Vulnerability model emphasises that individuals with Schizophrenia have a biologically mediated vulnerability to stressful events that can result in acute psychosis[11]. Therefore individuals who have achieved remission on medication and those with residual symptoms may experience episodes of relapse when faced with significant stressors. Herz et al[12] stated that a full blown relapse is dependant upon the complex interaction between an individual's degree of vulnerability, nature of stressful event and presence of protective factors such as coping skills, social support and therapeutic interventions.

For such individuals, it is necessary to preempt the effect of a stressful situation to prevent a relapse if possible. Management of stress is focused on identification of possible stressors, facilitating use of structured problem solving by the individual and family, decreasing activities or interactions that increase stress levels and the use of stress management techniques such as relaxation training.

MANAGEMENT OF POOR SOCIAL SUPPORT

Poor social support contributes to a relapse in Schizophrenia in several ways. An individual who lacks family or social support may be more likely to default treatment if he is not supervised, if he lacks motivation or has financial difficulties that deter him from complying with treatment. Good social support also has a protective effect in helping the patients to overcome stressful situations. Therefore it is crucial that for such individuals who lack social support, social interventions such as financial support,

placements in staff supported accommodation and participation in social activities are provided.

Patients who are relapsing often become more isolative, withdrawn and amotivated, which may lead to them defaulting their outpatient appointments. When these individuals also have poor social support, the early signs of relapse may be missed, thus leading to a full blown relapse. Therefore, clinicians may have to use assertive outreach techniques to engage these patients and encourage them to seek treatment early. Case Managers that work within various psychiatric hospital settings often employ assertive outreach techniques such as contacting patients through phone calls, letters or even conducting home visits if they are concerned that the patient may be relapsing. These case managers or care coordinators not only act as a form of assertive outreach for such patients but also as a form of social and therapeutic support for patients who are able to identify their early warning signs. In such cases the case managers provide frequent monitoring of symptoms, conduct risk assessments, assist in problem solving and management of any precipitating stressors as well as coordinating any changes in the treatment with the psychiatrist or psychologist. These assertive outreach interventions aid in possibly engaging the patient and preventing a full blown relapse.

MANAGEMENT OF SUBSTANCE MISUSE, SMOKING AND OTHER MEDICATION

Individuals may experience a relapse of Schizophrenia due to misuse of substances such as alcohol or illicit drugs. These substances can precipitate or cause an exacerbation of psychotic symptoms due to a direct intoxication effect, as a withdrawal effect, through reduced metabolism of the antipsychotic medication or through an indirect effect on the individual's sleep pattern or mood.

Patients may also become noncompliant to the medication due to a potentiation of side effects, such as increased lethargy, drowsiness or impaired concentration, which the patient may misattribute as side effects solely due to the medication. Stimulants like Amphetamines and Cocaine can cause psychotic symptoms, whilst drugs like Cannabis may precipitate or trigger further episodes of relapse. Therefore it is imperative that individuals with a history of substance use are educated on the effects of the substance on their mental health and its impact on the risk of relapse of Schizophrenia.

Smoking also has the potential to cause relapses through its effect on antipsychotic medication. People with mental illness are 2-3 times more likely than the general population to develop and maintain a nicotine addiction. Cigarette smoke contains polycyclic hydrocarbons that are known to stimulate the hepatic microsomal enzyme system that is also responsible for metabolism of many psychotropic drugs. Therefore smoking can reduce the levels of some antipsychotic medications such as Haloperidol, Clozapine and Olanzapine. Hence, if a stable patient experiences recurrent relapses, a history of concurrent or episodic smoking must be elicited. Psychoeducation on the interaction between smoking and medication as well as interventions for smoking cessation must be offered in such situations.

Apart from substances such as alcohol and illicit drugs, it is essential to elicit if the individual has been taking any other prescription medicine or traditional medicine. Interactions may occur between antipsychotic medication and other prescription or traditional medicine which may lead to a lowering of the levels of the antipsychotic medication. For example, antacids and barbiturates may reduce levels of Chlorpromazine and Haloperidol. There have also been multiple case reports of contaminated traditional medicine containing steroids or small doses of amphetamines, which can cause psychotic symptoms. Certain prescription medications such as fluoroquinolones, isoretenoin, high doses of antihistamines, antidepressants, slimming pills such as phentermine and sibutramine can cause psychotic symptoms as an adverse effect. Therefore, in an individual with recurrent relapses, it would be essential to screen for any concurrent medication or substance use that may be the precipitating or causing the relapse.

MANAGEMENT OF HIGH EXPRESSED EMOTION

Brown et al[13] showed that patients with Schizophrenia who were discharged to live with their parents or spouses appeared to relapse more often then patients who lived with other relatives or non-relatives. This led to the concept of 'expressed emotion'. This term encompasses hostility, emotional over-involvement and critical comments displayed by the caregivers of a patient. It can be measured using the semi-structured Camberwell Family Interview. There have been several studies that have duplicated these findings of the negative effects of high expressed emotions on the risk of relapse in patients with Schizophrenia. Relapse rates were observed to be much lesser in families with low expressed emotions or where caregivers expressed more positive remarks towards the patients.

Therefore based on these findings, interventions are targeted towards reducing the level of high expressed emotions in caregivers to manage to risk of relapse. Treatment of high expressed emotions involves family psychoeducation on the symptoms, treatment and prognosis of Schizophrenia, communication training, problem solving as well as developing coping strategies. Mari et al[14] showed that family interventions not only reduced the level of expressed emotions but also significantly increased compliance to medication and showed a reduction in hospitalisation when compared to a control group at 1 year follow up. This was supported by Randolph et al[15], whose study showed that behavioral family therapy was of benefit in reducing high expressed emotions as only 15% of the patients in the therapy group experienced a relapse when compared to a 55% relapse rate in the control group. This emphasises the importance of interventions to reduce high expressed emotions in order to reduce the risk of relapse in individuals with Schizophrenia.

CONCLUSION

A multitude of risk factors that can precipitate a relapse in Schizophrenia has been described above and the specific management of each individual factor has been specified. However, it is important to consider that a relapse may be secondary to any individual factor or several factors acting concomitantly. Therefore, a thorough history and assessment should be conducted to elicit all contributory factors and appropriate interventions undertaken to address them in order to prevent the onset of a full blown relapse or to help the individual to achieve remission of symptoms.

REFERENCES

1. Davis JM. Overview: Maintenance therapy in psychiatry: I. Schizophrenia. Am J Psychiatry 1975;132:1237-45.
2. Hogarty GE, Ulrich RF. The limitations of antipsychotic medication on schizophrenia relapse and adjustment and the contributions of psychosocial treatment. J Psychiatr Res 1998; 32:243-50. doi: 10.1016/S0022-3956(97)00013-7
3. Csernansky JG, Schuchart EK. Relapse and rehospitalization rates in patients with schizophrenia: effects of second generation antipsychotics. CNS Drugs 2002;16:473-84.
4. National Institute for Clinical Excellence. Guidance on the use of newer (atypical) antipsychotics drugs for the treatment of schizophrenia. NICE, 2002.
5. American Psychiatric Association. Practice guideline for the treatment of patients with schizophrenia, second edition. Am J Psychiatry. 2004;161:1-56.
6. Weiden PJ, Zygmunt A. medication noncompliance in schizophrenia. Part I: assessment. J Prac Psych Behav Health 1997;3:106-10.
7. Robinson D, Woerner MG, Alvir JM, Bilder R, Goldman R, Geisler S. Predictors of relapse following response from a first episode of schizophrenia or schiaffective disorder. Arch gen Psychiatry 1999;56:241-7.
8. Dixon L, Lehman A. Family interventions for schizophrenia. Schizophr Bull 1995;21:631-43. doi: 10.1093/schbul/21.4.631
9. Herz MI, Lamberti JS, Mintz J, et al. A program for relapse prevention in schizophrenia: A controlled study. Arch Gen Psychiatry 2000;57:277-83. doi: 10.1001/archpsyc.57.3.277
10. Kane JM, Davis JM, et al. A multidose study of haloperidol decanoate in the maintenance treatment of schizophrenia. Am J Psychiatry 2002;159:554-560. doi: 10.1176/appi.ajp.159.4.554
11. Zubin J, Spring B. Vulnerability: A new view of schizophrenia. J Abnorm Psychol 1977;86:103-26. doi: 10.1037/0021-843X.86.2.103
12. Herz MI, Lamberti JS. Prodromal symptoms and relapse prevention in schizophrenia, Schizophr Bull 1995;21:541-51. doi: 10.1093/schbul/21.4.541
13. Brown GW, Carstairs GM & Topping G. Post hospital adjustment of chronic mental patients. Lancet 1958:2;685-9. doi: 10.1016/S0140-6736(58)92279-7
14. Mari JJ, Streiner DL. An overview of family interventions and relapse on schizophrenia: meta-analysis of research findings. Psychological Medicine 1994;24:565-78. doi: 10.1017/S0033291700027720
15. Randolph ET, Elth S, Glynn SM et al. Behavioural family management in schizophrenia. Outcome of a clinic based intervention. British Journal of Psychiatry 1994;164:501-6. doi: 10.1192/bjp.164.4.501

LEARNING POINTS

- **Relapse of psychotic symptoms in Schizophrenia occurs in up to 40% of patients within a year of being hospitalised,**
- **A relapse may be secondary to any individual factor or several factors acting concomitantly. Risk factors that can precipitate a relapse in Schizophrenia are: significant residual psychopathology, poor compliance to medication, poor insight, substance misuse, interactions with other medication, poor social support, increased stress and caregivers with high expressed emotions.**
- **A thorough history and assessment should be conducted to elicit all contributory factors and appropriate interventions undertaken to address them in order to prevent the onset of a full blown relapse or to help the individual to achieve remission of symptoms.**
- **It is necessary to implement a proactive approach towards the prevention of relapses by using strategies such as psychoeducation and early identification of relapse signatures.**
- **More importantly, it should be emphasised that empowerment of the individuals in understanding and managing their illness is crucial.**

UNIT NO. 6

UPDATE ON MEDICATIONS IN SCHIZOPHRENIA

Dr Roger Ho Chun Man

ABSTRACT

Antipsychotics are a pharmacologically heterogeneous group of compounds, but all act as D2 dopamine receptor antagonists, an action linked to their antipsychotic effect. Today, sixty years on since 1952, we have the FGAs and the SGAs. These medications continue to be useful, and continue to have some troubling adverse effects. As a class, the FGAs are more likely to be associated with EPS but this is primarily true of medications that bind tightly with D2 neuroreceptors, such as haloperidol, and less true of medications that bind weakly, such as chlorpromazine. Anticholinergic effects are especially prominent with weaker-binding FGAs, as well as with the SGA clozapine. As a class, the SGAs, especially clozapine and olanzapine generally tend to cause more problems relating to the metabolic syndrome, such as obesity and type 2 diabetes mellitus. All antipsychotic medications are associated with an increased likelihood of sedation, sexual dysfunction, postural hypotension, prolonged QT interval and sudden death. Primary care physicians need to be familiar with the individual adverse effect profiles of these medications.

Keywords: Antispychotics, heterogeneous, dopamine receptor antagonists. First generation antipsychotics, second generation antipsychotics, extra-pyramidal symptoms, metabolic syndrome.

SFP2013; 39(1): 26-34

INTRODUCTION

The antipsychotics are the only class of drugs for which the evidence base shows consistent efficacy in treating the core symptoms of schizophrenia and schizophrenia-like illnesses (Mackin & Thomas, 2011)[1]. Antipsychotics are a pharmacologically heterogeneous group of compounds, but all act as D2 dopamine receptor antagonists, an action linked to their antipsychotic effect (Agid et al, 2007)[2].

Historically, two generations of antipsychotics are recognised. The "typical" (first generation) antipsychotic drugs (e.g haloperidol, chlorpromazine, and trifluoperazine) have been used to treat schizophrenia since the 1950s. The "atypical" (second generation) antipsychotic drugs (e.g. resperidone, olanzapine, and clozapine) were introduced into routine practice from the 1990s. Both classes are used in the acute phase of schizophrenia and related psychoses and for long term maintenance and prevention of relapse. Choosing the most appropriate drug and formulation for an individual may be more important than choosing the drug group.

This study unit updates the reader on several aspects of the medications in schizophrenia: treatment goals, mechanism of action of the antipsychotics, the typical antipsychotic drugs (FGAs) and atypical antipsychotic drugs (SGAs), adverse effects of antipsychotics, antipsychotic induced weight gain, and the use of antipsychotic medications in the different phases of schizophrenia.

CHANGES IN TREATMENT GOALS FOR SCHIZOPHRENIA

Figure 1 shows the changes in treatment goals for schizophrenia over the past decades as its psychopharmacology became better understood. Today, the goal of treatment is a good functional outcome targeted at remission and recovery.

Prior to the 1950s, treatment of psychotic disorders involved primarily institutional and supportive interventions, without effective treatment for the symptoms of these illnesses. (Hudepohl & Nasrallah, 2012).

In 1952, the arrival of the first antipsychotic medication chlorpromazine and with the initial success of this drug and other first generation antipsychotic medications effectively reduced the intensity of positive psychotic symptoms of hallucinations and delusions, allowing most institutionalised patients with schizophrenia to be discharged into community treatment. All in all, 51 neuroleptics from six chemical classes were developed; 12 are currently available in the USA (Hudepohl & Nasrallah, 2012; Nasrallah and Tandon, 2009)[3,4]. These are referred to as "first generation", "classic", "conventional", or "typical antipsychotics. Although useful in dealing with the positive psychotic symptoms, the first generation antipsychotics (FGAs) had a range of adverse effects, notably extrapyramidal symptoms (EPS) such as dystonia, parkinsonism, akathisia, and tardive dyskinesia.

In 1959, clozapine was introduced as the first antipsychotic drug synthesised without any risk of EPS, which led it to being labelled as an "atypical". It was initially marketed in Europe in 1972, but was withdrawn from the market in 1974 due to reports of many fatalities related to agranulocytosis. In 1989, clozapine was reintroduced in the USA after controlled studies showed efficacy in treatment-refractory patients with persistent delusions and hallucinations who had failed to respond to several FGAs. Weekly leukocyte monitoring was made a requirement for treatment, although less than 1% incidence was observed. (Hudepohl & Nasrallah, 2012)[3].

Following the approval of clozapine, other "atypical antipyschotics" were developed and approved by the Food and Drug Administration (FDA) which had lower levels of EPS and somewhat broader efficacy on mood and negative

ROGER HO CHUN MAN, Consultant and Assistant Professor, Department of Psychological Medicine, National University Health Systems

symptoms, mimicking the effects of clozapine without the risk of agranocytosis. (Hudepohl & Nasrallah, 2012)[3]

Today, sixty years on since 1952, we have the FGAs and the SGAs. These medications continue to be useful, and continue to have some troubling adverse effects. With a better understanding of these side effects, we are able to optimise the use of these medications despite the troubling side effects to achieve remission and recovery with better functional outcomes.

FIGURE 1. CHANGES IN TREATMENT GOALS FOR SCHIZOPHRENIA OVER THE PAST DECADES

1952	•	Reduction of (positive) psychotic symptoms – introduction of chlorpromazine
	•	Long-term treatment
1980	•	Negative symptoms
1990	•	Neuropsychological deficits
	•	Health-Related Quality of Life (HRQoL)/functional deficits
2000	•	Subjective well-being (SW)
	•	Early detection/delay of transition to psychosis
2005	•	Remission/recovery (functional outcome)

DOPAMINERGIC RECEPTOR BLOCKING IN THE MAJOR DOPAMINE PATHWAYS

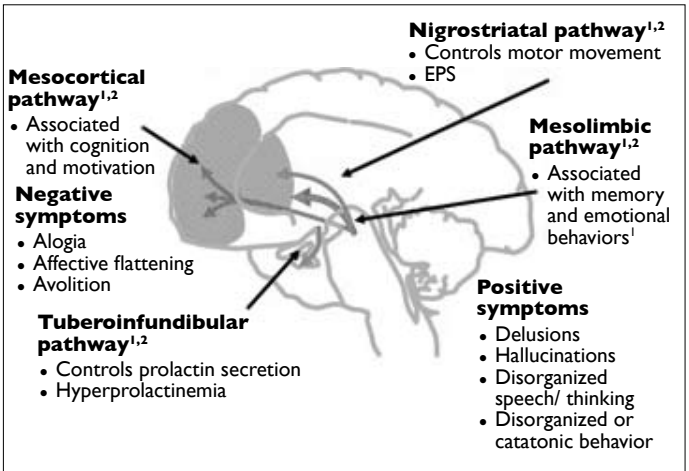
The dopamine hypothesis. The dopamine hypothesis of schizophrenia is currently used to explain the positive and negative symptoms of the disease. The postulate is that overactive mesolimbic dopamine (DA) neurons cause the positive symptoms of psychosis and the corollary that underactive mesocortical DA neurons, cause the negative, cognitive, and affective symptoms of schizophrenia.

The dopamine pathways are neural pathways in the brain which transmit the neurotransmitter dopamine from one region of the brain to another. There are 8 dopamine pathways in the brain, of which the four major ones are described below. See Figure 2.

Mesolimbic pathway – The mesolimbic pathway transmits dopamine from the ventral tegmental area (VTA) to the limbic system via the nucleus accumbens. The VTA is located in the midbrain and the nucleus accumbens is in the ventral striatum. Positive symptoms of schizophrenia (namely, delusions, and hallucinations) are believed to be the result of dopaminergic hyperactivity in the mesolimbic pathway of the brain. FGAs are antagonists at postsynaptic D2 receptors, and these treat the positive symptoms of schizophrenia by reducing dopaminergic activity. (Hudepohl & Nasrallah, 2012)[3].

Mesocotical pathway – The mesocortical pathway transmits dopamine from the VTA to the frontal cortex. FGAs also block D2 receptors in the mesocortical pathways, which can worsen the cognitive and negative symptoms of schizophrenia. FGAs bind to D2 receptors tightly and for long periods of time, which can lead to an increase in adverse effects (Hudepohl & Nasrallah, 2012)[3].

FIGURE 2. MAJOR DOPAMINE PATHWAYS



1. Kandel ER et al. *Principles of Neural Science.* 3rd ed. St Louis, MO: Elsevier; 1991.
2.Stahl SM. *Essential Psychopharmacology: Neuroscientific Basis and Practical Applications.* 2nd ed. New York, NY: Cambridge University Press; 2000.

Nigrostriatal pathway – The nigrostriatal pathway transmits dopamine from the substantia nigra to the striatum. This pathway is associated with motor control. Deficiency of dopamine production in the substantia nigra results in Parkinson's disease.

Tuberoinfundibular pathway – The tuberoinfundibular pathway transmits dopamine from the hypothalamus to the pituitary gland. In the tuberoinfundibular pathway from the hypothalamus to the pituitary gland, prolactin is under tonic inhibition of dopamine. D2 blockade results in decreased dopamine tone, thereby increasing the secretion of prolactin. While this state is normal during the postpartum period, it can lead to adverse effects in some patients treated with a FGA with high potency D2 neurorecepor blockade e.g. fluphenazine, haloperidol, thiothixene, and trifluoroperazine. Respiridone, which is the only SGA with prominent D2 blockade of this pathway, also has hyperprolactinemia as a adverse effect.

In the 1990s, the atypical antipsychotics were developed, branded, and marketed with a dual serotonin-dopamine receptor antagonism (SDA) mechanism of action whereby they simultaneously block both D2 and serotonin-2A (5HT-2A) receptors allowing for adequate antipsychotic effectiveness while lowering the risk of extrapyramidal symptoms (EPS). This improved neuromuscular safety profile occurs as the 5HT-2A receptor antagonism allows these atypical antipsychotics to be more selective at dampening mesolimbic DA activity while allowing less interference in the nigrostriatal DA pathway (Schwartz et al, 2012)[5].

The glutamine hypothesis. To be up to date, there is another hypothesis in the horizon that offers the glutamine hypothesis to explain the less than stellar results from the blocking of DA neurons. (Schawartz et al, 2012)[5]. Until more evidence is available, the dopamine hypothesis will continue to be the working hypothesis to explain the psychopharmacology of schizophrenia.

