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HEALTH EDUCATION & TRAINING INSTITUTE

ACUTE PSYCHIATRIC MANAGEMENT

3rd Edition

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FOREWORD

As trainee psychiatrists you will be dealing with the extraordinary range of human behaviours and predicaments. Your task will be to make sense of how others are making sense of their upturned worlds, their altered perceptions, the adversities that have befallen them. You will be privileged to have many people open their life stories to you, to trust your judgement and to look to you for the care they need. Also, there will be patients who do not see themselves as ill at all. If this is at times bewildering, even frightening for us as clinicians, spare a thought for the patient's experience. The patient brought to the hospital with his first episode of psychosis is entering a world completely alien and intimidating. The experience for his family will be almost as daunting.

Our role is to bring our knowledge, experience and compassion to such situations. This involves a certain kind of listening, seeing and feeling. The ability to listen to the patient's story so as to simultaneously hear the patient's experience, the chronology of symptoms, the possible aetiological factors and to understand the impact and meaning for the patient. Links are made, and hunches explored as a detective might solve a case. Diagnostic, behavioural and familial patterns are identified, several lines of inquiry are occurring at once. The patient and his/her family are engaged and included in the working up of an understanding and then a plan of action. Where there is fear and confusion: calm, reassurance and explanation are required; where there is distress: comfort and containment. These things are learnt in time, through study, watching and role mirroring, doing and practice.

This training manual was developed by an expert clinician editorial group of the Health Education and Training Institute and HETI's Psychiatric State Training Council. I hope this second edition of the Manual will provide a solid launching pad for a lifetime of learning.

Nick O'Connor
Chair, HETI Higher Education Governing Council

1 ASSESSMENT

1. ASSESSMENT

This section assumes a working knowledge of the process of taking a psychiatric history, formulating the case, discussing with senior clinicians when necessary and implementing an appropriate management plan. In addition, this section focuses on particular areas of practice where particular skills and knowledge are necessary in an acute setting.

LEARNING OBJECTIVES

- To assist the clinician in considering the various aspects of risk which are to be considered in the psychiatric assessment, and incorporating these finding into a sophisticated management plan

RISK FORMULATION

The consideration of the nature of risk an individual poses to themselves or others, as well as to various areas of their life and function, forms a key part of the formulation process. New South Wales Health offers standard risk assessment modules which are a necessary tool to use within the context of an assessment, however these are only a guide, and do not replace a sophisticated biopsychosocial approach to considering how risk has developed and presented in a person in the past, why and how it is occurring at present, and what circumstances may alleviate or enhance the likelihood of such risks presenting in the future.

RISK DOMAINS

The first areas of risk usually of concern to clinicians are those of "harm to self" and "harm to others". However, a sophisticated review of areas of risk must take into other considerations;

These may include;

- Sexual assault
- Sexual exploitation
- Traumatic stress before and during episode of care
- Financial risk
- Vocational risk
- Relationship vulnerability
- Parenting capacity
- Iatrogenic physical and psychological risk
- Reputation

Other areas of risk to consider of a more enduring nature may include;

- Risk of symptom persistence/incomplete recovery
- Sub optimal treatment adherence
- Family or cultural resistance
- Stigma
- Cognitive incapacity secondary to illness or treatment
- Difficulties in access
- Effect on vocation and lifestyle
- Family relationship and social consequences
- Physical ill health and poor treatment adherence
- Developmental disruption

CONSIDERATION OF RISK

While traditionally there is an expectation of psychiatrists being able to accurately predict risk, this is unrealistic, in that the predictive capacity of psychiatrists in regard to future harm has been shown to be low.

This is not to say that the assessment of risk is redundant in the psychiatric assessment.

Instead it is important for clinicians to recognise the limitations of such a process, and instead, in the process of assessment, work towards creating a formulation of risk which pays attention the the history of the individual, and integrates the trajectory of prior risk periods, if evident, and the current presentation evolution, to help establish, ideally in discussion with the individual, the appropriate route to help holistically provide care which through that process, manages the likelihood of identified risks eventuating.

ACUTE ISSUES

Some of the factors to be aware of in the acute setting relevant to the assessment of "risk to self and others" include;

- History of violence or self injurious behaviour
- Stated intention to harm self or others
- Violent thoughts and anger
- Substance intoxication
- Presence of command hallucinations
- Presence of misidentification delusions
- Changeability of mental state
- Impulsivity
- Attribution style

[1,2,3]

Overall, the goal for the clinician assessing a consumer is to comprehensively review the individual while being aware of past and current risk with a view to addressing this in a management plan.

Risk cannot be seen as a standalone task, and a "tick box" assessment does little to assist with the sophisticated assessment of an individual. Risk, and attempts to alleviate it, must be seen as part of a larger management plan.

It is essential that the issue of risk is discussed with a senior colleague, usually a psychiatrist or in some cases a senior emergency department clinician, with consideration then being made as to appropriate health district "care levels" and the use of special 1 to 1 nursing, as well as location of management (assuming that inpatient care is seen as the least restrictive option).

PSYCHIATRIC ASSESSMENT AFTER SELF-HARM

LEARNING OBJECTIVES

- Understand the nature of suicide attempts and deliberate self-harm
- Develop an approach to the assessment of people presenting with threatened or actual self-harm
- Formulate a management plan for a patient presenting with self-harm

1. Steadman HJ, Cocozza JJ, 1980. "The prediction of dangerousness- Baxtrom: A case study". In: G. Cooke, ed. *The Role of the Forensic Psychologist.* Springfield, Il.: Thomas. (pp. 204-21 5).
2. Appelbaum P, Guthiel T. *Clinical Handbook of Psychiatry & the Law.* Philadelphia: Lippincott, Williams & Wilkins. 2007
3. Monahan J, Steadman H, Silver E, et al. *Rethinking Risk Assessment: The MacArthur Study of Mental Disorder and Violence.*New York: Oxford University Press. 2001

INTRODUCTION

All suicide attempts and expressions of suicidal intent should be taken seriously regardless of whether the individual has made multiple past attempts of low lethality, regardless of the presence of a suspected personality disorder and even if it has been suggested that the attempt was with the aim to manipulate others.

At times a patient's suicidal gesture will be described as 'attention-seeking'. This term is often used in derogatory terms and is best avoided as it is likely to negatively influence an otherwise objective risk assessment.

SUICIDE AND DELIBERATE SELF-HARM

There is a view that self-harm attempts can be categorised into 'serious suicide attempts' and more impulsive forms of deliberate self-harm (DSH). The former is typically associated with severe mental illness, high intended lethality and attempts to avoid rescue. The latter is considered a manifestation of personality disorder or acute crisis, where there are impulsive, poorly planned attempts at self-harm.

This rule of thumb may be a misleading dichotomy as, regardless of the potential for death or serious injury in the DSH category, the rates of completed suicide years after a seemingly minor episode of so called 'deliberate self-harm' are significant.

An example is an Australian study, which followed patients from 1975 onwards. Of those who had made an attempt at deliberate self-harm in the mid 1970's, 4% had completed suicide at 4 years, 4.5% at ten years and 6-7% by 18 years[4].

RISK FACTORS/AETIOLOGY

Demographic/Social

There are increased rates of completed suicide and DSH in the elderly and in young males. Men are more likely to complete suicide, whereas women make more attempts. There is an increased suicide risk if a male is widowed, divorced or separated. Other demographic factors that may increase suicide risk include living alone, social isolation, unemployment, financial difficulties and recent legal difficulties. Suicide risk is heightened when there is a family history of suicide or psychiatric illness.

Psychiatric

DISORDERS ASSOCIATED WITH SUICIDE INCLUDE:

Affective disorders	60% of completed suicides
Alcohol and drug abuse	25% of completed suicides
Psychotic illness	10% of completed suicides
Personality disorders	5% of completed suicides

Up to 20% of people who complete suicide are intoxicated at the time of their death. Alcohol and drug intoxication affects judgment and impulsivity. Important psychological factors associated with suicide include:

- Hopelessness
- Low self-esteem
- Loss experiences
- Conflict
- Bereavement
- Early life trauma

Most importantly, a history of a past suicide attempt is the strongest clinical predictor of a future attempt.