TYPICAL ANTIPSYCHOTICS – FIRST GENERATION ANTIPSYCHOTICS (FGAS)

Potency

The FGAs can be divided into 3 classes based on their potency of dopamine blockade in comparison to effects ast other neurotransmitter receptors, and the dose needed to achieve therapeutic effectiveness. See Table 1.

Mechanism of action

FGAs are antagonists at postsynaptic D2 receptors in the mesolimbic pathway. D2 blockade in the mesocortical pathways also occurs, which can worsen the cognitive and negative symptoms of schizophrenia. In addition to D2 antagonism, FGAs also have blockade effects at M1 muscarinic cholinergic receptors leading to anticholinergic symptoms of constipation, dry mouth, blurred vision, urinary symptoms, and sedation; blockade at H1 histamine receptors leading to sedation and weight gain; and blockade at alpha1-adrenergic receptors leading to dizziness, orthostatic hypotension, and sedation.

High potency D2 neuroreceptor blockers (e.g. Haloperidol) have more EPS and less histaminic e.g. sedation, alpha adrenergic (e.g. orthostatic hypotension) and anticholinergic effects (e.g. dry mouth) effects. Low potency D2 neuroreceptor blockers (e.g. Chlorpromazine) have fewer EPS but more H1, a1, and muscarinic blocking effects.

Efficacy and indications

FGAs are indicated for treatment of the positive symptoms of schizophrenia and schizoaffective disorder in the acute stage as well as for long-term maintenance. Negative symptoms (e.g. apathy, anhedonia, avolition, and alogia, can be worsened through the use of these medications. Cognitive dysfunction and dysphoria are also observed when EPS emerges.

ATYPICAL ANTIPSYCHOTICS – SECOND GENERATION ANTIPSYCHOTICS (SGAS)

Whilst the FGAs were successful at treating the symptoms of schizophrenia and triggering the deinstitutionalisation movement, most patients with psychotic disorders were still not able to regain social functioning. The search for medications to deal with FGA treatment-resistant patients resulted in the introduction of clozapine and other antipsychotics which are more effective than the FGAs for both the positive and negative symptoms of schizophrenia. These were the SGAs and were modelled after clozapine's neuroreceptor profile of greater serotonin 5-HT2A antagonism than dopamine D2 antagonism. Table 2 shows selected SGAs and the year they were introduced.

Mechanism of action

SGAs employ both serotonin and dopamine antagonism to target symptoms, and this distinguishes them from the FGAs, the latter having mainly strong dopamine antagonism. In the SGAs, D2 antagonism tends to be more specific in they target mesolimbic and mesocortical pathways and have less effect on nigrostriatal pathways, leading to less risk of EPS. Of the SGAs, respiridone is different in that it has a higher affinity of the D2 receptor and hence has a dose related increase in EPS as well as prolactin.

Serotonergic antagonism occurs primarily at the 5-HT2A neuroreceptor. Blockade of these neuroreceptor in the cortex leads to decreased glutamate release from the cortical glutamate projections in the ventral tegmental area (VTA). This leads to decreased excitation of dopamine neurons in the VTA and further blockade of positive symptoms of schizophrenia.

SGAs also have some effects on cognitive, negative, and affective symptoms of schizophrenia. These symptoms are thought to be due to low dopamine activity in mesocortical pathways. 5-HT2A blockade leasds to increased frontal dopamine (by releasing 5-HT inhibition of dopamine), which may be the

TABLE 1. SELECTED FIRST GENERATION ANTIPSYCHOTICS

Drug	Initial dose (mg)	Maintenance dose (mg)	Maximum dose (mg)	Dopamine D2 neuroreceptor potency
Chlorpromazine	75	200-400	1000	Low
Thioridazine	25-150	75-400	800	Low
Perphenazine	12-24	8-24	64	Medium
Fluphenazine	2.5-10	1-5	40	High
Haloperidol	2-6	12-18	40	High
Thiothixene	5-10	15-30	60	High
Trifluoperazine	2-15	6-20	80	High
Depot antipsychotics (long acting)				
Flupenthixol decanoate (Fluanxol depot)	5-40	20-80/4 weeks	80/2 weeks	High
Fluphenazine decanoate (Modecate)	2.5-12.5	12.5-100/2-4 weeks	50-100/2-4 weeks	High
Zuclopenthixol acetate (Clopixol acuphase)	50-150/2-3 days		150/day X 4 days	High
Zuclopenthixol decanoate (Clopixol)	100-400	150-300/2-4 weeks	400/2 weeks	High

TABLE 2. SELECTED SECOND GENERATION ANTIPSYCHOTICS

Drug	Year introduced	Usual daily dosage mg
Aripridazole	2002	10-30
Clozapine	1989	300-600
Olanzapine	1996	10-20
Quetiapine	1998	250-600
Respiridone	1994	3-6
Ziprasidone	2001	40-80
Depot injection – Long acting antipsychotic		
Respiridone (Consta) Inj		25-37.5mg/2 weeks

mechanism with which these medications target these negative, cognitive and affective symptoms. In addition to 5-HT2A blockade, the SGAs have effects at other serotonin receptors. They also work at other DA receptors as well as muscarinic, histaminic, and alpha-adrenergic receptors. The SGAs may also have effect in the insulin regulation system.

Aripiprazole as a SGA deserves special mention as a partial D2 agonist, leading to effective reduction in positive psychotic symptoms with minimal reisk of EPS. In the mesolimbic pathways, aripiprazole exerts D2 antagonism, leading to reduction of dopamine output and reduction of positive psychotic symptoms. In the nigrostraital pathways, however, partial D2 antagonism prevents reduction of dopamine tone and leads to normal functioning. Akathisia may however emerge transiently during the initiation of aripiprazole.

SGAs have low affinity to dopamine D2 receptors and, compared to FGAs, dissociate more easily from D2 neuroreceptors. Landmark positron emission tomography (PET) studies by Kapur and Seeman, 2001 (Hudepohl & Nasrallah, 2012), showed that transient occupancy (60-65%) of D2 neuroreceptors is sufficient for antipsychotic activity and results in a lower incidence of EPS and other motor side-effects. This "hit and run" theory is common to the SGAs and explains improved tolerability of these medications. The PET D2 occupany studies also found that EPS emerges when 78% or higher occupancy of the D2 neuroreceptors occur. (Hudepohl & Nasrallah, 2012)[3].

Efficacy and indications

All of the SGAs have an FDA indication for treatment of schizophrenia, for both acute exacerbation and long-term maintenance treatment. The SGAs are mainly effective for the treatment of positive symptoms (delusions, hallucinations, thought disorder), and to a lesser extent for negative symptoms (apathy, blunted affect, asociality, lack of motivation), and cognitive symptoms (impairments in executive functions and memory). Maintenance treatment is indicated to prevent psychotic relapse.

Clozapine has two unique indications in the treatment of schizophrenia. It is approved for use only in treatment-resistant and refractory schizophrenia given its risk of agranulocytosis as a life threatening adverse effect. Current treatment recommendations state that a patient must fail an adequate trial of two SGAs prior to a trial of clozapine. It is also the only drug that is FDA-approved for the treatment and prevention of suicidality in patients with schizophrenia.

ARE SGAs MORE EFFECTIVE THAN FGAs?

For two decades, the SGAs have dominated the market under the assumption that they are more effective than the FGAs. The results of two publicly funded trials in US designed to evaluate the effectiveness of the antipsychotics under real-world conditions have called into question these prescribing preferences.

The Clinical Anti-psychotic Trials of Intervention Effectiveness study (CATIE). This study was designed to compare the FGA perphenazine with several SGAs using "all cause discontinuation" as a proxy measure for effectiveness (Muench & Hamer, 2010; Lieberman et al, 2005)[6,7].

The Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS). This study measured quality of life and other effectiveness measures. (Muench & Hamer, 2010; Jones et al, 2006)[6,8].

Neither study demonstrated a clear difference in effectiveness between FGAs and non-clozapine SGAs.

Meta-analysis. A meta-analysis in 2009 by Leucht et al of 150 double blind clinical trials, involving 21533 patients further clarified the situation. (Gupta, 2010; Leucht et al, 2009)[10,11]. Four SGAs were found to be better than FGAs for overall efficacy (both positive and negative symptoms). Among them, the effect size was largest for clozapine –0.52 (95% CI –0.75 to –0.29, P<0.001), olanzapine –0.28 (–0.38 to –0.18, p <0.0001) and lastly rispiridone –0.18 (–0.22 to –0.05, p = 0.002). The other SGAs (aripiprazole, quetiapine, zotepine, ziprasidone, sertindole) were not more efficacious than FGAs, even on negative symptoms. EPS, expected, were prevalent in FGAs. On the other hand, SGAs (except ziprasidone and aripiprazole) induced more weight gain. Similarly, some drugs were better for depressive symptoms (namely, amisulpride, clozapine, olanzapine, aripiprazole, and quetiapine).

In the 2009 guideline, NICE no longer recommends SGAs as a first-line treatment which was its recommendation in 2002. (NICE, 2009)[9]

The implications of three studies quoted above and the position of NICE are now clear. SGAs are not always superior. In some patients, FGAs may be more effective and better tolerated than the SGAs. With the exception that clozapine is more effective for treatment resistant patients, the choice of antipsychotic should depend on the potential for adverse effects in individual patients. General comparison between the FGA and SGA classes are less helpful than comparisons among specific medications because each presents its own challenges in terms of balancing effectiveness with safety and tolerability. (Muench & Hamer, 2010)[6].

ADVERSE EFFECTS OF ANTIPSYCHOTIC MEDICATIONS

The use of antipsychotic medications is a balance between the benefit of relieving psychotic symptoms and the harm of troubling adverse effects.

As a class, the FGAs are more likely to be associated with EPS but this is primarily true of medications that bind tightly with D2 neuroreceptors, such as haloperidol, and less true of medications that bind weakly, such as chlorpromazine. Anticholinergic effects are especially prominent with weaker-binding FGAs, as well as with the SGA clozapine.

As a class, the SGAs, especially clozapine and olanzapine generally tend to cause more problems relating to the metabolic syndrome, such as obesity and type 2 diabetes mellitus.

All antipsychotic medications are associated with an increased likelihood of sedation, sexual dysfunction, postural hypotension, prolonged QT interval and sudden death.

Primary care physicians need to be familiar with the individual adverse effect profiles of these medications. Vigilance for the occurrence of adverse effects, willingness to adjust or change medications as needed or work with psychiatric colleagues to do so, and the preparedness to treat any resulting medical sequelae will result in better functional outcome of patients with schizophrenia.

The comparative risk of these adverse effects amongst them are shown in Table 3.

Extrapyramidal symptoms (EPS)

Antipsychotic medications cause four main extrapyramidal symptoms: pseudoparkinsonism, akathisia, acute dystonia, and tardive dyskinesia. The first three usually begin within a few weeks of starting a new medication (or increasing the dosage). These symptoms may cause discomfort, social stigma, and poor compliance.

Pseudoparkinsonism. This is a reversible syndrome of tremulousness in the hands and arms, rigidity in the arms and shoulders, bradykinesia, akinesia, hypersalivation, masked facies, and shuffling gait. The bradykinesia or akinesia can create a diagnostic dilemma, with symptoms resembling depression or even the negative symptoms of schizophrenia (i.e., an inability to pay attention, the loss of a sense of pleasure, the loss of will or drive, disorganization or impoverishment of thoughts and speech, flattening of affect, and social withdrawal). Dosage reduction helps.

Akathisia. This is a feeling of inner restlessness which can be manifested as excessive pacing or inability to remain still for any length of time. Differentiating akathisia from psychiatric anxiety and agitation can be difficult. Treatment consists of dosage reduction when possible, or the addition of a low-dose beta blocker, such as propranolol (Inderal) at 20 to 80 mg per day.

TABLE 3. COMPARATIVE RISK OF ADVERSE EFFECTS OF ANTIPSYCHOTIC MEDICATIONS*

Adverse effect	Low potency FGAs@	High potency FGAs#	SGAs Aripiprazole	Clozapine	Olanzapine	Quetiapine	Respiridone	Ziprasidone
Extrapyramidal symptoms	+	+++	+	0	+	0	++	+
Sedation	+++	+	+	+++	++	++	+	+
Seizures	+	+	+	+++	+	+	+	+
Prolonged QT interval	++$	+	+	+	+	+	+	++
Postural hypotension	+++	+	+	+++	+	++	++	+
Anticholinergic effects	+++	+	0	+++	+	+	0	0
Sexual dysfunction	+++	++	+	+	+	+	++	+
Hyper Prolactinemia	++	+++	0	0	+	0	+++	+
Neuroleptic malignant syndrome	+	++	+	+	+	+	+	+
Dyslipidemia	++	+	0	+++	+++	++	+	0
Type 2 diabetes mellitus	+	+	+	++	++	+	+	+
Weight gain	++	+	0	+++	+++	++	++	0

NOTES
0 = rare; + = low risk; ++ = medium risk; +++ = higher risk
FGAs = first generation antipsychotics; SGAs = second generation antipsychotics
** = Effects are approximate, and relative to other antipsychotic medications rather than absolute risk of an adverse effect occurring*
@ = FGAs with lower potency dopamine D2 neuroreceptor blockade, including chlorpromazine and thioridazine
 # = FGAs with higher potency dopamine D2 neuroreceptor blockade, including fluphenazine, haloperidol, thiothixene, and trifluoperazine. Please note that the FGA perphenazine is considered to have intermediate dopamine D2 neuroreceptor blockade, with an adverse effect profile between the low- and high-potency FGAs
$ = individually, thioridazine has a higher risk of prolonged QT interval and should be used only when no other appropriate options are available.
SOURCES: Muench & Hamer, 2010; Haddad & Shama, 2007; Gardner et al, 2005.

Dystonic reactions. These are spastic contractions of the muscles, including oculogyric crisis, retrocollis, torticollis, trismus, opisthotonos, or laryngospasm. These uncomfortable reactions can be life threatening if left untreated. Intervention requires administration of intravenous or intramuscular anticholinergic agents.

Tardive dyskinesia. This is an involuntary movement disorder occurring with long-term antipsychotic treatment; it may not be reversible even if the medication is discontinued. Tardive dyskinesia usually involves the orofacial region, but all parts of the body can be involved. Abnormal movements can include myoclonic jerks, tics, chorea, and dystonia. They become most evident when patients are aroused, but ease during relaxation and disappear during sleep. Risk factors for developing tardive dyskinesia include long-term therapy with FGAs at higher dosages, older age, female sex, and concurrent affective disorders. Attempts to treat tardive dyskinesia usually consist of discontinuing the offending agent.

Sedation

Sedation is common with antipsychotic medications and is dose related. It can be a cause of poor compliance and, if persistent, can interfere with social and vocational functioning. Low-potency FGAs and clozapine are the most sedating, with some effect from olanzapine and quetiapine. Somnolence can be alleviated by lowering the dosage, changing to a single bedtime dose, or switching to a less sedating medication.

Seizures

All antipsychotics can lower the seizure threshold. They should be used with caution in patients who have a history of seizures and in those with organic brain disorders. Depot antipsychotics should not be used in patients with epilepsy because they cannot be quickly withdrawn.

Prolonged QT interval

All antipsychotics can contribute to prolongation of ventricular repolarization (prolonged QT interval), which can in turn lead to torsades de pointes and sudden cardiac death. This effect is most marked with the low-potency FGA thioridazine and the SGA ziprasidone, and is dose dependent. The incidence of sudden cardiac death among patients taking antipsychotics is about twice that of the general population.

Postural hypotension

Orthostatic hypotension can occur with all antipsychotic medications, depending on the degree of α1-adrenorecep- tor antagonism, particularly with low-potency FGAs and clozapine. It can also occur with risperidone and quetiapine, especially with rapid titration. This effect is more common in older adults (with risk of falls), those on blood pressure medications, and those who have other cardiovascular diseases. With careful dose titration, patients may become tolerant to this effect. Decreasing or dividing doses or switching to a medication with a lesser antiadrenergic effect are treatment options.

Anticholinergic effects

Constipation, urinary retention, dry mouth, blurred vision and, at times, cognitive impairment are highly likely adverse effects of the low potency FGAs. Olanzapine and quetiapine also have been shown to do so at high dosages. Medication doses can be lowered or divided to reduce this problem.

Sexual dysfunction

Some 40% patients taking antipsychotic medications report problems with sexual dysfunction, which can lead to poor medication adherence. Use of antipsychotics can affect all phases of sexual function, including libido, arousal, and orgasm. Both FGAs and SGAs can impair arousal and orgasm in men and women.

Hyperprolactinemia

Antipsychotics cause high prolactin levels by blocking the normal tonic inhibition on pituitary mammotropic cells of dopamine produced in the hypothalamus. Hyperprolactinemia is common with the use of any FGA, as well as with the SGA risperidone and is dose dependent. Hyperprolactinemia can be asymptomatic, but may cause gynecomastia, galactorrhea, oligo- or amenorrhea, sexual dysfunction, acne, hirsutism, infertility, and loss of bone mineral density. Symptoms often appear within a few weeks of beginning the antipsychotic or increasing the dosage, but can also arise after long-term stable use. Presence of osteoporosis, sexual side effects, or prolactin-dependent breast cancer may necessitate switching to an antipsychotic that does not raise prolactin levels, such as aripiprazole or quetiapine.

Neuroleptic malignant syndrome

Neruoleptic malignant syndrome (NMS) is an idiosyncratic, life-threatening complication of treatment with antipsychotic drugs. The criteria for diagnosis are fever, severe muscle rigidity, and two of the associated symptoms: autonomic (namely diaphoresis, tachycardia), and mental changes (confusion to coma, mutism). The patient should be treated promptly: the causative drugs is stoped, the patient rehydrated, muscle relaxants like dantrolene or baclofen be considered and ventilator support if needed. Benzodiazepines can be given in severe agitation. Further investigations include blood counts, cultures, urine toxicology. The condition carries a risk of death and multi-organ failure, but given adequate supportive treatment the prognosis is good and there are usually no lasting sequelae. Approximately 2 weeks after resolution of NMS, treatment with a low-potency atypical antipsychotic shold be started at a low dose and slowly titrated in a monitored setting with careful assesment for signs of recurrent NMS.(Kipps et al, 2005)[14]

ANTIPSYCHOTIC INDUCED WEIGHT GAIN

Weight gain is a common adverse effect of using anti-psychotic medications, and can be rapid and difficult to control. Weight gain does not seem to be dose dependent within the normal therapeutic range. The effect is worse with clozapine and olanzapine; minimal with aripiprazole and ziprasidone; and intermediate with other antipsychotics, including low-potency FGAs.

Antipsychotic medications can contribute to a wide range of glycemic abnormalities, from mild insulin resistance to diabetic ketoacidosis, as well as worsening of glycemic control in patients with preexisting diabetes. Although FGAs and SGAs can cause these problems, risk is variable—the greatest risk is with clozapine and olanzapine.

Dyslipidemia is also associated with several antipsychotic medications, with increases noted primarily in triglyceride levels. Low-potency FGAs and the SGAs clozapine, olanzapine, and quetiapine are associated with a higher risk of hyperlipidemia. Overall, metabolic disturbances appear to be greatest with clozapine and olanzapine, intermediate with quetiapine and low- potency FGAs, and lowest with aripiprazole, risperidone, ziprasidone, and high-potency FGAs.

RECOMMENDATIONS ON THE USE OF MEDICATIONS IN THE DIFFERENT PHASES OF THE DISEASE

Acute phase management

- Prevent harm by hospitalisation.
- Reduce aggression and threat by rapid tranquilisation (oral lorazepam 1 to 2mg stat, olanzapine zydis 10mg stat or risperidone quicklet 1-2mg stat; if patient refuses oral medication, consider IM lorazepam 2mg stat, and/or IM haloperidol 5-10mg stat).
- Reduce acute symptoms by regular oral antipsychotics. Start at low dose and titrate upwards over 2 weeks. The choice of antipsychotics is based on risk and benefit ratio and patient's preference after explanation of various options. Close monitoring for 2 months to assess effectiveness.