[4] de Moore G, Robertson. A Suicide in the 18 Years After Deliberate Self-harm A Prospective Study. *The British Journal of Psychiatry.* 1996);169:489-49.

Medical

Medical illnesses that have been associated with an increased risk of suicide are shown in Table 1 (see below). Suicidal behaviour has been described in association with numerous medical illnesses, some of which are associated with significant morbidity or disability, others which lead to varying states of dysphoria, disinhibitIon or other neuropsychiatric sequelae. In some circumstances, suicidal behaviour may be induced by the neuropsychiatric adverse effects of treatments for conditions e.g. high dose corticosteroids or chemotherapeutic agents. Infection with HIV may be associated with stigma in some sections of the community, and thus lead to acute states of distress, which may increase the risk of suicide or self-harming behaviour. Frequently, suicidal behaviour emerges out of misunderstanding the illness, its treatment or prognosis.

ASSESSMENT OF ATTEMPTED SUICIDE AND DSH

1) Build Rapport

A patient who is being seen following self-harm or for the assessment of suicidal intent may be distressed, embarrassed or guarded and, therefore, maybe reluctant to engage or cooperate with history taking. However, patients are often relieved by the unburdening of their troubles rather than being annoyed or offended.

2) Psychiatric History

Information relating to the attempt or intent should be obtained in an open and direct manner without ambiguity so that mistakes are not made.

It may be helpful to introduce questions regarding suicide in a sequential manner. For example, starting with "With all these problems that you are now facing, have you ever thought that you would rather be dead?" If an affirmative answer is given then it could be asked "Have you ever thought about deliberately ending your life?", then "Have you thought about how you might do this?"

It is often useful to run through a chronological description of the events leading up to, during and after the self-harm or suicide attempt to asses the level of risk.

Features of the history to consider:

a) Prior Self-Harm:

- Significant acute psychosocial stressors (possible precipitating factors) or medical problems
- Low mood or symptoms of a major mental illness
- Feelings of being better off dead
- Feelings of hopelessness
- Drug or alcohol consumption
- Preparation for death; finalising will or life insurance, giving away possessions, writing a suicide note
- Onset of suicidal ideation
- Degree of planning (versus impulsivity)
- The patient's perception of the degree of lethality of the chosen means patient may strongly believe that five sleeping tablets would be lethal in overdose) and the patient's intent (e.g. to die, to escape problems, to sleep)

HIV/AIDS	Organic brain syndromes	Rheumatoid arthritis
Head Trauma	Spinal Cord injuries	Cancer
Epilepsy	Cardio Pulmonary disease	Cushings disease
Multiple Sclerosis	Chronic renal failure	Huntington's Chorea

Table 1

b) Events at the time of the suicidal act:

- The setting; where they at home with family around them or did they attempt suicide away from home or at a time when they knew no one would be around
- Was the patient intoxicated?
- Acute stress present? (e.g. argument with partner)

c) Post Self-Harm:

- Are they glad or disappointed that they are alive?
- Does the patient show remorse or regret about the attempt? (Shame or regret may be a good or bad thing: some patients will regret the hurt that loved ones may have felt and be less inclined to attempt suicide in the future; a person with low self-esteem may feel even more of a burden or worthless and therefore more determined to carry out further attempts)
- Actions or behaviour after self-harm or suicide attempt (e.g. immediately called someone for help or tried to hide the attempt from others)
- Continued access to suicidal means (e.g. does the security guard who presents after self-harm have access to a gun?)
- Willingness to engage with mental health services and accept treatment
- Ongoing or future suicidal intent or plans
- Plans for the future? Do they express plans to see friends, keep appointments or to try to obtain goals in the future?
- What supports are available in the community?

Has the self-harm served a purpose or helped out the patient in someway (e.g. release of frustration, mobilised the support of loved-ones) that may result in a reduction of risk?

If the patient denies further suicidal intent or plan following an attempt, what has changed? (e.g. an acute stressor has passed, they have come to a realisation that they are loved or that their death would be more significantly felt by others than they previously thought, social supports generated etc.) If there doesn't appear to be any change in the patient's situation following a serious suicide attempt but the patient is denying further suicidal intent then consideration should be given to whether the patient is being deliberately deceptive.

Look for discrepancies in the recall of events that may indicate that the patient is being deceptive (e.g. a patient may present after an 'accidental' injury or overdose in the context of significant psychosocial stressors and have significant risk factors for suicide but denies suicidal ideation or intent) Consider suicidal intent in a patient that has been involved in uncharacteristic risktaking behaviour; a patient presents obtunded after taking a large amount of benzodiazepines but upon awakening say that their intent was just to get some sleep.

The ability of the patient to guarantee their safety is not a reliable measure of risk.

d) Psychiatric history:

- Ask about previous suicide attempts; the psychosocial context in which they occurred, the method used, degree of intent and lethality and treatment sought or provided
- It is useful to obtain history regarding the patient's ability to engage with treating professionals or teams
- Presence or absence of diagnosed mental illness or personality disorder.

e) Collateral history:

It is important to obtain collateral history from past medical files, family, friends, general practitioner, treating psychiatrist or psychologist, or community mental health team

Issues of privacy and confidentiality must be weighed against the level of risk; if the patient

does not give consent to talk to third parties, then confidentiality may be broken if it is felt that the level of risk to the patient (or others) outweighs the patient's right to privacy; a judgement may also need to be made about whether there is enough concern to risk jeopardising the therapeutic alliance from contradicting the patient's wishes.

3) Medical/physical assessment:

- This will be guided by emergency department or medical staff
- Consider a paracetamol level and other drug screen after self-harm as a routine (not all patients are reliable historians), if the medications ingested are unknown or if there has been a suspected polypharmacy overdose
- Consider a longer period of medical observation for medications with unusual metabolism or those that are slow release
- Patients who are intoxicated with alcohol or other substances may need to be detained in hospital and observed until they are sober so that a more thorough risk assessment can be undertaken
- Assessment of cognitive function may be important as part of an assessment capacity if the patient is requesting to leave or to detect ongoing cognitive side effects of ingested substances.

MANAGEMENT/MODIFICATION OF RISK OF SUICIDE AND DSH

Medical management:

- This will be guided by the medical teams
- Sedative medication may be required to reduce distress or reduce risk of harmful behaviour
- It is important that a patient is medically stable prior to being transferred to a psychiatric ward.

Treatment setting:

- Does the patient need to be admitted or could treatment be provided in the community?
  a. This will depend on the patient's need for medical management, their degree of risk, level of support in the community and their willingness to engage in treatment.
- If the patient is to be admitted should this be as a voluntary patient or under the *Mental Health Act?*
  a. This will also depend on the degree of risk and the patients level of cooperation with treatment
  b. The least restrictive environment should be used.
- When a patient is admitted consideration will need to be given to the type of ward and the level of nursing care
  a. If the patient requires close nursing supervision or is at risk of absconding then it would be appropriate that patient is managed in a closed ward, or observation or high dependency unit
  b. For patients considered to be of high immediate risk of self-harm consideration should be given to 1:1 nursing care
  c. There may be a lower threshold for 1:1 nursing care on a medical or surgical ward as the expertise of the nursing staff to provide psychiatric care will be low.

Psychiatric management/modification of risk factors:

- Reduce psychological distress or symptoms
- Increase social support
- Offering alternatives to suicide (e.g. through problem solving techniques)
- Treat underlying psychiatric illness or substance abuse/dependence.