Initial treatment (MOH CPG 2011)[15]

- The patient's social supports, functioning and relative risk of self-harm or harm to others must be evaluated for choice of treatment setting.
- People newly diagnosed with schizophrenia should be offered oral antipsychotic medication. The recommended optimal oral dose of antipsychotics is 300–1,000 mg chlorpromazine equivalents daily for an adequate duration of 4–6 weeks.
- If there is inadequate response by 4–6 weeks or if patient develops intolerable side effects, the medication should be reviewed and another typical or atypical antipsychotics should be used.
- Long-acting depot antipsychotics should not be used for acute episodes because it may take 3–6 months for the medications to reach a stable steady state.
- Electroconvulsive therapy should be considered for patients who have not responded to an adequate trial of antipsychotics and for patients with life threatening symptoms such as catatonia and prominent depressive symptoms.

Stabilisation phase

- Offer psychoeducation to enhance knowledge of illness.
- Minimize the likelihood of relapse by ensuring compliance to medications. Long-acting depot (e.g. IM fluanxol, clopixol). antipsychotics may be indicated in patients in whom treatment adherence is an issue or when a patient expresses a preference for such treatment (MOH CPG 2011)[15]
- Reduce expressed emotion by family intervention.
- Enhance adaptation and coping to social and occupational disturbances by rehabilitation and occupational therapy.
- Facilitate continued reduction in symptoms and promote the process of recovery by psychological interventions e.g. cognitive behaviour therapy and problem solving therapy.
- Antidepressants should be considered when depressive symptoms emerge during the stable phase of schizophrenia (post-psychotic depression). Antidepressants should be used at the same dose as for treatment of major depressive disorder (MOH CPG 2011)[15].

Maintenance phase

- Ensure symptom remission or control by the lowest effective dose of antipsychotics, which should not be lower than half of the effective dose during the acute phase (MOH CPG 2011)[15].
- Monitor and manage adverse effects related to antipsychotics.
- Regular follow-up with a psychiatrist on a regular basis.
- For patient with poor social support, refer to the community psychiatric team for home visit.
- Oral antipsychotics should be used as first-line treatment for patients with an acute relapse of schizophrenia (MOH CPG 2011)[15].
- Patients receiving atypical antipsychotics should be monitored regularly for metabolic side effects (MOH CPG 2011)[15].
- Treatment options for schizophrenia patients who are pregnant should be individualised, with consideration of severity of previous episodes, previous response to treatment and the woman's preference. Abrupt cessation of medications should be avoided. (MOH CPG 2011)[15].

REFERENCES

1. Mackin P, Thomas SH. Atypical antipsychotic drugs. BMJ. 2011 Mar 4;342:d1126. doi: 10.1136/bmj.d1126. PubMed PMID: 21378070.
2. Agid O, Mamo D, Ginovart N, Vitcu I, Wilson AA, Zipursky RB, et al. Striatal vs extrastriatal dopamine D2 receptors in antipsychotic response—a double-blind PET study in schizophrenia. Neuropsychopharmacology 2007;32:1209-15.
3. Hudepohl NS, Nasrallah HA. Antipsychotic drugs. Handb Clin Neurol. 2012;106:657-67. doi: 10.1016/B978-0-444-52002-9.00039-5. Review. PubMed PMID: 22608650.
4. Nasrallah HA, Tandon. Classic antipsychotic medications. In: AF Schatzberg, CB Nemeroff (eds). The American Psychiatric Publishing Textbook of Psychopharmcology. 4th ed. American Psychiatric Publishing, Arlington, 2009:553-4.
5. Schwartz TL, Sachdeva S, Stahl SM. Glutamate neurocircuitry: theoretical underpinnings in schizophrenia. Front Pharmacol. 2012;3:195. doi: 10.3389/fphar.2012.00195. Epub 2012 Nov 26. PubMed PMID: 23189055; PubMed Central PMCID: PMC3505861.
6. Muench J, Hamer AM. Adverse effects of antipsychotic medications. Am Fam Physician. 2010 Mar 1;81(5):617-22. Review. PubMed PMID: 20187598.
7. Lieberman JA, Stroup TS, Mcevoy JP, et al., for the Clinical Antipsychotic Trials of Intervention effectiveness (CATIe) Investigators. effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med. 2005;353(12):1209-23.
8. Jones PB, Barnes TR, Davies L, et al. Randomized controlled trial of the effect on quality of life of second- vs first-generation antipsychotic drugs in schizophrenia: Cost Utility of the Latest Antipsychotic Drugs in Schizophrenia Study (CUtLASS 1). Arch Gen Psychiatry. 2006;63(10):1079-87.
9. National Institute for Health and Clinical Excellence. Core interventions in the treatment and management of schizophrenia in primary and secondary care (update). (Clinical guideline 82.) 2009. www.nice.org.uk/CG82.
10. Gupta S. First-generation vs second-generation antipsychotic drugs: The ongoing saga. Indian J Psychiatry. 2010 Jan;52(1):77. doi:10.4103/0019-5545.58904. PubMed PMID: 20174527; PubMed Central PMCID: PMC2824991.
11. Leucht S, Wahlbeck K, Hamann J, Kissling W. New generation antipsychotics versus low-potency conventional antipsychotics: a systematic review and meta-analysis. Lancet. 2003;361(9369):1581-9.
12. Haddad PM, Sharma SG. Adverse effects of atypical antipsychotics: differential risk and clinical implications. CNS Drugs. 2007;21(11):911-36.
13. Gardner DM, Baldessarini RJ, Waraich P. Modern antipsychotic drugs: a critical overview. CMAJ. 2005;172(13):1703-11.
14. Kipps CM, Fung VS, Grattan-Smith P, de Moore GM, Morris JG. Movement disorder emergencies. Mov Disord. 2005 Mar;20(3):322-34. Review. PubMed PMID: 15584031.
15. Verma S, Chan LL, Chee KS, Chen H, Chin SA, Chong SA, Chua W, Fones C, Fung D, Khoo CL, Kwek SK, Ling J, Poh P, Sim K, Tan BL, Tan C, Tan CH, Tan LL, Tay WK; MOH Clinical Practice Guidelines Workgroup on Schizophrenia. Ministry of Health clinical practice guidelines: schizophrenia. Singapore Med J. 2011 Jul;52(7):521-5; quiz 526. PubMed PMID: 21808964.

LEARNING POINTS

- **Antipsychotics are a pharmacologically heterogeneous group of compounds, but all act as D2 dopamine receptor antagonists, an action linked to their antipsychotic effect.**
- **As a class, the FGAs are more likely to be associated with EPS but this is primarily true of medications that bind tightly with D2 neuroreceptors, such as haloperidol, and less true of medications that bind weakly, such as chlorpromazine.**
- **Anticholinergic effects are especially prominent with weaker-binding FGAs, as well as with the SGA clozapine.**
- **As a class, the SGAs, especially clozapine and olanzapine generally tend to cause more problems relating to the metabolic syndrome, such as obesity and type 2 diabetes mellitus.**
- **All antipsychotic medications are associated with an increased likelihood of sedation, sexual dysfunction, postural hypotension, prolonged QT interval and sudden death.**

ASSESSMENT OF 30 MCQs

FPSC NO : 51
MCQs on SCHIZOPHRENIA
Submission DEADLINE : 9 APRIL 2013 12 NOON

INSTRUCTIONS

- **To submit answers to the following multiple choice questions, you are required to log on to the College On-line Portal (www.cfps2online.org).**
- **Attempt ALL the following multiple choice questions.**
- **There is only ONE correct answer for each question.**
- **The answers should be submitted to the College of Family Physicians Singapore via the College On-line Portal before the submission deadline stated above.**

1. The first psychotic episode of schizophrenia is often preceded by a prodromal phase lasting weeks or even years. Which of the following symptoms is NOT consistent with the prodromal phase?

(A) Delusions.
(B) Sleep disturbance.
(C) Poor concentration.
(D) Irritability.
(E) Anxiety.

2. About the symptoms that may be present in a patient with schizophrenia, which of the following symptoms is LEAST LIKELY to be present?

(A) Hallucinations.
(B) Delusions.
(C) Alogia.
(D) Grandiosity.
(E) Anhedonia.

3. About the age of onset of schizophrenia in men, which of the following is CORRECT?

(A) 10 – 20 years.
(B) 15 – 25 years.
(C) 20 – 30 years.
(D) 25 – 35 years.
(E) 30 – 40 years.

4. The genetic vulnerability in schizophrenia arises from a complex combination of multiple genes of small effect. Which of the following lifetime risk of schizophrenia is CORRECT?

(A) 25% for a child with patients who do not have the disorder.
(B) 13% for a child with one parent with schizophrenia.
(C) 30% for a child with both parents with schizophrenia.
(D) 60% for a child with a monozygotic twin with schizophrenia.
(E) The genetic vulnerability is too small to be of predictive value.

5. With regards to the longitudinal course of schizophrenia, what is proportion of patients will have a good outcome?

(A) Less than 10%.
(B) Less than 20%
(C) Less than 30%
(D) Less than 40%.
(E) Less than 50%.

6. The Global Assessment of Functioning (GAF) score is used to assess the level of functioning. What is the GAF score that defines recovery in schizophrenia?

(A) 45 or more.
(B) 50 or more.
(C) 55 or more.
(D) 60 or more.
(E) 65 or more.

7. In the Singapore EPIP, patients rated their satisfaction with the service provided by EPIP on the Client Satisfaction Questionnaire 8 (CSQ-8). At the end of 2 years what was the proportion of patients who rated the level of satisfaction as "good or better"

(A) 78.9%
(B) 84.9%
(C) 88.9%
(D) 94.9%
(E) 98.9%

8. The concept of early intervention for psychosis resulted in several intervention sites being set up across the world. Which of the following matching of programme and site is CORRECT?

(A) Early Assessment Service for Young People with Early Psychosis Programme – Norway.
(B) TIPS – Hong Kong.

(C) Lambeth Early Onset (LEO) Service – London.
(D) The Prevention and Early Psychosis Program for Psychosis (PEPP) – Calgary.
(E) Early Psychosis Program – Ontario.

9. The five most disabling conditions suffered by mankind are matched with their ranked order. Which of the matching is CORRECT?
(A) First – Dementia
(B) Second – Quadriplegia
(C) Third – Psychosis.
(D) Fourth – Paraplegia
(E) Fifth – Blindness.

10. Between April 2007 and March 2011, EPIP screened 1293 individuals and accepted 815 into the programme. What is the biggest referral source of such individuals?
(A) Counsellor from welfare organization or school.
(B) Police or Court.
(C) General Practice or Polyclinic.
(D) Hospital.
(E) Relatives, friends or self.

11. Schizophrenia is a complex, heterogeneous, and disabling psychiatric disorder. What is its worldwide prevalence rate?
(A) 1%
(B) 2%
(C) 4%
(D) 6%
(E) 8%

12. Bipolar disorder with psychotic features is a differential diagnosis of schizophrenia. Which of the following supports a diagnosis of Bipolar disorder?
(A) Rapid onset and family history of affective disorder.
(B) Hallucinations.
(C) Paranoia.
(D) Disorganised speech.
(E) Low energy.

13. Mental changes can occur with prescribed medications. Which of the medications and the mental changes is CORRECTLY paired?
(A) Corticosteroids and depression.
(B) Antidepressants and insomnia.
(C) Beta-blockers and mania.
(D) Anticholinergics and somnolence.
(E) Levodopa and hallucinations.

14. A schizoid personality disorder shares a common clinical feature with schizophrenia. What is it?
(A) Anhedonia.
(B) Asociality.
(C) Alogia.
(D) Avolition.
(E) Delusional.

15. A proportion of patients with schizophrenia have co-morbid psychiatric or medical conditions. What is the prevalence?
(A) More than 30%
(B) More than 40%
(C) More than 50%
(D) More than 60%
(E) More than 70%

16. What does the acronym GPPP stand for in the context of the collaboration between family doctors and the Institute of Mental Health in Singapore?
(A) General Practitioner-Patient Project.
(B) Generalist-Psychiatrist-Patient Partnership.
(C) GP Partnership Programme.
(D) General Practitioners' Psychosis Project.
(E) Generalist-Patient Psychosis Programme.

17. The GPPP is a collaboration for the care and management of patients with mental illness in the community. What is the type of patients managed in this collaboration?
(A) Socially isolated patients.
(B) High risk patients.
(C) Unemployed patients.
(D) Financially needy patients.
(E) Stable patients.

18. About the patients suitable to be referred to family doctors in the GPPP, which of the following inclusion criteria is CORRECT?
(A) Patients not hospitalized within the last 6 months.
(B) Patients requiring the same maintenance medications for the last 6 weeks.
(C) Patients who are unemployed.
(D) Patients who cannot afford expensive consultation fees.
(E) Patients staying alone.

19. About the patients suitable to be referred to family doctors in the GPPP, which of the following IS NOT an exclusion criteria?
(A) Olanzapine prescription.
(B) Disruptive personality disorder.
(C) Substance use.
(D) Formal psychotherapy.
(E) Benzodiazepine-only prescription.

20. About the satisfaction with the GPPP collaboration, what is the level of patient satisfaction in the 2011 survey?
(A) 58.1%
(B) 62,1%
(C) 78.6%
(D) 82.1%
(E) 98.6%

21. One of the problems of schizophrenia is the high rate of relapse of psychotic symptoms. What is the proportion of patients who may relapse within a year of being hospitalized?

(A) Up to 20%.
(B) Up to 25%.
(C) Up to 30%.
(D) Up to 35%.
(E) Up to 40%.

22. Treatment resistant schizophrenia is defined as little or no symptomatic response to at least 2 antipsychotic trials of treatment at therapeutic dose range and adequate trial of treatment duration. What is defined as adequate treatment duration?

(A) At least 4 weeks.
(B) At least 6 weeks.
(C) At least 8 weeks.
(D) At least 10 weeks.
(E) At least 12 weeks.

23. In a patient with proven treatment resistant schizophrenia, what is the drug of choice?

(A) Aripiprazole.
(B) Haloperidol.
(C) Olanzapine.
(D) Respiridone.
(E) Clozapine.

24. Early recognition of an impending relapse helps in early treatment and avoidance of hospitalization. Which of the following is an early symptom?

(A) Hallucinations.
(B) Delusions.
(C) Difficulty concentrating.
(D) Asociality.
(E) Anhedonia.

25. About relapse in schizophrenia, identification of triggers is important. Which of the following is the LEAST LIKELY trigger?

(A) Cocaine use.
(B) Alcohol use.
(C) Cannabis use.
(D) Low expressed emotion of caregivers.
(E) Alcohol usage.

26. Antipsychotics used in treatment of schizophrenia are heterogeneous compounds. They nevertheless share a common effect that is efficacious. What is that?

(A) They all block 5-HT2A neuroreceptors
(B) They all block D2 dopamine neuroreceptors.
(C) They all block M1 muscarinic neuroreceptors.
(D) They all block alpha1-adrenergic neuroreceptors.
(E) They all block H1 histamine neuroreceptors.

27. The typical antipsychotics or First generation antipsychotics are divided by potency into high, intermediate and low. Which of the following has low potency?

(A) Thioridazine.
(B) Haloperidol.
(C) Perphenazine.
(D) Trifluoperazine.
(E) Fluphenazine.

28. In a patient with osteoporosis, an antipsychotic that does not raise prolactin levels is desired. Which of the following antipsychotic will therefore be a good choice?

(A) Thiothixene.
(B) Aripiprazole.
(C) Respiridone.
(D) Chlopromazine.
(E) Thioridazine.

29. A patient with schizophrenia has a BMI of 29. Which of the following antipsychotics will be a good choice?

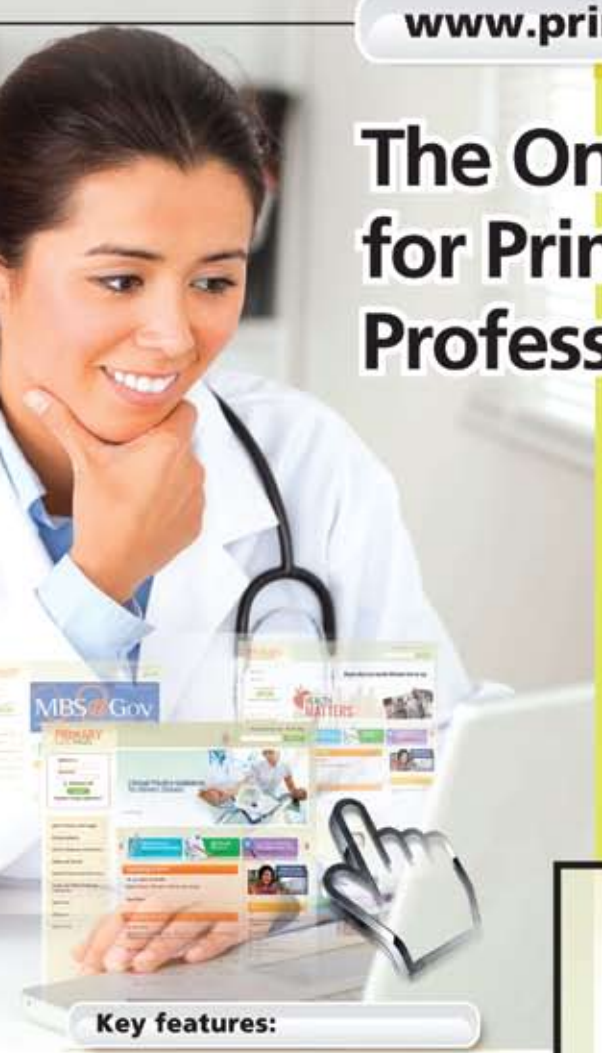
(A) Haloperidol.
(B) Quetiapine.
(C) Olanzapine.
(D) Zoprasidone.
(E) Clozapine.

30. Akathisia is an extrapyramidal symptom of antipsychotic therapy. Apart from dose reduction, which of the following medications helps to ameliorate this adverse effect?

(A) Benzodiazepine.
(B) Vitamin D.
(C) Propranolol.
(D) Baclofen.
(E) Dandrolene.

www.primarycarepages.sg

The Online Gateway for Primary Care Professionals

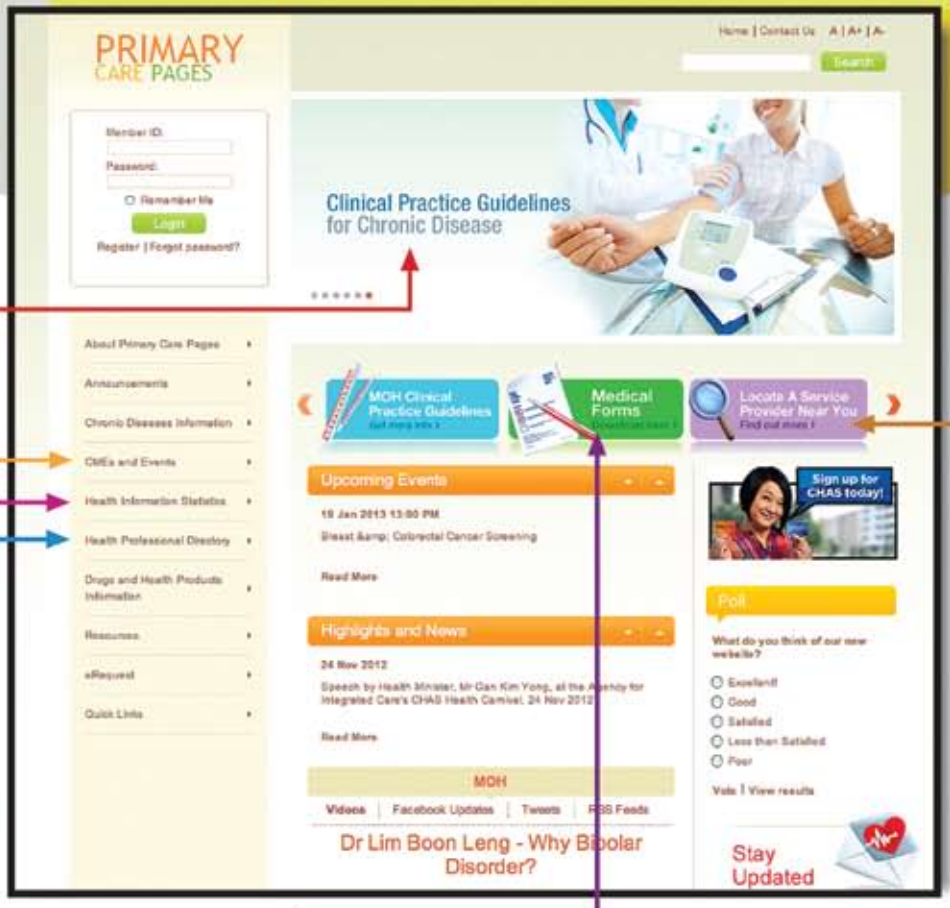


WWW.AIC.SG

The Primary Care Pages (PCP) is a one-stop portal for Primary Care Professionals. An initiative by Agency for Integrated Care (AIC), the PCP website aims to foster stronger partnership with Healthcare Professionals by providing a single platform for them to network and to access updated, consolidated and comprehensive information and applications.