THE PSYCHIATRIC ASSESSMENT OF ABORIGINAL AND TORRES STRAIT ISLANDER PEOPLES

LEARNING OBJECTIVES

- To assist the clinician in completing a culturally sensitive bio-psychosocial assessment of Aboriginal and Torres Strait islander peoples

Aboriginal peoples endorse the broader, more holistic concept of social and emotional health and wellbeing rather than mental illness. The separation of mind and body often used in Western mental health is less relevant to Aboriginal peoples. Indigenous perceptions of mental health incorporate the mind, body, spirituality, environment (including relationships with family, land and culture) and socio political factors, which have contributed to the development of disorder. When one or more of these elements of health is compromised the person may be predisposed to physical or mental problems.

General principles

- The centrality of relationships – establishing trust and a genuine connection is imperative, and can form a significant barrier to the clinical assessment if not given consideration.
- The consumer is the whole family so it is important to establish who is important to the individual being assessed in the "here and now". Support and engage the family in care of the individual.
- Recognise diversity between and within Aboriginal cultures and avoid assumptions.
- Recognise that history affects current day relationships. The high level of individual and societal trauma experienced by indigenous peoples and the consequent level of caution in engaging with non-indigenous authority figures must be kept in mind.
- TIme in establishing relationships is even more important in indigenous people. A genuine and personal connection may be critical to successful engagement. A clinicians readiness to listen intently will allow for a sense of being heard and understood.
- Cultural safety – establish respect, trust and a genuine partnership that values Aboriginal cultural identity, and an environment where people feel safe and empowered to express their cultural identity and may actively participate.

Start interviews by building rapport: be introduced to the patient by a familiar staff member, consider greeting the patient with a loose handshake and brief eye contact, ensure adequate personal space, and give an explanation of who you are and of your role.

Consider commencing the interview with a genogram. This helps to quickly establish family relationships, losses, and living arrangements and conveys interest in the patient as a person. It also places the patient in the position of expert. Use non-threatening statements (such as commenting on events within a community or the person's life) to put people at ease, without being over baring.

Create a problem list with the patient. This focuses the interview on the patient's priorities. Use humour, especially at your own expense. Keep language simple and clear. Make the patient a cup of tea, a gesture which symbolises hospitality, humility, freeness with time.

Communication

- Informed listening: demonstrate an understanding about salient background matters that put the patient's story in a context. Listen to both silences and what is said.

- Use openended questions. Indigenous people may feel confronted by direct questioning and give any answer, whether correct or not, in order to deflect attention. It is more important to make a connection with the patient, so talk about things other than the mental health issue first, talk around topics, and accept that not all information may be gathered in one sitting, but that investment in the relationship is most important.
- Talk at an appropriate pace and wait patiently for a response (quick responses are seen as impolite), and be aware that anxiety about the interview may affect behaviour.
- Particular cultural considerations include not referring to a dead person by name, taboos associated with the use of personal names, recognising that spiritual experiences are not necessarily psychotic, observing cultural norms (e.g. brief or intermittent eye contact, sit beside rather than opposite the patient), checking relationships and sense of belonging to country and family, awareness of the significance of spiritual issues and recognition of the effect of gender of the interviewer (if opposite to the patient, they may feel uncomfortable and unable to disclose information) and transference issues.
- Obtain corroborative information from family, Aboriginal health workers and other involved clinicians and members of the community. Concerns about confidentiality must be weighed up, but obtaining accurate information is important. Clarify which family members are significant and address confidentiality and consent to give information early in the process.

MENTAL STATE EXAMINATION

Appearance, behaviour, rapport: Establishing the patient's usual level of self care may help distinguish what is pathological (for example hygiene, the state of clothing) from normal grooming; recognising that scars may be the result of traditional rituals and not self-harm; appreciating that shyness is common and so avoidance of eye contact may not represent illness.

Speech: Responses may be delayed, softly spoken and short. The clinician must also consider the patient's familiarity with English.

Mood: If mood is not volunteered, then offering suggestions with words commonly understood in the local community (e.g. "wild" for anger, "silly" for euphoric, "weak" for depressed and "strong" for good or well).

Affect: Crying is uncommon as many Aboriginal children brought up traditionally are taught not to cry as it may cause sickness. Shyness and shame may also be mistaken for a flat or depressed affect. A patient may appear blank or expressionless with the clinician and yet be animated and reactive with relatives or familiar people.

Thought form: Disturbances of thought form may be more difficult to detect if the patient is not fluent in English. Seek the opinion of relatives, Aboriginal health workers and liaison officers.

Thought content: Interpreting the clinical significance of thought content requires awareness of accepted cultural beliefs. Check with the Aboriginal liaison officer or other clinician. For example, in some communities in far North Queensland black magic may be considered a cause of sickness or death and it may be accepted that the spirits of the deceased move around the living and are perceptible at times.

Perceptual abnormalities: Fleeting visual hallucinations such as spirits may be reported in the context of intense emotional experiences. However, auditory hallucinations are more likely to indicate mental illness.

Cognition: Be aware of biases which may adversely affect performance on Western psychological tests. Check knowledge of familiar material (e.g. sporting teams), observe behaviour in the community

(assesses performance in everyday tasks), and check their cognitive reputation (talk to people close to the patient).

Time: Aboriginal people often place events in a circular, rather than linear, pattern of time. Events are placed in time according to their relative importance for the individual, with more important events located as 'closer in time'. Assess event/time orientation using culturally and personally relevant events such as 'memory milestones' (e.g. seasons, deaths, and family gatherings). Assess cortical function by having the patient name common objects, copy a drawing of 2 intersecting boomerangs, Luria hand sequences and primitive reflexes.

Insight and judgement: Take into account cultural beliefs and norms, including traditional explanations of illness.

PSYCHOPATHOLOGY IN THE GENERAL MEDICAL SETTING

LEARNING OBJECTIVES

- Describe the features of depression, anxiety and psychosis in medically ill patients
- Outline investigation and management of such presentations

INTRODUCTION

The following provides an overview of assessment and initial management of the medically ill patient in a general hospital setting.

Psychiatric practice in the medical setting:

- *Referral* – it is important to get a clear idea from the treating team what question is being asked or what is being requested of the psychiatric team; it is helpful to get accurate information regarding the patient's medical illness, management and prognosis as the information will help shape the formulation and guide psychiatric treatment
- *Assessment* – start by reading the patients current and past medical files; check recent medical investigations and the medication chart; when interviewing the patient, initially focus on their medical predicament so that the patient feels their physical complaints are being taken seriously (some patients will feel that a psychiatric referral has been organised as it felt that the patient's problem is in their head); consider the interplay between the patient's coping styles, the medical problem and the psychiatric problem generating the consultation; detailed cognitive testing and assessment of capacity are often required
- *Investigation* – consider further investigations (e.g. TFT, syphilis serology, B12, folate, CT/MRI and gather collateral information)
- *Management* – be aware of drug interactions and how the medical problem(s) may alter the pharmacokinetic or pharmacodynamic properties of the psychotropic medication proposed; consider medications with alternate routes of administration if the patient is nil by mouth or refusing treatment; manage risk; determine whether detainment and treatment is necessary under 'Duty of Care', a Guardianship order or the *Mental Health Act*; communicate suggestions clearly to the treating team

Interactions between medical and psychiatric problems[5]*:*

- Psychiatric presentation of a medical condition or treatment (e.g. delirium)
- Psychiatric reactions to a medical condition (e.g. depression in the setting of cancer)

[5] Modified from: *Massachusetts General Hospital Handbook of General Hospital Psychiatry,* fifth edition.

- Medical/physical presentation of a psychiatric condition or treatment (e.g. conversion disorder, metabolic complications of antipsychotic use)
- Comorbid medical and psychiatric conditions (e.g. a patient with schizophrenia is admitted with exacerbation of asthma).

DEPRESSION IN THE MEDICAL SETTING:

1) Epidemiology:

- Prevalence of major depression in elderly inpatients is 10-30%[6]
- Prevalence of depression in inpatients with congestive heart failure 20-37%[7]
- Rate of major depression following myocardial infarction may be as high as 16-23%[8]
- 6 month mortality following MI 17% in depressed group compared to 3% in controls[9]
- 30% of patients depressed after stroke, associated with increased mortality[10]

2) Diagnosis

- Firstly consider whether the patient's predominant symptom is depressed mood, if not the patient may appear depressed or be psychomotor retarded secondary to delirium, dementia or a frontal lobe syndrome, or may have emotional lability secondary to central nervous system disease
- If the patient's mood is depressed then consider whether the depressed mood is a psychological reaction to illness, secondary to a medical problem or a primary psychiatric illness
- Sadness or grief may be appropriate to the situation but a major depressive episode is never appropriate
- Medical conditions commonly associated with depression include:
  i. Pancreatic carcinoma
  ii. Cerebrovascular disease
  iii. HIV/AIDS
  iv. Ischaemic heart disease
  v. Hypothyroidism
- Neurovegetative symptoms are of limited use in depression in the medical setting as they may be the result of a medical illness; however, these symptoms may be useful for diagnostic purposes if they are out of proportion to what would be expected from the medical illness or if a temporal association between the illness and the symptoms is lacking
- Anhedonia is another important symptom; if the patient does not derive pleasure from visits from family or friends then a major depression may be present
- Suicidal ideation may also indicate a major depression.

3) Management

If a major depression is thought to be secondary to a medical illness then consider whether management will involve treating the underlying cause or whether the depression needs to be treated separately.

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6. Cole MG, McCusker J, Ciampi A, Windholz S, Latimer E, Belzile E. The prognosis of major and minor depression in older medical inpatients. *American Journal Geriatric Psychiatry.* 2006;14(11):966-975.

7. Koenig HG. Recognition of depression in medical patients with heart failure. *Psychosomatics.* 2007;48:338-347.

8. Schleiffer SJ, Macari-Hinson MM, Coyle DA, et al. The nature and course of depression following myocardial infarction. *Archive Int Med.* 1989;149:1785-1789.

9. Roose SP, Glassman AH, Seidman SN. Relationship between depression and other medical illnesses. *JAMA.* 2001;286(14):1687-1690.

10. Morris PLP, Robinson RG, Andrzejewski P, Samuels J, Price TR. Association of depression with 10-year poststroke mortality. *American Journal Psychiatry.* 1993;150:124-129.

Choice of antidepressant will depend on:

- The most troubling target symptom (e.g. insomnia)
- The side effect profile (e.g. avoid tricyclic antidepressants if cardiac abnormalities are present as these may cause lengthening of PR and QT intervals)
- Potential drug interactions (check the effect of the drug on the P450 microsomal enzyme system)

ANXIETY IN THE MEDICAL SETTING

1) Diagnosis:

First consider whether the anxiety would be within normal limits for the situation or pathological *The Massachusetts Handbook for Hospital Psychiatry* makes this differentiation by focusing on the following features:

- Autonomy – "has a life of its own"
- Intensity – the level of distress
- Duration – persistent rather than transient
- Behaviour – avoidance or withdrawal

Pathological anxiety may result from:

- The patient's reaction to the meaning and implications of medical illness or to the medical setting, based on personality, past individual experiences of the disease or experiences of a loved one, symbolic of early life experiences, conditioned responses
- A physical disorder
- An underlying psychiatric disorder

Medical Illnesses mimicking an anxiety disorder:

- Endocrine disorders – Cushing's syndrome, Addison's disease, carcinoid syndrome, diabetes, hyperthyroidism, pheochromocytoma, testicular deficiency
- Drug-related – intoxicated (analgesics, antidepressants, chemotherapy, thyroxine, sympathomimetics), withdrawal (alcohol, opiates, benzodiazepines)
- Cardiovascular and circulatory – arrhythmia, mitral valve prolapse, myocardial infarction
- Respiratory – asthma, pneumothorax, pulmonary embolism
- Immunological/connective tissue disorder – SLE, PAN
- Metabolic – acidosis, electrolyte abnormalities
- Neurologic – tumours, syphilis, cerebrovascular disease, encephalopathy, epilepsy, Huntington's, multiple sclerosis, organic brain syndrome
- Gastrointestinal – peptic ulcer, colitis
- Infectious diseases – AIDS, malaria, tuberculosis, hepatitis

Clues to a medical cause of anxiety in this population:

- Illness and treatment with known association to symptoms of anxiety
- Presence of physical symptoms with lack of psychological symptoms
- Late onset of anxiety
- A lack of personal or family history of anxiety
- Absence of significant life events heralding or exacerbating anxiety symptoms
- A lack of avoidance behaviour
- A poor response to antianxiety agents

2) Management:

Anxiety managed with:

- Education – about anxiety and the medical illness (e.g. about misconceptions)
- Support
- CBT
- Medication – the short-term use of benzodiazepines (particularly if there is an immediate need for a response while the patient is in hospital), antidepressants, atypical antipsychotic for its anxiolytic effects.

PSYCHOTIC SYMPTOMS IN THE MEDICALLY ILL

LEARNING OBJECTIVES

- Assist the clinician in developing an approach to the medically unwell patient presenting with psychotic symptoms

Psychotic symptoms can present in the context of a variety of medical conditions as a distinct sequelae of the physical condition.

Psychotic symptoms can often be misidentified when a patient may clearly be delirious, such that a careful assessment is required to ensure appropriate management strategies are instigated.

Some medical illnesses associated with psychotic symptoms are shown in table 1 (see below).

- Assessment requires a medical history, review of systems, family history and physical examination. Cognitive testing should also be performed – deficits in attention, orientation and memory suggest delirium or dementia rather than a primary psychotic illness.
- Consider temporal course – chronic, episodic or recent onset.
- Consider drug-induced psychosis if the psychosis is of new onset, there is no family history or if the psychosis starts in hospital.
- Perform investigations as indicated by clinical index of suspicion.
- Consideration of competency – should the patient be managed under 'duty of care', Guardianship order or the Mental Health Act?

  Patients with primary psychotic illnesses can pose problems for nursing staff; e.g. they may be paranoid, disorganised and engage in inappropriate behaviour while on the ward, prominent negative symptoms will make patients seem apathetic or unappreciative and they may have poor hygiene. The psychiatrist may have to explain these difficulties and associate them with their illness rather than personality flaws.

Management of psychotic patients in a medical setting:

- Clarify the diagnosis.
- If an antipsychotic is going to be used, important that this is communicated to the treating psychiatrist or other medical practitioner so that the medication is not continued indefinitely and risk of exposure to side effects in the case of an organic psychotic illness that may have a short duration.
- Watch for dystonias in patients receiving high potency typical antipsychotics (haloperidol) especially in younger patients.
- Be aware of drug interactions and monitor for side effects (e.g. cardiac disturbance).

Epilepsy	Head trauma	Dementia	Cerebrovascular disease
Space occupying lesions	Hydrocephalus	Multiple sclerosis	Neuropsychiatric disorders
Autoimmune disease (SLE, paraneoplastic syndromes)	Infections (including encephalitis HIV, neurosyphilis)	Endocrine conditions including hypoglycaemia, addisons, cushings, thyroid conditions	Narcolepsy
Nutritional deficiencies	Metabolic disorders including porphyria	Medications	Substances including alcohol, steroids, amphetamine, cannabis, cocaine

Table 1

GAY, LESBIAN, BISEXUAL, TRANSGENDER AND INTERSEX (LGBTI) PATIENT ASSESSMENT AND HEALTH CARE PROVISION

LEARNING OBJECTIVES

- Describe the specific health needs of LGBTI consumers of mental health services
- Outline the principles of an inclusive approach to the mental health needs of LGBTI consumers.

INTRODUCTION

Lesbian, Gay, Bisexual, Transgender and Intersex (LGBTI) people make up a significant proportion of the Australian population.

The Australian Human rights commission states "Australians of diverse sexual orientation, sex or gender identity may account for up to 11% of the Australian population"[11].

The barriers faced by this population in accessing mental health services remain significant, with large percentages of the population reporting a need to hide their sexuality when accessing services.