The key features of PCP seek to facilitate networking and to promote collaboration among general practitioners, restructured hospitals and the intermediate and long-term care sector.

Key features:



Clinical Practice Guideline

Access chronic disease clinical practice guidelines.

CMEs and Events

Access a consolidated calendar of events including CME talks, symposium, workshop and more from the hospitals.

Health Statistics / Information

Access the latest Singapore Health Statistics.

Health Professional Directory

Publish the medical services provided in your clinic.

Medical Forms

Download medical forms including hospital referrals and CHAS patients forms.

Service Locator

Locate the nearest medical and community healthcare service provider.

For more information, please contact: **Agency for Integrated Care (AIC)**
Tel: +65 6603 6800 • Email: gp@aic.sg

Visit PCP to find out more about the Foreign Domestic Worker Grant and how GPs can help in disability assessment.

READINGS

- A Selection of Ten Current Readings on Topics Related to Schizophrenia

A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO SCHIZOPHRENIA –

some available as free full-text and some requiring payment

Selection of readings made by A/Prof Goh Lee Gan

READING 1 – PRIMARY CARE PROVIDERS' ROLE IN THE CARE OF PATIENTS WITH SCHIZOPHRENIA

Viron M, Baggett T, Hill M, Freudenreich O. Schizophrenia for primary care providers: how to contribute to the care of a vulnerable patient population. Am J Med. 2012 Mar;125(3):223-30. doi: 10.1016/j.amjmed.2011.05.002. Review. PubMed PMID: 22340915.

URL: http://www.sciencedirect.com/science/article/pii/S0002934311003858 -- payment required

Massachusetts General Hospital Schizophrenia Program, Boston, USA. mviron@partners.org

Comment in Am J Med. 2012 Mar;125(3):219-20.

ABSTRACT

Patients with schizophrenia represent a vulnerable population with high medical needs that are often missed or undertreated. Primary care providers have the potential to reduce health disparities experienced by this population and make a substantial difference in the overall health of these patients. This review provides primary care providers with a general understanding of the psychiatric and medical issues specific to patients with schizophrenia and a clinically practical framework for engaging and assessing this vulnerable patient population and assisting them in achieving optimal health. Initial steps in this framework include conducting a focused medical evaluation of psychosis and connecting patients with untreated psychosis to psychiatric care as promptly as possible. Given the significant contribution of cardiovascular disease to morbidity and mortality in schizophrenia, a top priority of primary care for patients with schizophrenia should be cardiovascular disease prevention and treatment through regular risk factor screening, appropriate lifestyle interventions, and other indicated therapies.

 PMID: 22340915 [PubMed - indexed for MEDLINE]

READING 2 – COMPULSORY COMMUNITY TREATMENT ORDERS MIGHT REDUCE MORTALITY AMONG PATIENTS WITH PSYCHIATRIC DISORDERS

Kisely S, Preston N, Xiao J, Lawrence D, Louise S, Crowe E. Reducing all-cause mortality among patients with psychiatric disorders: a population-based study. CMAJ. 2013 Jan 8;185(1):E50-6. doi: 10.1503/cmaj.121077. Epub 2012 Nov 12. PubMed PMID: 23148054; PubMed Central PMCID: PMC3537812.

URL: http://www-ncbi-nlm-nih-gov/pmc/articles/PMC3537812/pdf/1850e50.pdf - Free full text

Ballenden House, Edinburgh, UK. marktaylor2@nhs.net

ABSTRACT

BACKGROUND: Among patients with psychiatric disorders, there are 10 times as many preventable deaths from physical disorders as there are from suicide. We investigated whether compulsory community treatment, such as community treatment orders, could reduce all-cause mortality among patients with psychiatric disorders.

METHODS: We conducted a population-based survival analysis of an inception cohort using record linking. The study period extended from November 1997 to December 2008. The cohort included patients from all community-based and inpatient psychiatric services in Western Australia (state population 1.8 million). We used a 2-stage design of matching and Cox regression to adjust for demographic characteristics, previous use of health services, diagnosis and

length of psychiatric history. We collected data on successive cohorts for each year for which community treatment orders were used to measure changes in numbers of patients, their characteristics and outcomes. Our primary outcome was 2-year all-cause mortality. Our secondary outcomes were 1-and 3-year all-cause mortality.
RESULTS: The study population included 2958 patients with community treatment orders (cases) and 2958 matched controls (i.e., patients with psychiatric disorders who had not received a community treatment order). The average age for cases and controls was 36.7 years, and 63.7% (3771) of participants were men. Schizophrenia and other nonaffective psychoses were the most common diagnoses (73.4%) among participants. A total of 492 patients (8.3%) died during the study. Cox regression showed that, compared with controls, patients with community treatment orders had significantly lower all-cause mortality at 1, 2 and 3 years, with an adjusted hazard ratio of 0.62 (95% confidence interval 0.45-0.86) at 2 years. The greatest effect was on death from physical illnesses such as cancer, cardiovascular disease or diseases of the central nervous system. This association disappeared when we adjusted for increased outpatient and community contacts with psychiatric services.
INTERPRETATION: Community treatment orders might reduce mortality among patients with psychiatric disorders. This may be partly explained by increased contact with health services in the community. However, the effects of uncontrolled confounders cannot be excluded.
PMCID: PMC3537812 PMID: 23148054 [PubMed - in process]

READING 3 – COST EFFECTIVE STRATEGIES

Chisholm D, Saxena S. Cost effectiveness of strategies to combat neuropsychiatric conditions in sub-Saharan Africa and South East Asia: mathematical modelling study. BMJ. 2012 Mar 2;344:e609. doi: 10.1136/bmj.e609. PubMed PMID: 22389339; PubMed Central PMCID: PMC3292519.

URL: http://www-ncbi-nlm-nih-gov/pmc/articles/PMC3292519/pdf/bmj.e609.pdf - full free text

Department of Health Systems Financing, World Health Organization, 1211 Geneva, Switzerland. chisholmd who.int

ABSTRACT
OBJECTIVE: To assess the comparative costs and effects of interventions to combat five neuropsychiatric conditions (schizophrenia, bipolar disorder, depression, epilepsy, and heavy alcohol use). DESIGN: Cost effectiveness analysis based on an epidemiological model.
SETTING: Two epidemiologically defined World Health Organization sub-regions of the world: countries in sub-Saharan Africa with very high adult and high child mortality (AfrE); and countries in South East Asia with high adult and high child mortality (SearD).
DATA SOURCES: Published studies, costing databases.
MAIN OUTCOME MEASURES: Cost per capita and cost per disability adjusted life year (DALY) averted, expressed in international dollars ($Int) for the year 2005.
RESULTS: Across 44 assessed intervention strategies for the five neuropsychiatric conditions, cost effectiveness values differed by as much as two orders of magnitude (from $Int100-250 to $Int10,000-25,000 for a year of healthy life gained). In both sub-regions, inpatient based treatment of schizophrenia with newer antipsychotic drugs was the most costly and least cost effective strategy. The most cost effective strategies in the African sub-region related to population based alcohol control, while in the South East Asian sub-region the most cost effective intervention was drug treatment of epilepsy in primary care. The cumulative cost per capita of the most cost effective set of interventions covering all five conditions was estimated at $Int4.90-5.70. This package comprises interventions for epilepsy (older first line antiepileptic drugs); depression (generically produced newer antidepressants and psychosocial treatment); bipolar disorder (mood stabiliser drug lithium); schizophrenia (neuroleptic antipsychotic drugs and psychosocial treatment); and heavy alcohol use (increased taxation and its enforcement, reduced access, and, in the African sub-region, advertising bans and brief advice to heavy drinkers in primary care).
CONCLUSIONS: Reallocation of resources to cost effective intervention strategies would increase health gain, save money and help implement much needed expansion of services for neuropsychiatric conditions in low resource settings.
PMCID: PMC3292519 PMID: 22389339 [PubMed - indexed for MEDLINE]

READING 4 – TREATMENT OF HALLUCINATIONS IN SCHIZOPHRENIA SPECTRUM DISORDERS

Sommer IE, Slotema CW, Daskalakis ZJ, Derks EM, Blom JD, van der Gaag M. The treatment of hallucinations in schizophrenia spectrum disorders. Schizophr Bull. 2012 Jun;38(4):704-14. doi: 10.1093/schbul/sbs034. Epub 2012 Feb 24. Review.
PubMed PMID: 22368234.

URL: http://schizophreniabulletin.oxfordjournals.org/content/38/4/704.full.pdf+html – payment required

Neuroscience Division, Psychiatry Department, University Medical Centre Utrecht & Rudolf Magnus Institute of Neuroscience, University Medical Center Utrecht, PO Box 85500, 3508 GA, Utrecht, the Netherlands. i.sommer@umcutrecht.nl

ABSTRACT
This article reviews the treatment of hallucinations in schizophrenia. The first treatment option for hallucinations in schizophrenia is antipsychotic medication, which can induce a rapid decrease in severity. Only 8% of first-episode patients still experience mild to moderate hallucinations after continuing medication for 1 year. Olanzapine, amisulpride, ziprasidone, and quetiapine are equally effective against hallucinations, but haloperidol may be slightly inferior. If the drug of first choice provides inadequate improvement, it is probably best to switch medication after 2-4 weeks of treatment. Clozapine is the drug of choice for patients who are resistant to 2 antipsychotic agents. Blood levels should be above 350-450 μg/ml for maximal effect. For relapse prevention, medication should be continued in the same dose. Depot medication should be considered for all patients because nonadherence is high. Cognitive-behavioral therapy (CBT) can be applied as an augmentation to antipsychotic medication. The success of CBT depends on the reduction of catastrophic appraisals, thereby reducing the concurrent anxiety and distress. CBT aims at reducing the emotional distress associated with auditory hallucinations and develops new coping strategies. Transcranial magnetic stimulation (TMS) is capable of reducing the frequency and severity of auditory hallucinations. Several meta-analyses found significantly better symptom reduction for low-frequency repetitive TMS as compared with placebo. Consequently, TMS currently has the status of a potentially useful treatment method for auditory hallucinations, but only in combination with state of the art antipsychotic treatment. Electroconvulsive therapy (ECT) is considered a last resort for treatment-resistant psychosis. Although several studies showed clinical improvement, a specific reduction in hallucination severity has never been demonstrated.
PMID: 22368234 [PubMed - indexed for MEDLINE]

READING 5 – COMPARING EFFICACY AND SAFETY OF INDIVIDUAL SECOND GENERATUIB ANTIPSYCHOTICS VS FIRST GENERATION ANTIPSYCHOTICS

Zhang JP, Gallego JA, Robinson DG, Malhotra AK, Kane JM, Correll CU. Efficacy and safety of individual second-generation vs. first-generation antipsychotics in first-episode psychosis: a systematic review and meta-analysis. Int J Neuropsychopharmacol. 2012 Dec 3:1-14. [Epub ahead of print] PubMed PMID: 23199972.

URL: http://journals.cambridge.org/action/displayAbstract?fromPage=online&aid=8768990 – payment needed

The Zucker Hillside Hospital, Psychiatry Research, North Shore - Long Island Jewish Health System, New York, USA.

ABSTRACT
Because early treatment choice is critical in first-episode schizophrenia-spectrum disorders (FES), this meta-analysis compared efficacy and tolerability of individual second-generation antipsychotics (SGAs) with first-generation antipsychotics (FGAs) in FES. We conducted systematic literature search (until 12 December 2010) and meta-analysis of acute, randomized trials with ≥1 FGA vs. SGA comparison; patients in their first episode of psychosis and

diagnosed with schizophrenia-spectrum disorders; available data for psychopathology change, treatment response, treatment discontinuation, adverse effects, or cognition. Across 13 trials (n = 2509), olanzapine (seven trials) and amisulpride (one trial) outperformed FGAs (haloperidol: 9/13 trials) in 9/13 and 8/13 efficacy outcomes, respectively, risperidone (eight trials) in 4/13, quetiapine (one trial) in 3/13 and clozapine (two trials) and ziprasidone (one trial) in 1/13, each. Compared to FGAs, extrapyramidal symptom (EPS)-related outcomes were less frequent with olanzapine, risperidone and clozapine, but weight gain was greater with clozapine, olanzapine and risperidone. Pooled SGAs were similar to FGAs regarding total psychopathology change, depression, treatment response and metabolic changes. SGAs significantly outperformed FGAs regarding lower treatment discontinuation, irrespective of cause, negative symptoms, global cognition and less EPS and akathisia, while SGAs increased weight more ($p < 0.05$-0.01). Results were not affected by FGA dose or publication bias, but industry-sponsored studies favoured SGAs more than federally funded studies. To summarize, in FES, olanzapine, amisulpride and, less so, risperidone and quetiapine showed superior efficacy, greater treatment persistence and less EPS than FGAs. However, weight increase with olanzapine, risperidone and clozapine and metabolic changes with olanzapine were greater. Additional FES studies including broader-based SGAs and FGAs are needed.
PMID: 23199972 [PubMed - as supplied by publisher]

READING 6 – RELAPSE PREVENTION IN SCIZOPHRENIA

Kishimoto T, Agarwal V, Kishi T, Leucht S, Kane JM, Correll CU. Relapse prevention in schizophrenia: a systematic review and meta-analysis of second-generation antipsychotics versus first-generation antipsychotics. Mol Psychiatry. 2013 Jan;18(1):53-66. doi: 10.1038/mp.2011.143. Epub 2011 Nov 29. PubMed PMID: 22124274; PubMed Central PMCID: PMC3320691.

URL: http://www.nature.com/journal/v18/n1/pdf/mp2011143a.pdf -- payment required

Division of Psychiatry Research, The Zucker Hillside Hospital, North Shore-Long Island Jewish Health System, Glen Oaks, NY 11004, USA.

ABSTRACT
Few controlled trials compared second-generation antipsychotics (SGAs) with first-generation antipsychotics (FGAs) regarding relapse prevention in schizophrenia. We conducted a systematic review/meta-analysis of randomized trials, lasting more than 6 months comparing SGAs with FGAs in schizophrenia. Primary outcome was study-defined relapse; secondary outcomes included relapse at 3, 6 and 12 months; treatment failure; hospitalization; and dropout owing to any cause, non-adherence and intolerability. Pooled relative risk (RR) (±95% confidence intervals (CIs)) was calculated using random-effects model, with numbers-needed-to-treat (NNT) calculations where appropriate. Across 23 studies (n=4504, mean duration=61.9±22.4 weeks), none of the individual SGAs outperformed FGAs (mainly haloperidol) regarding study-defined relapse, except for isolated, single trial-based superiority, and except for risperidone's superiority at 3 and 6 months when requiring ≥3 trials. Grouped together, however, SGAs prevented relapse more than FGAs (29.0 versus 37.5%, RR=0.80, CI: 0.70-0.91, P=0.0007, I(2)=37%; NNT=17, CI: 10-50, P=0.003). SGAs were also superior regarding relapse at 3, 6 and 12 months (P=0.04, P<0.0001, P=0.0001), treatment failure (P=0.003) and hospitalization (P=0.004). SGAs showed trend-level superiority for dropout owing to intolerability (P=0.05). Superiority of SGAs regarding relapse was modest (NNT=17), but confirmed in double-blind trials, first- and multi-episode patients, using preferentially or exclusively raw or estimated relapse rates, and for different haloperidol equivalent comparator doses. There was no significant heterogeneity or publication bias. The relevance of the somewhat greater efficacy of SGAs over FGAs on several key outcomes depends on whether SGAs form a meaningful group and whether mid- or low-potency FGAs differ from haloperidol. Regardless, treatment selection needs to be individualized considering patient- and medication-related factors. PMCID: PMC3320691 [Available on 2013/7/1] PMID: 22124274 [PubMed - in process]

READING 7 – PHARMACOLOGIC TREATMENT OF FIRST EPISODE SCHIZOPHRENIA

Thomas SP, Nandhra HS, Singh SP. Pharmacologic treatment of first-episode schizophrenia: a review of the literature. Prim Care Companion CNS Disord. 2012;14(1). doi:pii: PCC.11r01198. 10.4088/PCC.11r01198. Epub 2012 Jan 5. PubMed PMID: 22690369; PubMed Central PMCID: PMC3357581.

URL: http://www-ncbi-nlm-nih-gov/pmc/articles/PMC3357581/ - full free text

Departments of General Adult Psychiatry (Drs Thomas and Nandhra) and Early Intervention (Dr Thomas), Coventry and Warwickshire Partnership Trust, Warwickshire; and Department of Social and Community Psychiatry, Health Sciences Research Institute, University of Warwick, Coventry (Dr Singh), United Kingdom.

ABSTRACT

OBJECTIVE: To review the evidence base for the efficacy and tolerability of antipsychotic medication for the treatment of the first episode of schizophrenia.

DATA SOURCE: MEDLINE databases were searched for published articles in English over the last 25 years, from January 1986 to January 2011, on choice of antipsychotic treatment for the first episode of schizophrenia, with an emphasis on efficacy and tolerability of antipsychotic drugs in the acute phase of psychotic illness.

STUDY SELECTION: The keywords antipsychotic drugs and schizophrenia were used in combination with drug treatment, pharmacologic treatment, efficacy, and tolerability in addition to atypical antipsychotics, first-generation antipsychotics, second-generation antipsychotics, first-episode psychosis, and acute psychotic episode.

DATA SYNTHESIS: At present, there is no convincing evidence to guide clinicians in choosing a single first-line antipsychotic that is effective in treating the positive and negative symptoms of the first episode of schizophrenia. Even though second-generation antipsychotic drugs offer potential benefits in terms of less extrapyramidal side effects and some benefits in treating negative, affective, and cognitive symptoms, these drugs are not without their own side effects.

CONCLUSIONS: With the introduction of a number of second-generation antipsychotic drugs there have been significant advances in antipsychotic drug treatment over the last decade. Despite these advances, there are still a number of limitations in continued use of some antipsychotic medications due to their efficacy and tolerability issues in the acute and early maintenance phases of psychosis. Active research in this area would provide more promising results of improved efficacy and tolerability of antipsychotic medication.

PMCID: PMC3357581 PMID: 22690369 [PubMed - in process]

READING 8 – ORAL VS LONG ACTING INJECTABLE ANTIPSYCHOTICS

Zhornitsky S, Stip E. Oral versus Long-Acting Injectable Antipsychotics in the Treatment of Schizophrenia and Special Populations at Risk for Treatment Nonadherence: A Systematic Review. Schizophr Res Treatment. 2012;2012:407171. doi: 10.1155/2012/407171. Epub 2012 Feb 15. PubMed PMID: 22966436; PubMed Central PMCID: PMC3420751.

URL: http://www.hindawi.com/journals/sprt/2012/407171/ - free full text

Département de Psychiatrie, Université de Montréal, Montréal, Québec, Canada 2900.

ABSTRACT

Long-acting injectable antipsychotics (LAIs) should offer better efficacy and tolerability, compared to oral antipsychotics due to improved adherence and more stable pharmacokinetics. However, data on LAIs has been mixed, with some studies finding that they are more effective and tolerable than oral antipsychotics, and others finding the contrary. One possibility for the disparate results may be that some studies administered different

---

antipsychotics in the oral and injectable form. The present systematic review examined the efficacy and tolerability of LAIs versus their oral equivalents in randomized and naturalistic studies. In addition, it examined the impact of LAIs on special populations such as patients with first-episode psychosis, substance use disorders, and a history of violence or on involuntary outpatient commitment. Randomized studies suggest that not all LAIs are the same; for example, long-acting risperidone may be associated with equal or less side effects than oral risperidone, whereas fluphenazine decanoate and enanthate may be associated with equal or more side effects than oral fluphenazine. They also suggest that LAIs reduce risk of relapse versus oral antipsychotics in schizophrenia outpatients when combined with quality psychosocial interventions. For their part, naturalistic studies point to a larger magnitude of benefit for LAIs, relative to their oral equivalents particularly among first-episode patients.
PMCID: PMC3420751 PMID: 22966436 [PubMed]

READING 9 – MAINTENANCE PHASE ANTIPSYCHOTIC TREATMENT

Takeuchi H, Suzuki T, Uchida H, Watanabe K, Mimura M. Antipsychotic treatment for schizophrenia in the maintenance phase: a systematic review of the guidelines and algorithms. Schizophr Res. 2012 Feb;134(2-3):219-25. doi: 10.1016/j.schres.2011.11.021. Epub 2011 Dec 10. Review. PubMed PMID: 22154594.

URL: http://www.sciencedirect.com.libproxy1.nus.edu.sg/science/article/pii/S0920996411006190 - payment required

Keio University, School of Medicine, Department of Neuropsychiatry, Tokyo, Japan. hirotak@dk9.so-net.ne.jp

ABSTRACT
OBJECTIVE: Antipsychotic treatment strategy for the maintenance phase of schizophrenia has been inconsistent in the literature. The purpose of this systematic review is to overview recommendations in various guidelines and algorithms.
METHODS: The guidelines and algorithms for schizophrenia that were published or updated in English after 2000 were searched, using Medline, PubMed, EMBASE, and PsycINFO with the following key words: guideline, algorithm, schizophrenia, and psychosis (last search: July 2011). The reference lists of the relevant reports were also examined.
RESULTS: Fourteen guidelines and algorithms were identified; only five of them clearly defined terms about the maintenance phase and treatment. Ten of 11 guidelines and algorithms did not recommend discontinuation of antipsychotics within five years; six of them partially recommended antipsychotic discontinuation for patients with first-episode schizophrenia exclusive. All nine guidelines and algorithms that referred to intermittent or targeted antipsychotic strategy endorsed against this strategy. Although being a hot topic of controversy, dose reduction of antipsychotics or lower dose therapy in the maintenance phase compared to the acute dosage is not recommended on the whole concerning atypical antipsychotics, whereas dose reduction appears sometimes considered acceptable for typical antipsychotics.
CONCLUSION: What constitutes maintenance phase and its treatment in schizophrenia has not yet been established in the literature. While discontinuation and intermittent or targeted strategies are not generally recommended, there is controversy regarding dose reduction or lower dose therapy, especially with regards to atypical antipsychotics. Further evidence is needed in order to derive treatment recommendations on antipsychotics in this critical treatment phase of schizophrenia.
 PMID: 22154594 [PubMed - indexed for MEDLINE]

READING 10 – ANTICHOLINERGIC MEDICATION DISCONTINUATION IN PATIENTS RECEIVING ANTIPSYCHOTICS

Desmarais JE, Beauclair L, Margolese HC. Anticholinergics in the era of atypical antipsychotics: short-term or long-term treatment? J Psychopharmacol. 2012 Sep;26(9):1167-74. doi: 10.1177/0269881112447988. Epub 2012 May 31. Review. PubMed PMID: 22651987.

URL: http://jop.sagepub.com/cgi/pmidlookup?view=long&pmid=22651987 – payment required

Clinical Psychopharmacology and Therapeutics Unit, Allan Memorial Institute, McGill University Health Centre, Montreal, QC, Canada. julie.desmarais@mail.mcgill.ca

ABSTRACT

Anticholinergic agents are usually prescribed to prevent or treat antipsychotic-induced extrapyramidal symptoms. Their long-term benefits are questionable and they carry diverse adverse effects, including cognitive impairment and worsening of tardive dyskinesia. This literature review explores the impact of anticholinergic medication discontinuation on movement disorders, cognition and psychopathology in patients receiving antipsychotics. Medline, Embase and PsycInfo were searched from 1950 to July 2011 using "cessation /withdrawal /discontinuation /stopping" with "anticholinergic*" or "antiparkinson*" and "neuroleptic*" or "antipsychotic*". Additional articles were obtained by searching the bibliographies of relevant references. Earlier studies of anticholinergic agent discontinuation in patients receiving first-generation antipsychotics reported relapse rates of extrapyramidal symptoms between 4% and 80%, reflecting the heterogeneity of the studies. Two recent studies of patients prescribed second-generation antipsychotics obtained relapse rates of 4% and 33%. Some studies suggest improvement in tardive dyskinesia with cessation of anticholinergics. Four studies examined the effects of anticholinergic agent discontinuation on cognition and all observed an improvement post-discontinuation. Changes in symptoms of schizophrenia with anticholinergic discontinuation are conflicting, with more recent studies suggesting an improvement. Given their questionable benefit with continued use, clinicians should consider a gradual withdrawal of anticholinergic agents in stable patients receiving antipsychotics.

PMID: 22651987 [PubMed - indexed for MEDLINE]

ORIGINAL PAPER

- **Advice for Individuals Travelling to High Altitude**

ADVICE FOR INDIVIDUALS TRAVELLING TO HIGH ALTITUDE

Dr Lee Eng Sing, Dr Lee Meng Kam Richard, Dr Aw Lee Fhoon Lily

ABSTRACT

More people are traveling to remote places for leisure and business. It is not uncommon for patients to get medication and advice for travel to high altitudes. Although high altitude cerebral and pulmonary oedemas are more frequent at very high and extreme altitudes, they may sometimes occur at lower altitudes and lead to fatalities. Even though acute mountain sickness (AMS) is generally deemed benign, it can easily wreck a holiday. The Lake Louise Score Questionnaire is a useful screening tool for AMS and it can be self-administered during travel. Non-pharmacological means in the prevention and treatment of AMS, especially acclimatisation, are the most important. Pharmacological prevention and treatment strategies should be used as a useful adjunct. This paper provides an approach to the provision of education and advice for high altitude travel in the primary care setting.

Keywords: Acute Mountain Sickness; high altitude illness; prevention; treatment

SFP2013; 39(1): 48-54

INTRODUCTION

The ease of travel has allowed more people to pursue leisure activities at remote places. These destinations include places of high altitudes. The allure of the summit, picturesque sceneries, skiing and mountain trekking are some of the common reasons why equatorial Singaporeans are drawn to such destinations.

For the majority of people who travel to high altitude, most will return from their sojourn with no ill effects. Morbidities are common but rarely does fatality occur[1]. Most of the deaths reported were caused by accidents at extreme altitudes[2]. These accidents may be attributable to altitude-induced hypoxia causing misjudgments and disorientation.

As family physicians, we sometimes have healthy individuals or patients with chronic diseases coming to us for advice or medications for such travels. It is therefore imperative that we should get ourselves acquainted on the subject matter to give the most evidence-based and unbiased advice. Most of the time, all it needs is to warn patients of certain precautions or to assess for possible exacerbation of pre-existing illnesses. Infrequently, we may have to firmly advise a patient not to participate in such an activity.

This review aims to give an overview of the problems that individuals may encounter at high altitudes for short holidays or business trips. It provides a basic understanding of illnesses that can occur at high altitudes and recognition of these illnesses. The emphasis of this article is on the guidelines for prevention, the critical steps in the treatment and management of AMS. Appropriate advice in a primary care setting is included. High altitude destinations commonly visited by Singaporeans are summarised in Appendix 1. (This a personal search from the google search engine of individual countries and areas that Singaporeans commonly visit after interviewing a travel agent in Singapore)

METHODOLOGY

A PubMed search was conducted using keywords like "prevention", "treatment", "acute mountain sickness" and "high altitude illness". Relevant articles were selected from this list and from the references of the articles. UpToDate and The International Mountaineering and Climbing Federation (UIAA) website (http://www.theuiaa.org/medical_advice.html) were also consulted.

WHAT HAPPENS AT HIGH ALTITUDE?

At sea level, barometric pressure is 760 mmHg; atmospheric partial pressure of Oxygen (pO_2) is 159 mmHg; and inspired pO_2 is 150 mmHg or 21% of Oxygen[3]. The inspired Oxygen is primarily dependent on the barometric pressure. Barometric pressure decreases in a non-linear way with increasing elevation. As such, the availability of inspired pO_2 lowers as one ascends.

In this article, the following definition for altitudes are used:

Intermediate altitude	1,500-2,499m
High altitude	2,500-3,499m
Very high altitude	3,500-5,499m
Extreme altitude	> 5,500m

Table 1 summarises the notable changes of a human body at increasing altitude.

LEE ENG SING, Family Physician, Associate Consultant, National Healthcare Group Polyclinics

LEE MENG KAM RICHARD, Family Physician, Associate Consultant, National Healthcare Group Polyclinics

AW LEE FHOON LILY, Consultant Family Physician, Private Practice

Appendix 1: Some common high altitude destinations visited by Singaporeans

Country	Place of interest	Highest altitude
Singapore		0-166m (highest point is Bukit Timah Hill) - For reference
Himalaya		
Bhutan		Cultural tours do not reach altitudes higher than 3,500m. All treks reach at least 3,500m; some go as high as 5,000m
China	Tibet	
	Lhasa (Capital)	3,658m
	Lalung-La Pass	5,050m
	Gyatsola Pass	5,220m
	Karola Pass	5,010m
	Kambala Pass	4,974m
India	Sikkim	
	Gangtok (Capital)	1,780m
	Goechala Pass	5,000m
	Jammu	
	Kishtwar High Altitude National Park	The altitudinal level of the park ranges from 1,700 to 4,800m above sea level
Nepal	Kathmandu (Capital)	1,400m
	Jomson (City)	2,700m
	Langtang (City)	3,307m
	Trekking in Annapurna	Thorung La Pass at 5,416m
	Trekking in Muktinath	Muktinath Shrine at 3,170m
	Trekking in Everest	Mera Peak 6,476m; Tesi Lapcha Pass 5,755m; French Col 5,240m; Dhampus Pass 5,155m
	Phoksumdo Lake	3,627m
Ski Resorts		
Austria	Austrian Alps	Up to 3,800m
China	Jade Dragon Snow Mountain (Lijiang Yunan)	4,516-4,700m
	Duolemeidi Mountain Resort (Zhangjiakou Hebei)	1,500-2,174m
	Kanas International Ski Resort (Xinjiang)	1,000-2,000m
	Dagu Glacier (Sichuan)	3,617-4,843m
Japan	Happo-One (Hakuba, Nagano)	760-1,831m
South Korea	Yongpyong Resort	700-1,458m
Switzerland	Swiss Alps	Up to 2700m. The highest mountain in the Alps is Mont Blanc (4,810m)
China	Sichuan	Altitude of Jiuzhaigou ranges from 1,998 to 2,140m, at the mouth of Shuzheng Gully, to 4,558 - 4,764m on Mount Ganzigonggai at the top of Zechawa Gully.
	Jiuzhaigou	
	Huangshan	The Huangshan mountain range comprises many peaks, some more than 1,000m high. The three tallest and best-known peaks are *Lotus Peak* (Lian Hua Feng 1,864m, *Bright Summit Peak* (Guang Ming Ding 1,840m, and *Celestial Peak* (Tian Du Feng, literally *Capital of Heaven Peak* 1,829m)
Kyrgyzstan	Great Silk Road Tour	The average altitude is about 2,500m.
	Issyk-Kul Lake	1,607m (second largest mountain lake)
Malaysia	Mount Kinabalu	The summit (known as Low's Peak) is 4,095m.
Peru	Puno (City) - Lake Titicaca	3,827m
	Machu Picchu	2,430m. Usually travel from Cusco, the nearest city - 3,500m
	Arequipa - Colca Canyon	2,325m
USA (Colorado Springs)	Denver (City) (Rocky Mountain National Park)	1,570m. The Manitou and Pikes Peak Cog Railway will take one up to the summit of summit of Pikes Peak at 4,300m.

Table 1: Summary of the changes an individual undergo at increasing altitude[3, 6, 32]

Altitude	Changes
Intermediate (1500-2499m)	Physiological changes detectable. Arterial oxygen saturation > 90%. Altitude illness possible but rare. Equivalent in altitude to commercial aircraft pressurised cabin during flight.
High (2500-3499m)	Altitude illness common with rapid ascent. Decreased exercise performance and increased ventilation. Complex reaction time slows.
Very High (3500-5499m)	Altitude illness common. Arterial oxygen saturation < 90% (75-85%). Marked hypoxemia during exercise and sleep. Learning and special memory impaired. Psychomotor impairment detectable.
Extreme (>5500m)	Progressive deterioration of physiological function outstrips acclimatisation. Arterial oxygen saturation 58-75%. Memory retrieval impaired. MRI shows cortical atrophy above 7000m. 32% of climbers have hallucinations above 7500m. Altitude above 8000m is generally accepted as the death zone.

HIGH ALTITUDE ILLNESS

High Altitude Illness (HAI) describes the cerebral and pulmonary syndromes that occur after an initial climb to high altitude or following a new ascent while already at high altitude[4]. The full pathophysiology of HAI is yet to be elucidated[5]. It is characterised by three distinct clinical presentations[6]. These are namely Acute Mountain Sickness (AMS) that is the commonest and mildest form, High Altitude Cerebral Oedema (HACE) and High Altitude Pulmonary Oedema (HAPE) that are the more severe forms. The latter two can lead to fatalities if not treated early.

Another distinct clinical presentation – Chronic Mountain Sickness (CMS), occurs in people who stay at high altitude for long periods. This entity will not be discussed in this paper.

Acute Mountain Sickness (AMS)

Historical records as far back as 2000 years ago have reported symptoms very similar to AMS[7,8]. It affects 22-53% of travelers to altitudes between 1,850m-4,240m[9]. As one ascends, the atmospheric pO_2 lowers and therefore the risk of developing AMS increases. For example, AMS affects close to 25% of travelers at an altitude of 2500m but up to 75% of travelers at an altitude of 4500m[10].

AMS is defined as headache in an unacclimatised individual plus the presence of one or more of the following symptoms[11, 12,13]:

- Gastrointestinal (anorexia, nausea or vomiting)
- Lassitude or fatigue
- Dizziness or lightheadedness
- Insomnia

The headache commonly starts as a tension-like band that eventually generalises[1]. It may sometimes mimic a classical migraine. The headache worsens with movements and especially when lying supine. Vomiting usually relieves it.

Sleep is particularly disturbed at high altitude and is a dominant symptom of AMS[10]. Travelers often complain of abbreviated and restless sleep especially on the first night[14]. This is due to periodic breathing with apnoeic episodes, a form of Cheyne-Stokes respiration[4,15].

AMS is usually a benign condition that is unpleasant and self-limiting. When staying at the same altitude without further ascent, it commonly resolves within 24-48 hrs [6]. Any individual with persistent AMS that does not resolve should be considered with high suspicion of developing HACE or HAPE. A past history of AMS is a good predictor for development of AMS especially when the conditions of ascent are similar[4].

The Lake Louise Score Questionnaire (LLSQ) is commonly used for diagnosis of AMS. A score greater than 4 in the LLSQ has a sensitivity of 78% and a specificity of 93% for the diagnosis of AMS (Appendix 2). The LLSQ also has an additional clinical assessment score that registers change in mental status, ataxia and peripheral oedema on a severity scale[16].

High Altitude Cerebral Oedema (HACE)

HACE is often thought of as a continuum of AMS[4]. The headache is of a more severe form and worsens in the morning. The afflicted person may behave strangely before exhibiting detectable neurological signs. Without early intervention, an afflicted person develops globalised encephalopathy, becomes comatose and dies[11].

High Altitude Pulmonary Oedema (HAPE)

HAPE seems to be of a different entity altogether and causes higher mortality when compared to HACE[17]. Symptoms of HAPE include breathlessness with coughing of pinkish, frothy sputum[9]. It most commonly occurs within 48-120 hrs after exposure to a high altitude. It can develop without preceding AMS or HACE. Without early intervention, a person may progress to respiratory failure[18].

According to the Lake Louise Consensus[13], it is diagnosed as follows:

- At least two of the following symptoms
  a. Dyspnoea at rest
  b. Cough
  c. Weakness or decreased exercise performance
  d. Chest tightness or congestion
- At least two of the following signs:
  a. Crackles or wheezing in at least one lung field
  b. Central cyanosis
  c. Tachypnoea
  d. Tachycardia

OTHER ILLNESSES AT HIGH ALTITUDE

It is natural for doctors and potential travelers to dwell only on HAI. However, exposure to high altitude also carries other risks. Proximity to the sun causing heat stroke and ultraviolet keratitis can happen. Exposure to cold may cause hypothermia and frost bite. Other environmental changes at high altitude that potentially can pose hazards to an individual include irradiation and decrease in humidity.

PREVENTION OF AMS

Non-pharmacological means for prevention of AMS

Travel agencies commonly do not provide enough time for tourists to acclimatise. For example, most tour packages travelling to Lhasa in Tibet reach an altitude of 4000m in less than two days.

Giving enough time for acclimatisation is the most reliable method for prevention of AMS. Experts advise that at altitude of more than 2500m, progress should not be more than 300-500m per day for sleeping altitude and should include a rest day (no ascent and no vigorous activities) every 3-4 days[3,19].

Climb high and sleep low is the maxim for high altitude travel[20]. Avoid sleeping above 2800m on the first night of travel[4]. Residing or having brief climbs above 1500m in the weeks before a high-altitude trip may hasten acclimatisation[21]. Acclimatisation is not a permanent phenomenon even for dwellers who have their usual residence at high-altitude.[18] Oxygen supplementation can help to prevent AMS[22]. Heavy physical exertion at high altitude has been shown to increase the risk of sudden cardiac death[23].

Adequate rest, appropriate hydration, avoidance of alcohol and sedatives are also important preventive measures.

Pharmacological means for prevention of AMS

Acetazolamide and dexamethasone are commonly used for the prophylaxis of AMS. Other drugs for prevention of HAI have never been proven[24]. Gingko biloba was a major contender a few years ago but has recently been refuted[25].

Acetazolamide

Acetazolamide is safe and 60-80% effective for AMS[17,26]. Studies have shown that acetazolamide at a dosage of 125-250 mg twice daily can help to prevent AMS. However, complete understanding of its protection in AMS remains speculative.

Side effects of the drug include paraesthesia, altered taste and hangover feeling[27]. Uncommon adverse drug reactions are rashes and blood dyscrasias. Fatal drug reactions may include Toxic Epidermal Necrolysis, Stevens-Johnson syndrome and renal failure1. It may therefore be prudent to try out the drug many days before travel to ascertain that there are no side effects.

Although acetazolamide is generally safe for individuals with no chronic diseases, avoidance and special precautions with certain medical conditions or concomitant drugs should be practiced.

Dexamethasone

Dexamethasone minimises the effects of AMS without improving the acclimatisation process[28]. A return of the symptoms of AMS may occur and develop rapidly when the drug is abruptly terminated. Dexamethasone is useful for individuals who cannot tolerate acetazolamide as prophylaxis[6].

Caution is advised for diabetic patients who have poorly controlled glycemia. It is also prudent to avoid in individuals at risk for peptic ulcer disease or upper gastrointestinal bleed. For those who travel to rural places frequently, it may be prudent to avoid this drug as it may worsen amoebiasis and strongyloidiasis. Potential tendon rupture may occur especially when individuals are taking dexamethasone with fluroquinolones in the management of traveler's diarrhoea[28]. Side effects of steroids such as euphoria and mania may also occur[12].

TREATMENT OF AMS

Non-Pharmacological treatment of AMS

Measures like sleeping propped up[1], rest, proper hydration (not vigorous hydration), avoidance of alcohol are all that is required for simple headaches.

The best treatment for AMS is to stop further ascent, descend within 24 hrs if symptoms do not resolve or descend urgently if respiratory or neurological symptoms develop[6]. It is important that the rest of the tour members do not help carry the unwell for further ascent.

An individual afflicted with AMS should not descend alone in case symptoms worsen[17]. Debilitating illness, tough terrain and/or bad weather conditions can make descent difficult. Occasionally, the descending route may involve further ascent before eventually declining. An alternative route may have to be sought in such cases with a guide familiar with the local terrain. The Gamow bag (portable hyperbaric bag) and supplemental Oxygen may be useful in instances when descent is impossible.