BACKGROUND

Homosexuality was only decriminalised in recently in Australia. The first state to pass this was South Australia in 1975 and the last Tasmania in 1997. A number of other legislative changes have also taken place to address discrimination against the LGBTI community. These have included amendments to the age of consent laws, superannuation laws and in more recent time formal acknowledgment of relationships. These changes have paralleled increasing visibility and acceptance of LGBTI people amongst mainstream society. Despite increasing acceptance, LGBTI people continue to face discrimination, marginalisation, family and peer rejection, stigmatisation, harassment and violence. LGBTI people who are migrants or in older age groups may have experienced greater discrimination, marginalisation, harassment and violence as a result of their sexual orientation or gender identity. These experiences negatively impact on people's health and wellbeing.

LGBTI AND HEALTH OUTCOMES

We know that LGBTI people in Australia have disproportionately negative health outcomes in comparison with the rest of the population. They experience higher rates of depression and anxiety disorders, psychological distress, alcohol, tobacco and other drug use and are more likely to have ever been homeless and to have no contact with family. They also experience higher rates of suicidal ideation and self-harm and are 4 times more likely to have attempted suicide, with even higher rates for transgender people, LGBTI youth and aboriginal people. Reliable mortality statistics for these populations remains highly problematic as sexual orientation, sex identity and gender identity are not identified in most existing data collection mechanism and may not be known by family and friends at the time of death.

Research demonstrates that these negative outcomes are related to the social determinants of health such as discrimination, isolation and marginalisation. These determinants also contribute to barriers to accessing health and support services. In addition, generic health interventions and prevention strategies have failed to be inclusive of LGBTI people and their needs. Social inclusion is recognised as a critical factor in the health and wellbeing of people globally and steps to address

11. https://www.humanrights.gov.au/face-facts-lesbian-gay-trans-and-intersex-people3fn1

this in health and social services is an important step toward reducing the negative impact of the social determinants of health on LGBTI community.

FORMULATING A CLINICAL APPROACH TO LGBTI PATIENTS

A number of recommendations have been made to mainstream providers of health to facilitate an approach that is inclusive of LGBTI people.

- That LGBTI communities be recognised as a higher risk group for depression, anxiety, psychological distress, substance use and suicide.
- Awareness of the social determinants of health which negatively impact LGBTI individuals health and their access to mainstream services.
- Awareness of the potential impact of prior discrimination, harassment, violence, marginalisation or insensitive treatment on LGBTI people. Awareness that LGBTI migrants and individuals from older age groups may have experienced greater exposure to such adverse experiences.
- LGBTI individuals may not have disclosed their sexual preference or gender identity to family, friends, work colleagues or employers because of fear of discrimination or margininalisation. Due attention to the privacy of this information should be taken and not discussed with other parties without the individuals consent.
- Addressing "hetero-centrism" and discrimination against LGBTI people within mainstream services.
- Develop cultural competency of mainstream service providers to provide non-discriminatory, culturally appropriate, inclusive services to the LGBTI community.
- Recognise LGBTI people as individuals rather than as part of a stereotyped group.
- When seeing transgender or gender non-conforming persons, use their preferred name, pronoun and terms. If unsure, ask "how would you like to be addressed"?
- As with all patients, sensitive questions should be prefaced with an explanation about why the information is needed.
- Consider a collaborative and inclusive approach to service provision through involvement of appropriate LGBTI health services.

NOTES

2 TREATMENTS

2. TREATMENTS

This section pays particular to treatment issues arising in the acute setting of psychiatry.

LEARNING OBJECTIVES

- To acquire an understanding of general actions and side effect potentials for various psychotropic agents.

ANTIPSYCHOTICS, ANTIDEPRESSANTS AND LONG ACTING INJECTABLES; A BRIEF OVERVIEW

ANTIPSYCHOTICS

Various terms are used to refer to antipsychotic medication, with a common distinction being placed upon them as being either "typical" or "atypical" in their action, with "typical" generally referring to the older group of medications, with a particular mode of action and side effect profile, with "atypical" referring to newer agents with differing side effects and receptor affinities.

Typical antipsychotic agents include:

- Haloperidol
- Chlorpromazine
- Zuclopenthixol
- Flupenthixol
- Fluphenazine

The action of these agents is to block dopamine D2 receptors, the over activity of which is associated with symptoms of psychosis.

Atypical antipsychotic agents include:

- Aripiprazole
- Olanzapine
- Risperidone
- Paliperidone
- Quetiapaine
- Ziprasidone
- Amisulpiride
- Lurasidone
- Clozapine

There are significant differences between the mode of action between the various antipsychotics in the "atypical" group above. Clozapine for example, has poor affinity at the D2 receptor and is more active at the dopamine D1, D3 and D4 receptors as well as serotonin, histamine and muscarnic receptors. Different agents in this group have varying potency for the various serotonin sub receptors. Aripiprazole is described as a "novel" antipsychotic given its different properties to other, atypical agents, in that it is a partial agonist at D2, while also regulating serotonin function.

In general terms, the most immediate concerns as regards side effects differ between typical

and atypical antipsychotic medicines. A working knowledge of side effect profiles of individual agents is important for the prescriber.

Typical agents are associated with a higher likelihood of the development of extrapyramidal side effects, specifically;

- Dystonias
- Akathisia
- Parkinsonism
- Tardive dyskinesia

Atypical agents are generally associated with metabolic syndrome factors, specifically;

- An increased likelihood of weight gain/BMI
- Hyperlipidaemia
- Hyperglycaemia
- Hypertension
- Increased weight circumference

CLOZAPINE

LEARNING OBJECTIVES

- Understand the role and efficacy of clozapine in the management of treatment refractory schizophrenia
- Recognise the appropriate monitoring of medical parameters during clozapine initiation and maintenance therapy

INTRODUCTION

Clozapine is still the only drug of proven efficacy in treatment-resistant schizophrenia[1]. The significant response of neuroleptic-resistant schizophrenia patients to clozapine validates its efficacy in this group. Clozapine is of proven superiority over first generation antipsychotics[2] and has a response rate of 50% among previously treatment-refractory patients and 76% among treatment-intolerant patients[3]. The benefits of clozapine are seen in reduction of positive and negative symptoms of schizophrenia, as well as reduction in aggression and suicide[4].

Clozapine is available under special access provisions of the pharmaceutical benefits scheme. Clozapine can only be prescribed by psychiatrists or general practitioners who have registered with an appropriate clozapine patient monitoring service whose remit is to monitor patients receiving clozapine for haematological abnormalities.

INITIATION OF CLOZAPINE THERAPY

The initiation of clozapine therapy requires the informed consent of the patient, or where appropriate, the Mental Health Review Tribunal. The risks of agranulocytosis, myocarditis and metabolic complications and the steps undertaken to minimise these must be explained to the patient. The patient must then be registered with the CPMS and baseline white cell count (WCC) and neutrophil count (NC) must also be provided. The patient's blood type must also be identified.

1. Baldessarini RJ, Frankenburg FR. A novel antipsychotic agent. New England Journal Medicine. 1991;324(11):746-54 and UK clozapine study group. The safety and efficacy of clozapine in severe treatment-resistant schizophrenic patients in the UK. *British Journal Psych*. 1993;150-54.
2. Kane J, Honigfield G, Singer J, et al. Clozapine for the treatment-resistant schizophrenic; results of a US multicenter trial.*Psychopharmacol.* 1989;99:560-63.
3. Lieberman JA, Safferman AZ, Pollack S, et al. Clinical effects of clozapine in chronic schizophrenia: response to treatment and predictors of outcome. *American Journal Psych.* 1994;151:1744-52.
4. Meltzer HY. Suicide and schizophrenia; clozapine and the InterSept study. *Journal Clinical Psych.* 1999;60(Suppl 12):47-50.

CLINICAL WORK-UP FOR CLOZAPINE THERAPY

Different clinical services have varied protocols for 'clozapine workup' however the common components of such a work up are shown in Table 1.