Pharmacological treatment of AMS

Simple analgesia (non-narcotics) such as aspirin, paracetamol and ibuprofen may reduce headache caused by AMS. Antiemetics like metoclopramide and prochlorperazine may be used for nausea[6]. Short-acting benzodiazepines may be used for individuals bothered by insomnia[15]. Drugs should be used mainly to aid descent[6]. It should not be used as an aid for further ascent. Table 2 summaries the common drugs used for prevention and treatment of AMS.

Table 2: Summary of pharmacological agents for AMS prevention and treatment [6,16,27]

Prevention	Treatment
• Acetazolamide 125-250mg bd (taken one day before the ascent for at least 3-5 days for the first part of a trip or the full duration of ascent)	• Acetazolamide 250mg bd
• Dexamethasone 2mg qds or 4mg bd	• Dexamethasone 4mg qds

SPECIAL GROUPS OF INDIVIDUALS

It is generally safe for patients with chronic diseases such as diabetes, epilepsy, hypertension and stable ischaemic heart disease to travel provided their conditions are well-controlled[1,6]. The UIAA (The International Mountaineering and Climbing Federation or Union Internationale des Associations d'Alpinisme) has provided a helpful guide on this topic[29].

Patients with asthma or chronic obstructive pulmonary disease should be warned that, contrary to what is commonly believed, air quality might not be better at high altitude. Emissions from diesel trucks and wood burning especially in areas such as the Himalayas may cause poor air quality in the early mornings and evenings. Valleys within the mountains may also trap particulate air pollutants during temperature inversions.[9]

As long as one is physically fit, age is not an obstacle to high altitude travel[27]. Children are at the same risk of suffering from AMS as adults. However, recognition of symptoms in pre-verbal children may be delayed due to their inability to communicate effectively[6]. Excessive crying, poor appetite, lethargy and vomiting

in pre-verbal children should be assessed with AMS in mind[30].

There are not many studies on pregnant women travelling to high altitude. It may be wise to advise those with low-lying placenta, pre-eclampsia and pregnancy-induced hypertension to avoid such travel[27]. Both acetazolamide and dexamethasone are pregnancy class C drugs.

GENERAL ADVICE IN A PRIMARY CARE SETTING

Places at high altitude have always been held with mystique and there is an inexplicable lure of summits of mountains to mankind. With increased affluence and ease of travel, more Singaporeans will be travelling to such destinations. An approach to the provision of education and advice for high altitude travel in the primary care setting is proposed. It will be prudent to get the following information before dishing out advice to an individual intending to travel to high altitude:

1. Proposed rate of ascent and mode of transport
2. Previous history of HAI
3. Current and past medical history
4. Current medications and drug allergies
5. Purpose of ascent

The following proposal is not meant for adventurers who do competitive mountain climbing or skiing; or who ascend to extreme altitudes e.g., Mount Everest Expedition (altitude of 8850m); or people who have decided to migrate and stay long-term in high altitude.

1. Find out from the travel agency the exact itinerary. There should be contingency plans for travelers who suffer from AMS. Choose one that has a flexible itinerary to allow for days of rest if necessary.
2. Screen for medical conditions that are absolutely contraindicated e.g., pulmonary hypertension, etc.[9,18,29,31]
3. Profile the risk of individuals intending to travel to high altitude and provide the suggested advice as indicated in Table 3. This is an important step as a history of previous HAI, rapid ascent to a high altitude due to tight schedule in a travel itinerary and/or existence of cardio-pulmonary conditions will deem a potential traveler to be at high risk of developing HAI.
4. Explain that the level of fitness, gender and age of an individual are not reliable predictors of AMS.[5,32]
5. Provide a copy of LLSQ (Appendix 2) for self-assessment so that individuals may seek help early if indicated.
   a. If the score is between 3-5, mild AMS is present. Travelers are advised to rest and avoid further ascent. Non-pharmacological measures as described above are to be instituted. Serial evaluations of LLSQ are recommended to assess the condition.
   b. If symptoms resolve and the score is less than 3, further ascent may be appropriate. If symptoms do not resolve and the score is still within 3-5, descend within 24 hours.
   c. If analgesia, anti-emetics or short-acting benzodiazepines are used or the score is 6 or more on the LLSQ, dexamethasone (if not already started and not contraindicated) may be initiated to minimise the symptoms of AMS. Arrangements for immediate descent with medical attention from a doctor trained in high-altitude medicine should be made.
   d. If HACE or HAPE develop, arrangements for immediate descent and medical treatment from a doctor trained in high-altitude medicine should be made.
6. Reinforce non-pharmacological measures as first line.
7. A moderate degree of physical conditioning should be initiated before participating in unaccustomed physical activities e.g., skiing.
8. Common illnesses like traveler's diarrhoea and possible physical injuries should be discussed. It is important to entertain other possible diagnoses when AMS is presented e.g., hypoglycaemia, dehydration, exhaustion, or hypothermia.[3,17]
9. Get good travel insurance.
10. Finally, discuss prophylaxis and treatment. Prophylactic medication is only indicated in those with a known history of HAI or those who cannot avoid rapid ascent.

Table 3: Risk profiling and suggested advice for individuals travelling to high altitude for leisure[4]

Risk of HAI	Description	Suggested Advice
Low	• No history of HAI & initial destination < 2800m (sleeping altitude) • ≥ 2 days to reach destination • ≤ 500m/day of ascent once over 2500m	• Non-pharmacological measures • Education
Moderate	• Previous history of AMS & initia destination < 2800m (sleeping altitude) • No history of AMS & initial destination < 3000m in < 2 days • > 500m/day of ascent once over 2800m	• Non-pharmacological measures • Education • Consider acetazolamide or dexamethasone (if unable to tolerate the former)
High	• History of HACE or HAPE & initial destination > 3000m in < 2 days • History of AMS & < 3000m in < 2 days • >500m/day of ascent once over 3000m; rapid guided ascents • Predisposing medical conditions e.g. COPD, pulmonary hypertension etc.	• Non-pharmacological measures • Education • Discuss possibility of cancelling trip • Refer for further assessment e.g., treadmill ECG

Appendix 2: Lake Louise Score Questionnaire (LLSQ)

(Downloaded from www.treksafe.com.au/medical/documents/LakeLouisescore_001.pdf)

A diagnosis of AMS is based on:
1. A rise in altitude within the last 4 days
2. Presence of a headache

PLUS

3. Presence of at least one other symptoms
4. A total score of 3 or more from the questions below.

SELF-REPORT QUESTIONNAIRE

Add together the individual scores for each symptom to get the total score.

Headache	No headache	0
	Mild headache	1
	Moderate headache	2
	Severe headache, incapacitating	3
Gastrointestinal Symptoms	None	0
	Poor appetite or nausea	1
	Moderate nausea &/or vomiting	2
	Severe nausea &/or vomiting	3
Fatigue &/or Weakness	Not tired or weak	0
	Mild fatigue/weakness	1
	Moderate fatigue/weakness	2
	Severe fatigue/weakness	3
Dizziness/ Lightheadedness	Not dizzy	0
	Mild dizziness	1
	Moderate dizziness	2
	Severe dizziness, incapacitating	3
Difficulty Sleeping	Slept as well as usual	0
	Did not sleep as well as usual	1
	Woke many times, poor sleep	2
	Could not sleep at all	3
	TOTAL SCORE	

Total score of
3-5 : Mild AMS
6 or more : Severe AMS

NOTE:
- Do not ascend with symptoms of AMS
- Descend if symptoms are not improving or getting worse
- Descend if symptoms of HACE or HAPE develop

REFERENCES

1. Clarke C. Acute mountain sickness: medical problems associated with acute and subacute exposure to hypobaric hypoxia. Postgrad Med J 2006;82(973):748-53. doi: 10.1136/pgmj.2006.047662
2. Pollard AJ. Altitude induced illness. BMJ 1992;304(6838):1324-5. doi: 10.1136/bmj.304.6838.1324
3. Gallagher SA, Hackett PH. High-altitude illness. Emerg Med Clin North Am 2004;22(2):329-55, viii. doi: 10.1016/j.emc.2004.02.001
4. Gallagher SA, Hackett P, Rosen JM. High altitude illness: Physiology, risk factors, and general prevention. UpToDate 2010.
5. Roach RC, Hackett PH. Frontiers of hypoxia research: acute mountain sickness. J Exp Biol 2001;204(Pt 18):3161-70.
6. Barry PW, Pollard AJ. Altitude illness. BMJ 2003;326(7395):915-9. doi: 10.1136/bmj.326.7395.915
7. Gilbert DL. The first documented description of mountain sickness: the Andean or Pariacaca story. Respir Physiol 1983;52(3):327-47. doi: 10.1016/0034-5687(83)90089-0
8. Gilbert DL. The first documented report of mountain sickness: the China or Headache Mountain story. Respir Physiol 1983;52(3):315-26. doi: 10.1016/0034-5687(83)90088-9
9. Luks AM, Swenson ER. Travel to high altitude with pre-existing lung disease. Eur Respir J 2007;29(4):770-92. doi: 10.1183/09031936.00052606
10. McMurray SJ. High altitude medicine for family physicians. Can Fam Physician 1994;40:711-8.
11. Wilson MH, Newman S, Imray CH. The cerebral effects of ascent to high altitudes. Lancet Neurol 2009;8(2):175-91. doi: 10.1016/S1474-4422(09)70014-6
12. Bia FJ. Current prevention and management of acute mountain sickness. Yale J Biol Med 1992;65(4):337-41.
13. The Lake Louise Consensus on the Definition of Altitude Illness. http://www.high-altitude-medicine.com/AMS-LakeLouise.html [Last modified 8-May-2000 assessed 1 Sep 2012 2000.]
14. Weil JV. Sleep at high altitude. High Alt Med Biol 2004;5(2):180-9. doi: 10.1089/1527029041352162
15. Beaumont M, Batejat D, Pierard C, Van Beers P, Philippe M, Leger D, et al. Zaleplon and zolpidem objectively alleviate sleep disturbances in mountaineers at a 3,613 meter altitude. Sleep 2007;30(11):1527-33.
16. Maggiorini M, Muller A, Hofstetter D, Bartsch P, Oelz O. Assessment of acute mountain sickness by different score protocols in the Swiss Alps. Aviat Space Environ Med 1998;69(12):1186-92.
17. Schoene RB. Illnesses at high altitude. Chest 2008;134(2):402-16. doi: 10.1378/chest.07-0561
18. Maloney JP, Broeckel U. Epidemiology, risk factors, and genetics of high-altitude-related pulmonary disease. Clin Chest Med 2005;26(3):395-404, v. doi: 10.1016/j.ccm.2005.05.002
19. Hackett PH, Roach RC. High-altitude illness. N Engl J Med 2001;345(2):107-14. doi: 10.1056/NEJM200107123450206
20. British Mountaineering Council Information Service Information Sheets.
21. Muza SR, Beidleman BA, Fulco CS. Altitude preexposure recommendations for inducing acclimatization. High Alt Med Biol 2010;11(2):87-92. doi: 10.1089/ham.2010.1006
22. West JB. Oxygen enrichment of room air to relieve the hypoxia of high altitude. Respir Physiol 1995;99(2):225-32. doi: 10.1016/0034-5687(94)00094-G
23. Albert CM, Mittleman MA, Chae CU, Lee IM, Hennekens CH, Manson JE. Triggering of sudden death from cardiac causes by vigorous exertion. N Engl J Med 2000;343(19):1355-61. doi: 10.1056/NEJM200011093431902
24. Bartsch P, Bailey DM, Berger MM, Knauth M, Baumgartner RW. Acute mountain sickness: controversies and advances. High Alt Med Biol 2004;5(2):110-24. doi: 10.1089/152702904135210 8
25. Chow T, Browne V, Heileson HL, Wallace D, Anholm J, Green SM. Ginkgo biloba and acetazolamide prophylaxis for acute mountain sickness: a randomized, placebo-controlled trial. Arch Intern Med 2005;165(3):296-301. doi: 10.1001/archinte.165.3.296
26. Swenson ER, Teppema LJ. Prevention of acute mountain sickness by acetazolamide: as yet an unfinished story. J Appl Physiol 2007;102(4):1305-7. doi: 10.1152/japplphysiol.01407.2006

27. Rodway GW, Hoffman LA, Sanders MH. High-altitude-related disorders - Part II: prevention, special populations, and chronic medical conditions. Heart Lung 2004;33(1):3-12. doi: 10.1016/j.hrtlng.2003.08.003

28. Luks AM, Swenson ER. Medication and dosage considerations in the prophylaxis and treatment of high-altitude illness. Chest 2008;133(3):744-55. doi: 10.1378/chest.07-1417

29. Milledge JS, Kupper T. Consenses Statement of the UIAA Medical Commission. Vol. 13, People with Pre-Existing Conditions Going to the Mountains. 2008.

30. Samuels MP. The effects of flight and altitude. Arch Dis Child 2004;89(5):448-55. doi: 10.1136/adc.2003.031708

31. Higgins JP, Tuttle T, Higgins JA. Altitude and the heart: is going high safe for your cardiac patient? Am Heart J 2010;159(1):25-32. doi: 10.1016/j.ahj.2009.10.028

32. O'Connor T, Dubowitz G, Bickler PE. Pulse oximetry in the diagnosis of acute mountain sickness. High Alt Med Biol 2004;5(3):341-8. doi:10.1089/ham.2004.5.341

33. Imray C, Wright A, Subudhi A, Roach R. Acute mountain sickness: pathophysiology, prevention, and treatment. Prog Cardiovasc Dis 2010;52(6):467-84. doi: 10.1016/j.pcad.2010.02.003

Prism Section

- What Approach can Primary Care Physicians Adopt to Manage their Patient who is Upset as a Result of Adverse Effect from their Treatment?

PRISM SECTION

WHAT APPROACH CAN PRIMARY CARE PHYSICIANS ADOPT TO MANAGE THEIR PATIENT WHO IS UPSET AS A RESULT OF ADVERSE EFFECT FROM THEIR TREATMENT?

Dr Chan Hian Hui Vincent

ABSTRACT

The article explores the various approaches a doctor can use in managing and upset patient. These approaches include BATHE (Background-Affect-Troubles-Handling-Empathy), LEARN (Listen-Explain-Acknowledge-Recommend and Negotiate) and LEAP (Listen-Empathise-Agree-Partnership). We include a case study of a 16 year old patient who presented with a sore throat. She subsequently developed a rash after starting Amoxicillin, which was later changed to Augmentin. The doctor utilised the BATHE approach in managing the patient's unhappiness.

Keywords: Amoxicillin, Augmentin, rash, upset, approach, adverse effects

SFP2013; 39(1): 56-58

Patient's revelation: what happened?

NBR is a 16 year old Malay girl who was seen at a polyclinic for a suspected bacterial pharyngitis that had lasted 2 weeks. She was thus prescribed a course of oral Amoxicillin 500mg, by myself, to be taken thrice daily, together with other medications for symptom relief. She returned to the clinic again five days later, her symptoms persisted. During that consultation, the primary care physician noted that patient was only partially compliant with the prescribed Amoxicillin. My colleague thus decided to change the antibiotic to Augmentin 625 mg twice a day, with the view that this would improve patient's compliance to the treatment.

Two days later, patient returned to the clinic with her mother to see me. NBR developed a generalised rash involving the trunk, upper and lower limbs. NBR and her mother were upset with the adverse reaction. They attributed the change of antibiotic to be the cause of the rash.

CHAN HIAN HUI VINCENT, Family Physician, Deputy Clinic Director, SingHealth Polyclinics - Pasir Ris

Gaining insight into the case management: what are the issues?

How do physicians manage patients who are upset due to the development of ill effects from the prescribed treatment?

Patients who are upset as a result of adverse drug reactions are more likely to take on medico-legal actions against the medical practitioner. Ghandi (2000) reported lower patient satisfaction levels in cases where adverse drug reactions were encountered.[1] According to the Medico-legal database of the Medical Protection Society, 19% of medico-legal cases came from "prescribing" issues, of which antibiotic related adverse reactions formed a main group.[2] It is therefore important to engage patients who encounter adverse drug reactions and act to ensure a good therapeutic outcome.

There are several approaches which primary care physicians (PCP) can adopt to manage angry and difficult patients, or when dealing with an unexpected outcome to medical treatment. These approaches include:

1. **BATHE (Background-Affect-Troubles-Handling-Empathy)**
2. **LEARN (Listen-Explain-Acknowledge-Recommend and Negotiate)**
3. **LEAP (Listen-Empathise-Agree-Partnership)**
4. **ASSIST (Acknowledge-Sorry-Story-Inquire-Solution-Travel)**

Such approaches are applicable in situations when patients and their physicians have differing points of view. PCPs can use any of these approaches to achieve common understanding and agreement with their patients, so as to improve satisfactory outcomes.

The **LEARN** approach[3] includes first **L**istening and understanding the patient's point of view and then **E**xplaining the doctor's perception and assessment of the current clinical development of the subject. Next, both parties should **A**cknowledge differences and points of agreement. Once common understanding is achieved, the doctor can then **R**ecommend the appropriate treatment, and **N**egotiate for concordance with the patients on the agreed mode of management.

Table 2: Components of the LEARN approach

L	Listen with empathy and understanding the patient's perception of the problem.
E	Explain your perceptions and assessment of the problem
A	Acknowledge the differences and similarities
R	Recommend treatment
N	Negotiate agreement to treatment

The **LEAP** approach[4] includes: Listen, Empathise, Agree and Partner. Akin to the BATHE and LEARN approaches, the doctor first **L**istens to the patient and **E**mpathise with the patient's adverse experience. The doctor then works with the patient to **A**gree on common points, before **P**artnering the patient to achieve the best outcome.

Another method is the ASSIST approach[5], pioneered by the Cognitive Institute. Elements of this approach include: **A**cknowledging the patients concerns and complaints, and then saying **S**orry, while attempting to understand the patient's **S**tory by **I**nquiring about key facts along the way. Once common understanding between the doctor and the patient is achieved, they can then work towards a **S**olution and **T**ravel together along this path to resolve the issue fully.

Table 3: Components of the LEAP approach

L	Listen reflectively to patient's perception of the problems. Avoid giving one's own opinion of the situation right from the start of the consultation.
E	Empathise, strategically express empathy and if appropriate, normalise the experience
A	Agree and discuss only perceived problems. Then review the advantages and disadvantages of the proposed intervention or treatment. Finally repeat back and highlight the perceived benefits of this proposed intervention.
P	Partner the patient, and work on goals that both sides can agree upon.

Table 4: Components of the BATHE approach

B	Background: Use active listening to understand the story, the context and the patient's situation.
A	Affect: Name the emotion, acknowledge patient's anger and normalise the experience. Acknowledging their right to be angry will help start the healing process and solidify the therapeutic relationship.
T	Troubles: Explore what scares or troubles them the most about their present and future. Simply asking the question "Tell me what frightens you?" will help them to focus on circumstances they may not have considered.
H	Handling: Knowledge and positive action can help mitigate fears and reduce anger.
E	Empathy: By displaying empathy and concern you can help the person feel understood, less abandoned and alone.

Table 5: Components of the ASSIST approach

A	Acknowledge: The doctor must first acknowledge the patient's problem.
S	Sorry: The doctor must then express regret and empathy about the unexpected outcome.
S	Story: Getting the patient to relate his or her viewpoint, emotion and experience.
I	Inquire: Where doctors seek to ask relevant questions.
S	Solutions: Seeking the patient's ideas on how to move forwards.
T	Travel: Where doctors journey with the patient together to find solutions to the problems.

Study the management: how do we apply in our practice?

I chose the BATHE approach[6,7], to help me address the patient's and her mother's concerns in this case. This choice was made because the BATHE was developed as a rapid psychosocial intervention to assess the psychological factors that may contribute to patients' physical complaints. And in a pilot study, it was shown to be effective in showing patients the sympathy and concern of their attending primary care doctors.[8]

Table 6: Comparison of four approaches to manage and communicate unexpected adverse events

BATHE	LEARN	LEAP	ASSIST	Common components
Background Affect Troubled Empathy	Listen	Listen Empathise	Acknowledge Sorry Story Inquire	Listen to patients empathetically to understand their perceptions.
	Explain Acknowledge	Agree	Solution	Explain the doctor's perception of the problem and reconcile both viewpoints to create common understanding.
Handle	Recommend Negotiate	Partnering	Travel	Partner the patient in formulating a treatment plan that will achieve the best outcome.

Active listening techniques[9] are also important. This is reflected by repeating or paraphrasing what were said to signify our understanding of patient's narration of their experience and to clarify their areas of concerns. Next, we acknowledge empathetically that their concerns are important issues that must be addressed. We follow on with a list or summary of the patient's concerns and propose solutions to address each of their concerns. These steps will send a clear statement to the patient that we understand their concerns, feel for them and will partner them in resolving these important issues.

The first step is to understand the **Background** to the patient's and parental concerns by taking a detailed history of this generalised rash and its possible relationship to the prescribed oral antibiotics. I recognised that NBR and her mother were unhappy and slightly annoyed (patient's **Affect**) about the unexpected rash, as it began after taking the prescribed antibiotics.

I acknowledged that this was a real concern and proceeded to ask about what **Troubled** them most. Her mother highlighted that the previous doctor had erred in giving the patient Amoxicillin and Augmentin, thereby causing the rash. I then explained that her rash could be due either to a drug reaction or a viral infection such as infectious mononucleosis from the Epstein Barr Virus. The patient also expressed concern that the rash prevented her from commencing her part time vacation work as a retail assistant. She perceived that the rash would create a negative impression and impact on her customers.

I informed her that the rash would resolve after a period of few days and in the interim period of time, she could cover her exposed upper limbs with long sleeved attire. In addition, I suggested drug therapy with a course of prednisolone and antihistamines to expedite the rash resolution so that she could return to her part time work earlier.

To help them **Handle** the situation better, I explained that adverse drug reactions were rare and difficult to predict. For instance, one study reported that only 2.45% of children in ambulatory care developed rash due to drug reactions[10]. I also explained that there could be other reasons for the rash, such as a viral infection.

I proposed my treatment plan, which included a short course of Prednisolone 20mg OM for 5 days, along with a course of oral antihistamines. Patient was reassured that the rash was expected to resolve, and she should return if this rash failed to resolve or worsened.

I tried to display **Empathy** throughout the clinical consultation. In this way, the patient would feel that they were attended to closely. The doctor-patient relationship can also then be strengthened. NBR and her mother were satisfied with the explanation and treatment plan, and agreed to return if NBR remained unwell.

Patients can be upset as a result of experiencing unforeseen consequences of drug treatment such as cutaneous eruptions. The BATHE, LEARN, LEAP, ASSIST model of approaches can be used to manage such a situation to minimise adverse outcomes. Indeed, these 4 models are not validated for use in managing such cases, yet they are easy to remember and use. We thus propose that future studies to be undertaken to assess the validity of these 4 approaches. For doctors interested to know more about risks management in clinical practice, the Medical Protection Society offers courses such as "The Essential Risk Management Workshop series" which is available to all local doctors.

REFERENCES

1. Gandhi TK, Burstin HR, Cook EF et al, Drug Complications in Outpatients, J Gen Intern Med, 2000:15:149-154. doi: 10.1046/j.1525-1497.2000.04199.x

2. Sandars J, Cook G, Chapter 1, The Scope of the Problem, ABCs of Patient Safety, Wijey and Sons, 2007:1-3.

3. Berlin EA, Fowkes WC Jr. A teaching framework for cross-cultural health care-Application in family practice, In Cross-cultural medicine. West J Med 1983 Dec; 139:934-8.

4. Amador X. LEAP institute's: Listen-Empathise-Agree-Partner Approach.

5. The "ASSIST" Model for disclosing errors to patients. It is a central component of Mastering Adverse Outcomes, run by Medical Protection Society risk consulting. It was pioneered by Cognitive Institute, a subsidiary of MPS.

6. Stewart MR, Lieberman J J: The Fifteen Minute Hour: Applied Psychotherapy for the Primary Care Physician. 2nd Edition. Westport, CT: Praeger Publishing; 1993.

7. Wang-Cheng R. Dealing With the Angry Dying Patient, 2nd Edition. Fast Facts and Concepts. July 2006; 59. Available at: http://www.eperc.mcw.edu/fastfact/ff_059.htm.

8. Sandra R. Leiblum, PhD; Eliezer Schnall, PhD, Martin Seehuus, MA; Anthony DeMaria. To BATHE or Not to BATHE: Patient Satisfaction With Visits to Their Family Physician. Family Medicine. June 2008;40(6);407-11.

9. Wang EC, MD. Dealing with the Angry Patient. The Permanente Journal/ Spring 2003/ Volume 7 No. 2.

10. Taché SV, MD MPH. Prevalence of Adverse Drug Events in Ambulatory Care: A Systematic Review. Ann Pharmacother July/August 2011(45);7/8:977-89.

CHRONIC DISEASE MANAGEMENT PROGRAMME FOR SCHIZOPHRENIA

(REPRINTED FROM CHRONIC DISEASE MANAGEMENT PROGRAMME – HANDBOOK FOR HEALTHCARE PROFESSIONALS, 2009 EDITION)

1 INTRODUCTION

1.1 Schizophrenia is a major psychiatric disorder with a chronic and often disabling clinical course. It has an estimated lifetime prevalence of seven per thousand of the adult population worldwide. This disorder is characterised by a multiplicity of symptoms affecting the most fundamental human attributes: cognition, emotion and perception. The early age of onset, impairments in intellectual and psychosocial aspects of the individual's life as well as associated stigma, often bring to its victims and families significant emotional and financial distress.

2 SYMPTOMATOLOGY AND PRESENTATION

2.1 Each patient with the disorder will have a unique combination of symptoms and experiences and may present at various phases of their illness. Some might experience a prodromal phase where frank psychotic symptoms had not yet occurred. The prodromal phase is frequently characterised by non-specific symptoms such as depressed mood, anxiety, sleep disturbances, attenuated psychotic symptoms, social withdrawal and deterioration in academic or occupational functioning.

2.2 There are 4 main categories of symptoms in Schizophrenia: positive, negative, disorganized and cognitive symptoms. Various combinations of these symptoms may occur.

2.3 Positive symptoms are those that appear to reflect an excess or distortion of normal functions. Characteristic positive symptoms are delusions and hallucinations. Delusions are fixed, false and firmly held beliefs that are out of the socio-cultural and religious context of the affected individual. Usually, the patient would misinterpret sounds and actions of others as relating to themselves. They may also report unusual experiences or fear that their actions are being monitored and their lives might be in danger. Hallucinations are perceptions in the absence of a stimulus, in a conscious and awake person. Often hallucinations in Schizophrenia occur in the auditory modality and patients would complain of voices talking to them. They may also be noted to mumble, talk, laugh or gesticulate to themselves. Hallucinations could also occur in other sensory modalities such as vision, smell, touch and taste. If these are the predominant hallucinations, care must be exercised to exclude an organic cause for the psychosis.

2.4 Negative symptoms are those that appear to reflect a diminution or loss of normal functions. These often persist in the lives of people with Schizophrenia, even after resolution of positive symptoms, and are difficult to evaluate because they are not grossly abnormal as positive symptoms and may be caused by other factors such as antipsychotic medications. Typical negative symptoms are alogia (limited speech with consequent difficulty in maintaining a conversation), anhedonia (lack of pleasure or interest in life), avolition (lack of initiation, drive and energy), asociality (social withdrawal) and affect flattening (difficulty in expressing emotions). Patients seldom complain about negative symptoms, but their caregivers would report about their "laziness".

2.5 Disorganised symptoms include disturbances in thinking, speech and behaviour. They may talk irrelevantly, answer off the point or manifest bizarre behaviours. Cognitive symptoms include impairments in attention, concentration, memory and executive functioning. Cognitive symptoms have a significant impact on their social, occupational and academic functioning.

2.6 Schizophrenia is associated with significant psychiatric co-morbidities such as depression, anxiety disorders, post-traumatic stress disorders and substance use disorders. These co-morbidities could affect the clinical outcome and delay improvement. Occasionally, the patient with Schizophrenia may first present with features of depression or anxiety rather than complain of hearing voices. Therefore, the clinician should screen for the presence of these disorders during the clinical interviews.

2.7 In the assessment of the patient, it is important to obtain corroborative history from family, friends or caregivers. This is especially so in patients who are not forthcoming during the clinical interviews or downplay their symptoms. During the interview, it is also important to assess the social support system and the patient's self-care, as it will influence subsequent management plans.

2.8 Other important aspects of the interview include risk assessment and physical health. In the risk assessment, clinicians are specifically examining the patient for risk of harm to self and others. Patients suffering from Schizophrenia have an increased risk of suicide. A suicide risk assessment is provided at Annex 2C for reference. As a result of neglect and poor hygiene, they may become malnourished or suffer the physical consequences of it.

3 DIAGNOSIS AND DIFFERENTIALS

3.1 In the diagnosis of Schizophrenia, there are 2 widely used criteria internationally. The International Classification of Diseases (ICD) endorsed by the World Health Organisation, and the Diagnostic and Statistical Manual of Mental Disorders (DSM) published by the American Psychiatric Association.

3.2 Diagnostic guidelines for DSM-IV-TR

A. Characteristic symptoms: Two (or more) of the following, each present for a significant portion of time during a 1-month period (or less if successfully treated):

i) Delusions
ii) Hallucinations
iii) Disorganized speech (e.g., frequent derailment or incoherence)
iv) Grossly disorganized or catatonic behaviour
v) Negative symptoms, i.e., affective flattening, alogia, or avolition

Note: Only one Criterion A symptom is required if delusions are bizarre or hallucinations consist of a voice keeping up a running commentary on the person's behaviour or thoughts, or two or more voices conversing with each other.

B. Social/occupational dysfunction: For a significant portion of the time since the onset of the disturbance, one or more major areas of functioning such as work, interpersonal relations, or self-care are markedly below the level achieved prior to the onset (or when the onset is in childhood or adolescence, failure to achieve expected level of interpersonal, academic, or occupational achievement).

C. Duration: Continuous signs of the disturbance persist for at least 6 months. This 6-month period must include at least 1 month of symptoms (or less if successfully treated) that meet Criterion A (i.e., active-phase symptoms) and may include periods of prodromal or residual symptoms. During these prodromal or residual periods, the signs of the disturbance may be manifested by only negative symptoms or two or more symptoms listed in Criterion A present in an attenuated form (e.g., odd beliefs, unusual perceptual experiences).

D. Schizoaffective and Mood Disorder exclusion: Schizoaffective Disorder and Mood Disorder With Psychotic Features have been ruled out because either (1) no Major Depressive, Manic, or Mixed Episodes have occurred concurrently with the active-phase symptoms; or (2) if mood episodes have occurred during active- phase symptoms, their total duration has been brief relative to the duration of the active and residual periods.

E. Substance/general medical condition exclusion: The disturbance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition.

F. Relationship to a Pervasive Developmental Disorder: If there is a history of Autistic Disorder or another Pervasive Developmental Disorder, the additional diagnosis of Schizophrenia is made only if prominent delusions or hallucinations are also present for at least a month (or less if successfully treated).

3.3 Diagnostic Guidelines for ICD-10

3.3.1 The normal requirement for a diagnosis of Schizophrenia is that a minimum of one very clear symptom (and usually two or more if less clear-cut) belonging to any one of the groups listed as (a) to (d) below, or symptoms from at least two of the groups referred to as (e) to (h), should have been clearly present for most of the time during a period of 1 month or more. Conditions meeting such symptomatic requirements but of duration less than 1 month (whether treated or not) should be diagnosed in the first instance as acute Schizophrenia-like psychotic disorder and are classified as Schizophrenia if the symptoms persist for longer periods.

3.3.2 Although no strictly pathognomonic symptoms can be identified, for practical purposes it is useful to divide the above symptoms into groups that have special importance for the diagnosis and often occur together, such as:

a) thought echo, thought insertion or withdrawal, and thought broadcasting;
b) delusions of control, influence, or passivity, clearly referred to body or limb movements or specific thoughts, actions, or sensations; delusional perception;
c) hallucinatory voices giving a running commentary on the patient's behaviour, or discussing the patient among themselves, or other types of hallucinatory voices coming from some part of the body;
d) persistent delusions of other kinds that are culturally inappropriate and completely impossible, such as religious or political identity, or superhuman powers and abilities (e.g. being able to control the weather, or being in communication with aliens from another world);
e) persistent hallucinations in any modality, when accompanied either by fleeting or half-formed delusions without clear affective content, or by persistent over-valued ideas, or when occurring every day for weeks or months on end;
f) breaks or interpolations in the train of thought, resulting in incoherence or irrelevant speech, or neologisms;
g) catatonic behaviour, such as excitement, posturing, or waxy flexibility, negativism, mutism, and stupor;
h) "negative" symptoms such as marked apathy, paucity of speech, and blunting or incongruity of emotional responses, usually resulting in social withdrawal and lowering of social performance; it must be clear that these are not due to depression or to neuroleptic medication;
i) a significant and consistent change in the overall quality of some aspects of personal behaviour, manifest as loss of interest, aimlessness, idleness, a self-absorbed attitude, and social withdrawal.

3.4 In making a diagnosis of Schizophrenia, it is important to exclude certain differentials. Differential diagnoses can be categorised into functional psychiatric disorders and organic brain disorders.

3.5 Possible psychiatric differential diagnoses include schizoaffective disorder, bipolar disorder and delusional disorder. Some examples of organic brain disorders that may present with psychotic symptoms include delirium, drug- induced states in either intoxication or withdrawal phases, alcoholic hallucinosis, and intracranial pathologies such as meningo-encephalitis, epilepsy and brain tumours.

3.6 Therefore, in the evaluation of the patient, the following steps would be pertinent:

a) A complete history and mental state assessment;
b) A thorough physical examination to exclude some of the differential diagnoses;
c) Laboratory tests such as full blood count, renal and liver panel, thyroid function tests and other relevant investigations may be useful in the initial evaluation;
d) Neuroimaging such as CT or MRI scan of the brain may be necessary if neurological signs are present or intracranial causes are suspected.

4 TREATMENT

4.1 In the holistic management of patients with Schizophrenia, it is essential to consider bio-psycho-social aspects of care. Often, it is useful to enlist the assistance of a multidisciplinary team that includes a case manager, social worker, psychologist and occupational therapist in the assessment and planning of care in the early phase of illness, or when psychosocial aspects of care becomes predominant.

Biological interventions

4.2 Antipsychotic medications

4.2.1 Antipsychotic medications should be used as the first-line treatment for psychotic symptoms. Antipsychotic medications are divided into typical and atypical based on their propensity to cause extrapyramidal side effects (EPSE). Typical antipsychotics have been convincingly shown in numerous trials to be more effective than placebo in the treatment of positive symptoms, but have a greater propensity to cause EPSE. Atypical antipsychotics are equally efficacious in controlling psychotic symptoms, have a lower propensity to cause EPSE, but are generally more costly. Antipsychotic medications may come in various formulations such as tablets, capsules, oro-dispersible, liquid and injections. (refer to Table A.1 for a list of common antipsychotics and their dosage range)

4.2.2 In general, polypharmacy is avoided and antipsychotic medications are started at low doses and titrated upwards in accordance with clinical response and tolerability. It may take up to 2 weeks of antipsychotic medication at therapeutic dosage before clinical response begins. The patient may experience a few outcomes after initiation of medication; (a) adequate response and tolerable side effects, (b) adequate response but intolerable side effects, (c) inadequate response but tolerable side effects, (d) inadequate response and intolerable side effects and (e) refusal to adhere to medication (refer to Figure 1) for treatment algorithm).

FIGURE 1. TREATMENT ALGORITHM FOR SCHIZOPHRENIA

Sequential steps to take	Action
1	Diagnosis of schizophrenia
2	First line e.g. – FGA – Haloperidol, Trifluoperazine; SGA – Resperidone – adequate trial (4-6 weeks) If adequate response -- continue
3	If inadequate response -- Second line – SGA – Olanzapine, Aripiprazole, Quetiapine, Ziprasidone If adequate response without intolerable side effects – continue
4	If inadequate response – Third line – Clozapine If adequate response with intolerable side effects – continue
5	If inadequate response – Augment Clozapine with ECT, Lithium

4.2.3 In patients with adequate response but intolerable EPSE, anticholinergic medications such as benzhexol and benztropine may be prescribed. Usage of anticholinergic medications should be reviewed regularly and balanced against side effects such as dry mouth, constipation, confusion and cognitive impairment. If side effects are preventing upward titration of antipsychotic dosage, a switch in antipsychotic medication may be preferred.

4.2.4 In situations where patients prefer, or adherence to oral medications is doubtful, depot antipsychotic medications can be started. Currently, there are 3 main types of depot typical antipsychotic medications; fluphenazine, flupenthixol and zuclopenthixol and 1 available depot atypical medication, risperidone. In practice, a test dose of depot medication of much lower dose is given first and the patient monitored for up to a week; before a further top up dose of the depot medication is given. Oral antipsychotic medications will be tapered down gradually once the dose of depot antipsychotic medication is stabilised.

4.2.5 Clozapine is indicated for patients with treatment resistant Schizophrenia, defined as inadequate response to 2 trials of antipsychotics for 6 weeks at therapeutic dosages. Clozapine is reserved as third-line because of the need for regular haematological monitoring once started to prevent agranulocytosis. Therefore, patients on clozapine should be reviewed by psychiatrists.

4.3 Adjunct medications

4.3.1 Antidepressants such as selective serotonin reuptake inhibitors (SSRI), tricyclic antidepressants (TCA) are prescribed to manage co-morbid psychiatric illnesses such as Depression and anxiety disorders. Mood stabilisers such as sodium valproate and lithium are sometimes used as adjunctive treatments when patients have prominent mood features or are treatment resistant. Short- term benzodiazepines may be useful in management of agitation or disruptive behaviours. However, there should be due consideration of potential drug- drug interactions before prescribing multiple psychotropic medications.

4.4 Electroconvulsive therapy

4.4.1 Electroconvulsive therapy (ECT) is effective in catatonic patients, and is sometimes used in treatment resistant Schizophrenia.

Psychosocial interventions

4.5 Combination of pharmacotherapy and psychosocial interventions has synergistic effects and can improve the course of Schizophrenia. Interventions include basic psychoeducation and counselling that most healthcare professionals can provide, to more complex and specialised interventions such as individual, group or family psychotherapy and vocational rehabilitation.

4.6 Psychoeducation includes educating the patients and their caregivers about the illness, its course, prognosis, as well as treatment. Side effects of medications, costs and treatment options should be discussed where appropriate.

Follow up

4.7 This is one of the most important aspects of care in Schizophrenia. During the follow up appointments, the clinician has to evaluate various aspects of the management. Broadly, they may be categorised as symptoms, medications and physical health (refer to Table A.3).

4.8 Efficacy of treatment should be assessed at each review. This includes changes in symptoms and behaviours, either improvement or deterioration. Early signs of relapse should be sought and can be managed as an outpatient by adjustment of medications. Patients have their own unique relapse signature. The patient or caregiver might be able to describe early warning signs such as increasing intensity or frequency of hallucinations, mood changes or sleep disturbances. During this segment, clinicians should also evaluate for co-morbid psychiatric disorders such as depression.

4.9 Under the category of medications, adherence and side effects should be evaluated. Adherence can be evaluated by asking the patient or caregiver directly, or by asking them to bring their existing stock of medications to check for surpluses. Checking for treatment adherence is necessary as patients frequently reduce or stop their medications on their own for various reasons ranging from a lack of insight into the illness, to complacency once they feel improved. Medication side effects are common reasons why patients do not adhere to their prescription. Therefore, it is important to enquire and examine for the presence of side effects such as EPSE, excessive sedation, sexual dysfunction, and amenorrhoea in females (refer to table A.2).

4.10 Patients with Schizophrenia are at risk of metabolic syndrome and have higher mortality rates from cardiovascular diseases. Antipsychotic medications have been associated with hypertriglyceridemia, hypercholesterolemia, hyperglycemia and weight gain. Patients should also be encouraged to lead a healthy and active lifestyle to modify their cardiovascular risk profile. If necessary, lipid-lowering or oral hypoglycaemic agents should be prescribed to manage these disorders as laid out in the Ministry of Health's clinical practice guidelines.