Informed consent and registration with patient monitoring service
Weight, waist circumference, pulse, blood pressure
Full blood count with differential white cell count
Fasting glucose
Fasting cholesterol and triglycerides
ECG
Echocardiogram
Troponin
EEG (where indicated)

Table 1

The initiation of clozapine therapy ("Day 1") requires close monitoring of pulse, blood pressure, and temperature. There are rare instances of cardiovascular collapse described following the first dose of clozapine (6.25-12.5mg). This usually results from massive vasodilation. Isoprenaline infusion is the pressor of choice, as intravenous adrenaline may lead to further hypotension. Many services require inpatient admission for 'Day 1', however day-hospital admission is possible, assuming adequate resuscitation facilities are available. Some patients develop 'flu-like' symptoms in the initial phases of clozapine therapy, including pyrexia. This is not related to infection and, in the absence of abnormalities in neutrophil count, should not necessitate the cessation of clozapine.

MEDICAL REVIEW DURING DOSE TITRATION

The patient is usually reviewed weekly during the first 18 weeks of treatment. During this period, clozapine therapy is titrated up towards the usual therapeutic doses of 300-600mg per day in divided doses. Dose increments vary from 12.5-50mg per week, depending upon the patient's tolerance of treatment. Given the severity of illness usually associated with the need for clozapine therapy, there should be careful documentation of the patients progress (Table 2).

Recent progress/symptoms
Significant mental state features
Risk issues
Current clozapine dose and tolerability/efficacy
Blood results
Weight/BP/pulse/waist circumference
Plan

Table 2

CLINICAL MONITORING DURING CLOZAPINE THERAPY

a) Haematological

The most clinically significant adverse effect of clozapine therapy is the induction of agranulocytosis in up to 3% of patients. In order to prevent excess morbidity and mortality in clozapine therapy, the CPMS require regular testing of the patient's white cell count and neutrophil count in order for clozapine therapy to continue. The CPMS requires weekly leukocyte and neutrophil counts for the first 18 weeks of clozapine therapy and monthly for the duration of therapy. A leukocyte count of > 3.0 x 10^9/L or neutrophil count >1.5 x 10^9/L represents a contraindication to initiation of clozapine therapy, or grounds for closer monitoring or discontinuation of clozapine therapy. A leukocyte count < 3.5 x 10^9 or neutrophil count < 2.0 x 10^9 places a patient in the at-risk category (the "amber zone") and warrants closer haematological monitoring. There have been a variety of postulated

mechanisms of agranulocytosis in clozapine therapy, although the most likely cause is a toxic metabolite of clozapine, N-desmethylclozapine[5]. This compound is likely metabolized to an unstable compound which is toxic to haemopoietic precursors of both myeloid and erythroid lineages[4,5].

Benign ethnic neutropaenia

Benign ethnic neutropaenia (BEN) has been defined as "the occurrence of neutropaenia defined by normative data in white populations, in individuals or other ethnic groups who are otherwise healthy and who do not have repeated or severe infections"[4,6]. Between 25% and 50% of Africans and some ethnic groups in the Middle East, including Yemenite Jews and Jordanias have BEN. Individuals with BEN have a similar haematological response to infections as do those without BEN and do not show an increased incidence of infections[4,5]. Low baseline white cell counts have not been associated with agranulocytosis whilst on clozapine treatment and African American's do not appear to be at higher.

When neutrophil counts fall below predetermined levels, monitoring services require either repeat FBC in the case of "amber" alert, or cessation of clozapine in the case of "red" alert. In instances of BEN, baseline neutrophils may fall in the "amber" or "red" zone. An awareness of the possibility of benign ethnic neutropenia in patients allows collaboration with haematology and clozapine monitoring services and may also prevent unnecessary cessation of clozapine, or facilitate its use in those who would otherwise been deemed inappropriate[6,7].

Lithium, known to cause a relative leucocytosis, has been has been used to increase neutrophil counts in cases of BEN, or in clozapine induced neutropaenia in order to allow ongoing treatment with clozapine. Lithium does not protect against agranulocytosis. Neutrophil counts have been shown to have diurnal variation, characterised by lower counts in the morning. This phenomenon may be amplified by antipsychotic treatment. Case reports of morning pseudoneutropaenia during clozapine have not demonstrated an association with agranulocytosis. In instances of neutropaenia based on morning blood counts, a repeat count taken in the afternoon may prevent inappropriate cessation of clozapine.

b) Cardiac monitoring

Clozapine therapy has been associated with a variety of potentially lethal cardiac abnormalities, acute myocarditis and cardiomyopathy. The risk of myocarditis is highest in the first two months of treatment. Cardiomyopathy is rare, but generally occurs later in treatment. Pericarditis and pericardial effusion have also been associated with clozapine treatment. Tachycardia occurs in about 25% of patients and is also a potential indicator of myocardial disease. Persisting tachycardia beyond two months of treatment, or in association with other symptoms of cardiac failure, palpitations or angina pectoris warrant urgent medical review. A minority of clozapine-treated patients show ECG changes similar to those including S-T segment depression and flattening or inversion of T-waves. These may be benign abnormalities, but they also may be an indicator of myocarditis. The appearance of such anomalies warrants urgent cardiologist review. Patients with a history of cardiac illness or abnormal cardiac findings on physical

5. Gerson SL, Meltzer H. Mechanisms of clozapine-induced agranulocytosis. *Drug Saf.* 1992;7(Suppl 1):17-25.
6. Gerson SL, Arce C, Meltzer HY N-desmethylclozapine: a clozapine metabolite that suppresses haemopoiesis. *British Journal Haematol.* 1994;86:555-61.
7. Rajagopal S. Clozapine, agranulocytosis, and benign ethnic neutropenia. *Postgraduate medical journal.* 2012.

examination should have a cardiology review prior to commencement of clozapine therapy. Cardiac monitoring during clozapine therapy should include:

1. Routine pulse and BP measurement
2. Pre-treatment ECG (serial measurements depending upon clinical indications)
3. Baseline cardiac enzymes – CK-MB, troponin I, troponin T (serial measurements every 6-12 months)
4. Echocardiogram (pre-treatment and annual)

c) Monitoring clozapine levels

Measuring serum clozapine levels is usually done when there is non-response or partial response to treatment, or where there are questions of treatment adherence. In general, therapeutic levels of clozapine are 1.1 µmol/L (350 ng/mL); the literature recommends combined clozapine and norclozapine levels to be >1.3 µmol/L[8].

Clozapine levels should be checked in the following circumstances:

1. Where patients are on doses above 600mg daily or;
2. Where there are clinical indications of reduced effectiveness suggesting non-adherence or increased metabolism of uncertain origin;
3. Concomitant administration of the following medications (Table 3)

d) Neurological monitoring

Drug induced movement disorders are uncommon with clozapine therapy, however there should be routine examination assessing for obvious abnormal involuntary movements, parkinsonism, and motor restlessness. Seizures occur at a frequency of 1.3% of patients taking clozapine. Seizures tend to occur at low doses (< 300 mg/d) during the titration phase of treatment, and at higher doses (> 600 mg/d) during the maintenance phase. Patients with

PSYCHOTROPIC MEDICATION			
Sertraline	Phenytoin	Lithium	Citalopram
St Johns wort	Diazepam	Carbamazepine	Phenobarbitone
Haloperidol	Fluoxetine	Risperidone	Sodium Valproate
Fluvoxamine	Lamotrigine	Paroxetine	
SOCIAL/RECREATIONAL			
Caffeine	Nicotine	Grapefruit juice	
ANTIBIOTICS			
Ciprofloxacin	Clarithromycin	Rifampacin	
CARDIAC			
Lisinopril	Quinidine		
OTHERS			
Cimetidine	Disulfiram	Oral contraceptive pill	

Table 3

[8] Perry PJ, Miller DD, Arndt SV, et al. "Clozapine and norclozapine plasma concentrations and clinical response of treatment- refractory schizophrenic patients". *American Journal Psychiatry.* 1991;148:231-235.

a history of seizures or epilepsy are more likely to have seizures soon after initiation of therapy, on low doses. Such patients should have pre-treatment EEGs and routine monitoring as indicated by neurologist advice. Arguments exist as to whether patients taking clozapine doses of > 600 mg/day should undergo routine EEG monitoring. This is best individualised until clearer data is available regarding the cost-benefit of such monitoring.