5 WHEN TO REFER

5.1 Patients with the following indications should be referred to a psychiatrist for further assessment;

a) Initial assessment, diagnosis and initiation of treatment, when in doubt
b) Risk of violence to self or others
c) Unexpected changes in symptomatology
d) Drug-related complications
e) Treatment resistance
f) Switching to clozapine
g) Forensic or medico-legal issues

5.2 Special groups: pregnancy, paediatric or geriatric age group

5.3 If urgent, the patient can be referred to any hospital's emergency department for evaluation. The Institute of Mental Health also has a 24-hour Emergency Room that provides psychiatric consultations.

6 CLINICAL INDICATORS

6.1 Participating medical institutions must monitor the quality of care that patients receive and submit the following clinical indicators via electronic channels to MOH:

a) Clinical Global Impression (CGI) Scale
b) Consultation for CDMP Mental Health
c) Blood test for fasting lipid (only for patients on atypical antipsychotic medication)
d) Blood test for fasting glucose (only for patients on atypical antipsychotic medication)

6.2 The Clinical Global Impression (CGI) Scale is a simple, easy to administer 2-item scale (each item has 7 points) scale to indicate the severity and improvement of the mental condition. It is chosen as it can be applied to reflect severity and improvement in other mental conditions. The scoring details are further described in Annex 4-A.

6.3 As patient compliance to follow-up is an important aspect of care for patients suffering from mental illness, the Consultation for CDMP Mental Health (at least twice per year) is a key care compliance indicator for the Programme.

6.4 For Schizophrenia patients who are prescribed atypical antipsychotic medications, a blood test for fasting lipid and fasting glucose should be performed at least once yearly to alert doctors to possible development of metabolic syndrome, a known complication of treatment with atypical antipsychotics.

6.5 Table A2 summarises the clinical indicators required for monitoring patients with Schizophrenia. The tests for the indicated monitoring parameters should be carried out upon commencement of pharmacotherapy, and thereafter at the recommended frequencies are shown in Table A3.

7 RESOURCES

- DSM IV-TR Diagnostic criteria for Schizophrenia http://www.psychiatryonline.com/content.aspx?aID=8939#8939
- International Statistical Classification of Diseases and Related Health Problems, 10th Revision, Version for 2007 (ICD 10) http://apps.who.int/classifications/apps/icd/icd10online/

TABLE A.1. INITIAL DOSING AND CLINICAL TITRATION OF COMMONLY USED ANTIPSYCHOTIC MEDICATION IN SCHIZOPHRENIA

Antipsychotic	Usual Dosage Range (mg)	Common Side Effects	Remarks
1st Line Anti-psychotic Medication			
Typical Anti-psychotic Medication (FGA)*			
Haloperidol	5-20	1. Extrapyramidal side effects e.g. dystonia, akathisia, parkinsonism	Monitor for EPSE
Chlorpromazine	50-400	2. Tardive dyskinesia	
Trifluoperazine	10-20	3. Hyperprolactinemia (amenorrhoea, galactorrhoea and breast	
Sulpiride	400-800	enlargement in females, and impotence and gynaecomastia in males)	
		4. Antiadrenergic side effects e.g. postural hypotension, delayed ejaculation	
		5. Photosensitivity in chlorpromazine users	
Atypical Anti-psychotic Medication (SGA)*			
Risperidone	2-6	Rhinorrhoea, blocked nose and at higher dosages (more than 6 mg/day) the side effect profile is similar to typical antipsychotic medications with increased EPSE and hyperprolactinemia	Increased EPSE without improved efficacy above 6mg/day
Depot Injections			
Fluphenazine	12.5-75mg/2-6wk		Typical
Flupenthixol	20-40mg/2-4wk		Typical
Zuclopenthixol	200-400mg/2-4wk		Typical
Risperidone	25-37.5mg/2wk		Long-acting Atypical (Consta) injection
2nd Line Anti-psychotic Medication			
Amisulpride	50-800		
Olanzapine	10-25	Sedation, weight gain, postural hypotension and anticholinergic side effects	
Quetiapine	300-850	Sedation, postural hypotension, anticholinergic side effects	Safety and benefit of high doses (>800mg/day not yet established
Aripiprazole	10-30	Headaches, insomnia and anxiety	72-hr half-life; no evidence of improved efficacy > 20 mg/day
Paliperidone	3-12		
3rd Line Anti-psychotics – Only for treatment resistant Schizophrenia			
Clozapine[1]	200-500	Sedation, weight gain, hypersalivation, postural hypotension	Need to regularly monitor full blood counts

Footnotes
[1]To be prescribed only by psychiatrist in treatment resistant Schizophrenia.
** FGA = First generation antipsychotic medication*
** SGA = Second generation antipsychotic medication*
Uncommon side effects of antipsychotic medications – Neuroleptic malignant syndrome; Lowered seizure threshold; Transaminitis

TABLE A.2: CLINICAL INDICATORS FOR MONITORING SCHIZOPHRENIA PATIENTS

Clinical Indicator		Recommended Frequency	Remarks
1	Clinical Global Impression (CGI) Scale: a. Severity b. Improvement	At least once yearly	Provider-administered
2	Consultation for CDMP Mental Health	At least twice per year	Provider-administered
3	Blood test for fasting glucose	At least once yearly	Provider-administered; Only for patients on atypical anti-psychotics
4	Blood test for fasting lipid	At least once yearly	Provider-administered; Only for patients on atypical anti-psychotics

TABLE A.3. MONITORING PROTOCOL FOR PATIENTS ON ATYPICAL ANTI-PSYCHOTICS FOR METABOLIC SYNDROME

Monitoring Parameters	Initial Period After initial 12-24 weeks of treatment	Long-Term Quarterly	Every Year
Weight (BMI)		X	X
Blood Pressure	X		X
Fasting Plasma Glucose	X		X
Fasting Lipid Profile	X		X

ASSESSMENT OF SUICIDE RISK (Annex 2-C)

Assessment of suicide risk is critical. The patient may already have attempted suicide or performed an act of self-harm; it is important to ask. Suicidality is a psychiatric emergency that warrants immediate admission.

Presence of the following features indicates a risk of suicide:

- Demographic factors – the classic profile for a successful attempt is an elderly single male
- Other demographic factors include divorce, widowed, unemployed with no religion
- Poor or no social support
- Presence of a psychiatric condition: especially depression and Schizophrenia
- Comorbid substance abuse and dependence
- Personality traits: impulsive, poor coping with stress, borderline and anti-social personality disorders
- Presence of a painful debilitating condition
- Previous suicide attempts
- Family history of suicide
- Premeditation – e.g. timing and location of the attempt; collection of necessary materials; rehearsal of the act
- Last acts – e.g. writing goodbye letters; distributing personal belongings
- Effort to avoid detection – e.g. attempting suicide while alone in a locked room; choosing a time when the family is away or asleep
- Choosing a method that they perceive as lethal
- Regret that they are still alive
- Absence of specific plans and goals for the future; having nothing to live for

How to inquire about suicidal ideation

It can be very daunting to assess for suicidal ideation for the uninitiated. Rest assured that asking for suicidal ideations will not result in this happening. In fact, you are likely to miss it if you don't enquire. Here is a suggested flow for this line of questioning which is less challenging to ask:

1. "Do you sometimes have a feeling that life isn't worth living, or do you think about death much?"
2. "Do you sometimes think that if you died tomorrow from an accident or illness, that it just wouldn't matter?" ***(Passive ideation)***
3. "Have you had thoughts of killing yourself?" ***(Active ideation)***

CLINICAL GLOBAL IMPRESSION (CGI) SCALE (Annex 4-A)

Considering your total clinical experience with this particular population, how would you rate this patient's mental condition at this time?

1) Severity of Illness

1 = Normal (not at all mentally ill)
2 = Borderline mentally ill
4 = Moderately mentally ill
5 = Markedly mentally ill
6 = Severely mentally ill
7 = Extremely mentally ill

2) Global Improvement

0 = Not assessed
1 = Very much improved
2 = Much improved
3 = Minimally improved
4 = No change
5 = Minimally worse
6 = Much worse
7 = Very much worse

Guidelines and Information for Authors

The Singapore Family Physician

Authors are invited to submit articles for publication in *The Singapore Family Physician* on the understanding that the work is original and that it has not been submitted or published elsewhere. Your original article will be considered for publication on the understanding that they have to be approved by the Editorial Board via a double-blinded peer-review process and subject to revision. Authors are encouraged to consult the recommendations in the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* (http://www.icmje.org/index.html) which the SFP is in accord with.

The following types of articles may be suitable for publication: case reports/ study, original research works, audits of patient care, protocols for patient or practice management and letters to the Editor. The CME and review articles will be published under the prerogative of the Institute of Family Medicine (IFM) in the College of Family Physicians Singapore. The article should be written in British English, and not be more than 3000 words in length. This must be submitted in an electronic form and of a format that is compatible with major word processor applications. Submissions in Microsoft Word in Word 1997-2003 format (.doc) is preferred, later versions (.docx) will not be accepted.

From 31 January 2010 all articles submitted for publication must be submitted electronically through the ***SFP Editorial Manager***, our online submission and peer-review system which can be accessed at www.editorialmanager.com/sfp/default.asp.

All instructions for registration and submission can be found at the webpage. Authors and reviewers can follow clearly the progress of the manuscript submission and review process by logging into the ***SFP Editorial Manager***. An online users' guide, authors' and reviewers' instructions are also located at the website in case of queries and difficulties. Any problems encountered logging in can be addressed to editorialoffice@cfps.org.sg.

RECOMMENDED FORMAT FOR THE MANUSCRIPT

The submission should comprise of the following:

1. Title Page
2. Summary/ Abstract
3. Key Words
4. Text/ Manuscript (anonymised version)
5. Tables
6. Illustrations
7. Authors Agreement/ Copyright Assignment Form
8. Patient's Consent Form, if necessary (including consent for photograph or illustration taken of human subject)

and each one of these sections should start on a fresh page.

Authors are advised to ensure the anonymity of study subjects and patients by removing any and all information that could compromise their privacy from the submission.

The text should be typed in Arial font, 12 point size with a 1.5 line space.

The Title Page

- The title should be concise and highlight the key elements of the article.
- Include on the title page first name, qualifications, present appointments, type and place of practice of each contributor.
- Include name, address, handphone number and email address of the first author to whom correspondence should be sent.
- Insert at the bottom: name and address of institution or practice from which the work originated.

The Summary/ Abstract

- The summary should describe why the article was written and present the main argument or findings.
- Limit words as follows: 250 words for major articles; 200 words for case reports.

Key Words

- Add, at the end of summary in alphabetical listing, keywords of up to 5 in number which will be used for article indexing and retrieval under Medical Subject Headings or MeSH. MeSH is the NLM controlled vocabulary thesaurus used for indexing articles for WPRIM and PubMed. Please refer to www.nlm.nih.gov/mesh/ for details.

The Text/ Manuscript (full complete)

The text should have the following sequence:

- **Introduction:** State clearly the purpose of the article.

- **Methods:** Describe the selection of the subjects clearly. Give References to established methods, including statistical methods; provide references and brief descriptions of methods that have been published but are not well known. Describe new or substantially modified methods, giving reasons for using them and evaluate their limitations. Include numbers of observations and the statistical significance of the findings where appropriate.

  Drugs must be referred to generically; all the usual trade names may be included in parentheses.

  Dosages should be quoted in metric units.

  Laboratory values should be in SI units with traditional unit in parentheses.

  Do not use patients' names, initials or hospital numbers to ensure anonymity.

- **Results:** Present results in logical sequence in the text, table and illustrations.

- **Statistics:** Describe statistical methods which can be easily understood and verified by the reader. Use technical terms in its proper place, and where possible quantify readings and indicate errors of uncertainty and confidence intervals.

- **References:** The author(s) is/ are responsible for the accuracy and completeness of the references, which should be identified in the text by superscript Arabic numerals in the order of first citation and noted in numerical order at the end of the text.

  Digital Object Identifier (DOI) citation information must be included as a full DOI URL by prepending http://dx.doi.org/ to any DOI reference. To identify a DOI reference, please visit CrossRef at http://www.crossref.org/guestquery/ and enter in the reference information in the box provided to locate the DOI where available. Such DOI information will facilitate readers to trace referenced papers easily.

Where there are more than three authors, the first three should be named and then followed by et al.

Example:
Tan and Ho. Treat-to-target approach in managing modifiable risk factors of patients with coronary heart disease in primary care in Singapore:What are the issues? Asia Pacific Family Medicine, 2011;10:12. doi:10.1186/1447-056X-10-12.
Authors may wish to familiarise themselves with the AMA style for the citing of references for BioMedical publications at www.amamanualofstyle.com.

Tables
Tables should be submitted on a separate page. Label them in roman-numeric sequence [I,II,III etc] and ensure they are clear and with explanatory legends as required.

Illustrations
- Illustrations must be submitted in a separate page, and should be provided whenever appropriate. Illustrations should be cited in the text. When required, it is the author's responsibility to obtain permission to reproduce illustrations. Authors need to ensure that photographs, illustrations and figures do not contain any information that will reveal the identities of the patients and authors. From 1 January 2012, all photographs and illustrations taken from any human subject must be accompanied by the respective endorsed consent form. Clear captions to the figures should be provided.

Anonymised Text
As the original article will be subjected to a double-blinded peer review process, all identification of names and institutions have to be removed from this version to facilitate the peer review process.

Author Contributorship for Original Article Submission
Author details must be included in the relevant fields when submitting an article. Only those who have made substantial contributions to the study and/ or preparation of the article should be acknowledged as authors and named in full. The SFP follows the International Committee of Medical Journal Editors (ICMJE) criteria pertaining to authorship (refer to http://www.icmje.org/ethical_1author.html). The precise role(s) of each author should be included in the 'contributorship' declaration.

Declaration of Conflicts of Interest
The SFP requires the author(s) to provide full and detailed declarations of any conflicts of interest. Where there are none, please use the following declaration: *"The author(s) declare(s) that he/she/they has/have no conflict of interest in relation to this article."*

RECOMMENDED FORMAT FOR PRISM (Patients' Revelations as Insightful Studies of their Management) SECTION

Authors planning to submit their case studies to the PRISM section should structure their article according to these headings:

Title
- The title should be framed into a question to define the key focus of the case study.

Patient's revelation: What happened?
- The author(s) will provide a concise description of the setting on which the subject raised his/her medical or psychosocial issue pertaining to their health or disease management. It should cover the background, encounter and interaction of patient with the healthcare professional (doctor, nurse or allied healthcare professional). Author(s) should conceal the identity of the subject and/or related or accompanying personnel: abbreviation should be used instead, if necessary.

Gaining insight: What are the issues?
- The issue(s) raised by the patient should be framed into question(s). The question(s) will constitute a problem list and will serve as a focus for the management of this subject.

Study the management: How do we apply in our clinical practice?
- This section covers the approach to the management of the subject by the author(s). The author(s) should provide a literature review of current evidence, if any, of the basis of the subject's management, or to highlight the gaps of knowledge if such evidence is lacking. The author(s) will suggest ways to apply the new knowledge in clinical practice or to highlight the limitations of its applications, if any.

Conclusion
- The author(s) will provide a concise summary of the lessons learnt from this case study.

The article submitted to the PRISM section should be written by not more than three authors. Each article should not exceed 2000 words. Photographs or charts may be included but should conform to the specific instructions for any other articles submitted to The Singapore Family Physician.

Revised Manuscript Submission
Manuscripts may be returned to their respective authors for revision. This will be accompanied by an Editor's email for which comments and recommendations may be made. The authors are advised to read and to take note of these comments carefully and to revise their articles accordingly. The authors need to reply to the editor's email to outline their response before the resubmission of the revised manuscript. They should exclude the identity of the authors and their institutions, as the email may be redirected to the reviewers during the resubmission process. The resubmitted manuscripts should include the revised complete version, as well as the anonymised version as before.

Proofs
Prior to publication, the Editorial Team will copyedit the article to fit the format of the Journal. The author will be sent the copyedited proof of the article, and the author should read carefully the proof and give comments and/or confirmation within 48 hours of receiving the proof. This will greatly facilitate the SFP to proceed to printing without delay, or to have to go to print without the corresponding author's comments

Reprints
1 complimentary copy of the article will be given to the authors. Additional copies can be ordered at authors' rates at time of printing.

Correspondence & Enquiries should be addressed to:
The Honorary Editor, The Singapore Family Physician
College of Family Physicians Singapore
College of Medicine Building
16 College Road #01-02
Singapore 169854
Tel: 6223 0606 Fax: 6222 0204
Email: editorialoffice@cfps.org.sg

Circulation
The Singapore Family Physician is published quarterly. It is circulated to all Fellows, Collegiate Members, Ordinary Members and Associate Members of the College of Family Physicians Singapore, and to private and institutional subscribers. It is also published online and can be found at www.cfps.org.sg

The journal is also circulated to all relevant government, professional, medical and academic organisations in Singapore, sister Colleges overseas and to the World Organisation of National Colleges and Academies of General Practitioners/ Family Physicians (WONCA).

"The course has been helpful, I have gained a lot of knowledge, and it has made me feel more confident in dealing with the more common mental conditions like anxiety, depression and even in the detection of early mental psychosis.

– Dr Peter Yeo."

Graduate Diploma in Mental Health (GDMH)

The Institute of Mental Health collaborates with the Division of Graduate Medical Studies (DGMS), Yong Loo Lin School of Medicine, National University of Singapore to offer a part time Graduate Diploma in Mental Health (GDMH). This structured training programme is open to general practitioners who wish to gain insights into human psychiatry and knowledge on mental illness. Through this professional certification, participants will develop an in-depth understanding of the subject and learn the different approaches towards patient treatment. Clinical attachment opportunities will also be available.

Module 1: Introduction to Psychiatry
Module 2: Psychosis
Module 3: Mood, Anxiety and Grief
Module 4: Addiction / Personality Disorder
Module 5: Child and Adolescent Mental Health including Learning Disabilities
Module 6: Psychogeriatrics

Application starts from 1 March 2013 to 30 June 2013. For more information, please contact
Helen Ong: 6389 2968 / helen_bc_ong@imh.com.sg
Arthur Lim: 6389 2831 / arthur_tm_lim@imh.com.sg

INSTITUTE of MENTAL HEALTH
Loving Hearts, Beautiful Minds

NUS National University of Singapore

4th Intake September 2013
Government Subsidy Available.

ADMINISTERING CHAS

The Community Health Assist Scheme (CHAS), formerly known as Primary Care Partnership Scheme (PCPS) was enhanced in January 2012. To generate greater public awareness of CHAS, Agency for Integrated Care (AIC) embarked on a marketing campaign across media channels such as TV, radio, print and outdoor in 2012 and it has been well-received by the public. There are currently more than 240,000 CHAS beneficiaries. We are expecting the number of CHAS beneficiaries to reach more than 400,000 by the end of 2013.

AIC also seeks to support CHAS GPs/Dentists in administering the scheme at their clinics. We have developed easy-to-use guides to assist the doctors and clinic assistants. Newly accredited CHAS GPs/Dentists will receive all necessary collaterals and forms as a welcome pack from AIC to facilitate implementing the scheme at their clinics.

We have implemented several enhancements to CHAS claims portal to make the claims portal more user-friendly and easier to submit medical and dental claims. We welcome your continuous feedback on the use of the claims system. Look out for further enhancements that will be implemented in the coming year.

Participating in CHAS is now simpler than expected:

- There is no cap imposed on clinic charges. The fees are to be reasonable, taking into account that patients are from low to middle income background. Please note the cap limit on consultation at $4 and per medicine tablet at $0.70 for CHAS patients has not been applicable since Year 2009.
- You can potentially retain your regular patients. The number of CHAS cardholders is expected to exceed 400,000 by end 2013.
- You only need to obtain patient's consent through patient consent form once, at the first visit.
- CHAS GP clinics are able to directly refer CHAS patients to government restructured institutions, bypassing the polyclinics, for subsidised specialist treatment using the CHAS Referral Form. Please note that you would not be able to refer to a named specialist.
- The clinic has up to 30 days from patient's visit date to submit CHAS claims.
- You can contact AIC during office hours for assistance in administering CHAS at your clinic.

Agency for Integrated Care (AIC), which was set up by MOH to oversee healthcare integration in Singapore, is the one-stop contact point for GPs and Dentists for CHAS.

aic agency for integrated care

MINISTRY OF HEALTH SINGAPORE

For more details, please contact **CHAS GP Hotline +65 6632 1199** or **gp@chas.sg**.