OTHER SIDE EFFECTS OF CLOZAPINE THERAPY

Hyper-salivation and constipation are very common side effects. Hyper-salivation can be mitigated by 0.1% atropine mouthwash. If left untreated, constipation can become a serious problem with potentially fatal outcomes from bowel obstruction. There are isolated reports have been documented of clozapine-associated emergence of obsessive compulsive symptoms, priapism, allergic complications. pancreatitis, toxic hepatitis, elevation in creatinine kinase levels and diabetes-like symptoms.

CLOZAPINE CESSATION

Serious and potentially fatal adverse events mean that it can become necessary in some patients to abruptly cease clozapine. Other patients may become non-adherent with treatment for a range of reasons. Clozapine is the antipsychotic that has the strongest evidence for a withdrawal psychosis developing when the medication is discontinued. The onset of this withdrawal psychosis is typically within 24-48 hours of the abrupt discontinuation of clozapine. One previous review has suggested that the overall incidence of a supersensitivity psychosis following the abrupt withdrawal of clozapine is around 20%, but the actual incidence is probably higher than this. Psychotic symptoms occurring as direct result of antipsychotic medication withdrawal can be more extreme than symptoms occurring as part of the natural course of the illness. If clozapine is unable to be recommenced in a timely fashion, this can result in a severe and protracted relapse with an extended time to recovery and poorer outcomes. As part of the planning to commence clozapine, consideration needs to be given to supports that may be necessary to optimise adherence to medication, as poor adherence can potentially worsen outcomes for some patients.

If it is possible to gradually reduce clozapine this should ideally be done at a rate of 25mg every week to reduce the likelihood of a rebound psychosis developing.

LONG ACTING INJECTABLE MEDICATIONS

LEARNING OBJECTIVES

- Describe the various forms of injectable antipsychotics
- Understand the different pharmacological profiles of injectable antipsychotics

INTRODUCTION

The advent of long acting injectable antipsychotic medications (LAI) or ‘depot antipsychotics’ represented a major advance in the ambulatory treatment of patients with chronic psychotic disorders. LAIs enabled clinicians to ensure adherence to treatment and provided patients with greater capacity to live independently in the community. Over the last fifteen years technological advances allowing a more sophisticated method of delivery have resulted in several second-generation antipsychotics becoming available as LAIs.

PHARMACOKINETICS OF LAIS

General comments

One of the main advantages of all LAIs is that adherence is more explicit and concerns about covert non-adherence are removed. As LAIs are injected straight into the muscle, they also avoid problems that may occur with absorption from the gut and avoid first pass metabolism. LAIs can produce smoother plasma levels than when the same medication is administered in oral form. This may or may not translate into better tolerability.

Traditional LAI's

Older LAIs are manufactured as esters dissolved in oil. Following injection of the oil into the muscle, the esterified drug then slowly diffuses to the edge of the oil globules in which it is contained, where plasma esterases cleave the active compound. The active compound is then able to circulate in the plasma.

Most older LAIs reach a mild peak about 7 days following the injection. One exception to this is fluphenazine decanoate, which has a brief release spike in the first 24 hours after injection. With oil-based LAIs the rate of absorption into the plasma is slower than the rate of elimination

As absorption can occur over weeks to months, this means that the LAI can continue to have action for months after it is administered. Older LAIs can take some months to reach a steady state.

Microsphere technology

The first medication to utilize microsphere technology to achieve a prolonged delivery of antipsychotic was Risperdal Consta©.

Rather than being esterified and dissolved in an oily base, the medication is encapsulated in microspheres made out of a biodegradable copolymer of polyglactin. The microspheres require a chain of cold storage to ensure that they do not begin to break down ahead of administration. After injection into the muscle, the microspheres are slowly eroded and the antipsychotic is then released into the plasma.

Very little medication is released from the micropsheres until after 2-3 weeks and because of this, there is a need for oral supplementation over this period.

Crystal-based LAIs

Crystal based LAIs offer a more sophisticated means of delivering the medication that results in the immediate release of medication into the plasma and a much more predictable pharmacokinetic profile.

Olanzapine pamoate was the first antipsychotic to be manufactured as a crystal-based LAI. Following injection in the muscle, the crystal breaks down, such that a slow release of olanzapine into the plasma occurs.

One consideration particular to the olanzapine LAI is the possibility of a post-injection syndrome. This syndrome occurs in a small percentage of people after receiving the injection with signs and symptoms consistent with an olanzapine overdose. The exact mechanism of this syndrome is not completely understood, but is thought to occur by some of the medication crystals coming into direct contact with blood and being absorbed at a faster rate. The syndrome is a risk present every time the injection is given and requires the patient to remain at the health centre for 2hours of observation following administration.

Paliperidone palmitate comes in two forms, Invega Sustenna which is a monthly preparation, and Invega Trinza which is the first LAI which is formulated for quarterly administration in those who have tolerated Invega Sustenna for at least 3 months. These are also crystal based LAIs. Successful treatment for several months with Invega Sustenna prior to commencing Invega Trinza.

Abilify maintaina is the long acting preparation of Abilify (aripiprazole) . Aripiprazole maintains takes the form also of a crystaline substance. Administered to the deltoid of gluteal region, maximal plasma concentration is reached in 4-7 days post injection.

CHLORPROMAZINE EQUIVALENTS

Chlorpromazine equivalents (CPZe) are a means of comparing the relative potencies of different antipsychotic medications. It must be borne in mind that these equivalencies are an attempt to compare the complex effects of very different drugs. Equivalence doses are generally based on a synthesis of data such as the mean doses used in large populations, the relationship between

plasma level and effect, the relationship between dose and plasma level and PET imaging showing D2 receptor occupancy and effect[9]. The following table from the TRS Consensus guidelines[10] combines some of the currently accepted consensus values for CPZe.

ANTIPSYCHOTIC DRUG	DOSE EQUIVALENT TO 100MG CHLORPROMAZINE (ORAL)
Amisulpiride (oral)	100mg
Aripiprazole (oral)	2.5mg
Clozapine (oral)	100mg
Haloperidol (oral)	2mg
Olanzapine (oral)	4mg
Paliperidone (oral)	1.5mg
Quetiapine (oral)	150mg
Risperidone (oral)	1mg
Ziprasidone (oral)	40mg
Zuclopenthixol (oral)	20mg
Flupenthixol decanoate (IMI)	13mg every 2 weeks
Haloperidol decanoate (IMI)	33mg every 4 weeks
Zuclopenthixol Decanoate (IMI)	67mg every 2 weeks
Risperidone (LAI)	13mg every 2 weeks
Olanzapine (LAI)	75 mg every 2 weeks 135mg every 4 weeks
Paliperidone (monthly LAI)	27mg every 4 weeks

[9] Lambert T, Taylor J, 2011. Pharmacology of antipsychotic long-acting injections. In Antipsychotic Long-acting injections. *Oxford University Press.*

[10] Australian Consensus Panel for Treatment-Refractory Schizophrenia. Targeting treatment-refractory schizophrenia: A multidimensional outcomes approach to the diagnosis and management of incomplete recovery 2010; available at: www.trsconsensus.com.au

ANTIDEPRESSANTS

Like antipsychotic medications, there are various sub groups of antidepressants which it is important to have a general overview of.

Common groups include;

SSRI

- Selective serotonin re-uptake inhibitors
- Side effects can include nausea, headache, sleep disturbance, GI disturbance, sexual disfunction
- Agents include (but not limited to) escitalopram, sertraline, fluoxetine,

SNRI

- Serotonin nor-adrenaline re-uptake inhibitors
- Similar side effects to SNRIs, but more problematic in acute situation can be marked withdrawal or initiation syndromes characterised by extreme nausea, headaches, agitation, hence need for monitored, slow titrations and withdrawals.
- Agents include venlafaxine, duloxetine, desvenlafaxine

NASSA

- Noradrenergic and specific serotonergic activity
- Can have some similar side effects to SSRIs, however constipation, dry mouth, weight gain and fatigue can be more present
- Agents include mirtazapine, mianserin

TRICYCLICS

- This older group of medications if considered to be more likely to induce side effects, which include sedation, dry mouth, constipation, urinary retention, blurred vision, and orthostatic hypertension.
- More dangerous in overdose
- Agents include amitriptyline, nortriptyline

MONOAMINE OXIDASE INHIBITORS

- Also an older style of medication, often used when illness is perceived as more "resistant" to treatment
- Side effects include dry mouth, blurred vision, urinary hesitancy, constipation, orthostatic hypertension
- Patients using these agents must follow a specific diet, avoiding foods high in tyramine (including some beers, red wine, aged meats, some cheeses, fav beans, and vegemite) or risk a hypertensive crisis
- Agents include tranylcypromine and phenelzine

LITHIUM

Lithium has well-established efficacy as an antimanic agent and antidepressant in bipolar disorder, and for prophylaxis against mood episodes in bipolar disorder.

Lithium is probably more effective than the anticonvulsants in classical bipolar I disorder and in severe mania. It is one of the more effective augmentation strategies in major depression.

Around 50% of antidepressant non-responders achieve remission with added lithium.

Lithium is the most effective mood stabiliser at preventing suicide[11,12]. If a patient is having some breakthrough episodes on an anticonvulsant, a change to lithium is warranted.

Of those who cease lithium after achieving a good response, about 15% become relatively lithium resistant when relapse forces them to recommence it. For these reasons, requests by a patient with established bipolar disorder to have their mood stabiliser reduced or ceased should be firmly resisted.

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[11] Goodwin, et al. Suicide risk in bipolar disorder during treatment with lithium and divalproex. *JAMA.* 2003;290:1467.

[12] Tondo, et al. Lithium maintenance treatment of depression and mania in bipolar I or bipolar II disorders. *American Journal Psychiatry.* 1998;155:638.

Ceasing lithium quickly (over < 2 weeks) doubles the risk of relapse. Mixed or dysphoric mania, ultrarapid cycling bipolar disorder and personality disorder have a poor response to lithium, compared to anticonvulsants.

SOME IMPORTANT SIDE EFFECTS OF LITHIUM

Renal: There is a fall in GFR and rise in creatinine in around 15% of patients taking lithium in the long term, but this may be related to episodes of toxicity or cardiovascular problems than to lithium per se. It is more controversial whether lithium at a therapeutic blood level can cause permanent renal damage. Renal failure may certainly occur as a result of toxic levels of the drug, however. Lithium also commonly causes a concentrating defect at therapeutic levels, resulting in polyuria, which may progress to diabetes insipidus.

Warn patients to drink water for resulting thirst, rather than soft drinks or fruit juice, as these worsen weight gain. Abnormalities in renal function should be referred to a renal physician for investigation, as there are many possible causes.

Thyroid: Lithium suppresses the action of the thyroid, including the release of thyroid hormone from the gland. Clinical hypothyroidism occurs in up to 20% of people (especially women) taking lithium for ten years. A larger number have raised TSH with normal T4 (subclinical hypothyroidism)[13]. In the absence of pre-existing or familial thyroid disorder, thyroid function generally recovers on cessation of the drug. It is not necessary to cease lithium due to thyroid suppression. The patient should be warned at commencement that thyroid suppression is a possibility, and thyroxine replacement will be instituted if necessary. Endocrine referral may be of assistance. There is evidence that even subclinical hypothyroidism may destabilise bipolar disorder, and that thyroxine replacement helps in these cases.

Teratogenicity: Lithium is pregnancy category D. It causes serious malformations, especially cardiac anomalies such as Ebstein's, in 4-12% of exposed foetuses. 1st trimester exposure is especially risky.

OTHER SIDE EFFECTS

1. Fine intention tremor, occasionally so severe as to require cessation of the drug. Propranolol may help in some cases.
2. Significant weight gain (similar to valproate)
3. Cognitive dulling and mild memory impairment in some patients. Beware of confounding with mild depression or hypothyroidism.
4. Hair thinning
5. Acne
6. Benign T-wave flattening on ECG
7. Benign neutrophilia (WCC around 10.0 X 10^9 is common) due to increased mobilisation from bone marrow stores.

TOXICITY

Lithium is entirely excreted in the urine. Anything that impedes this excretion may cause blood levels to rise to toxic levels. Your patients will need to be warned to avoid:

1. Excessive lithium intake, for example, some patients take extra tablets on "bad days".
2. Missing blood tests. Regular tests are vital to detect gradually increasing lithium levels.
3. Dehydration, especially in summer. Some patients try to control the polyuria by reducing water intake, with disastrous results. Take extra fluids or reduce dose during severe diarrhoea or vomiting.
4. Medications that block excretion. All NSAIDS (now over-the-counter) can do this, with the exception of aspirin, and should be avoided.

[13]. Perrild, et al. Thyroid funciton and ultrasonically determined thyroid size in patients receiving long term lihtium treatment.*American Journal Psych.* 147:1518-21.

Warn the patient to check all prescription medications for interactions before commencing them. Thiazide diuretics (not loop diuretics such as frusemide) can increase lithium levels into toxic range.

5. Lithium toxicity can result in acute or chronic renal failure, seizures, coma, permanent neurotoxicity (especially cerebellar damage) or death. Dialysis is the treatment of choice at levels > 3.0mmol/L.

Symptoms include worsening tremor, worsening metallic taste in the mouth, nausea and fatigue, confusion, worsening polyuria and dehydration. Patients with mild symptoms should be advised to seek a trough lithium level within a day or so. Those with severe symptoms should cease taking lithium and present immediately at the emergency department for testing.

HOW TO PRESCRIBE LITHIUM

Before commencing: Take baseline TFTs, EUC and, if relevant, ßHCG. Warn patients about potential side effects, including renal and thyroid, and teratogenicity. Warn a manic patient and their family that post-manic depression is common, and is not the result of the mood stabiliser. They should seek treatment for this, if it occurs, and not cease the medication.

Dosing: 250mg lithium carbonate and 450mg slow release forms are available. The slow release form can be helpful in offering once daily dosing if needed to promote compliance or reduce daytime side effects such as tremor, and in reducing the otherwise daunting number of tablets that the patient must take. Start at around 500mg per day and test after 5-7 days, then adjust dose accordingly. Reduce this for the elderly, who have a lower GFR.

Blood levels: Blood levels are taken 12 hours post dose. On single daily dosing, the level will be ~20% higher than with bd dosing. Levels should be done at least weekly until the correct level is attained, and continued every 1-3 months in the long term. TFTs and EUC should be done 6 monthly. With bd dosing, aim for a serum lithium of 0.6 for augmentation in major depression, and 0.8 – 1.0 to treat acute mania. Bipolar prophylaxis is achieved for different patients with levels somewhere between 0.6 and 1.0. Titrate to response and side effects for the individual.

Insufficient Effectiveness: Check the serum level, as noncompliance is common. If changing to an anticonvulsant, leave lithium in situ until a good level of anticonvulsant is achieved, then taper lithium. If neither class is completely effective, use lithium in combination with one of the anticonvulsants.

ANTICONVULSANT MEDICATIONS IN PSYCHIATRY

In psychiatry, anticonvulsants are predominantly used as mood stabilisers in bipolar disorder. There is little evidence to support their use in unipolar depression. Patients poorly responsive to lithium should try an anticonvulsant, and vice versa. A combination of both classes is sometimes required for maximum efficacy in preventing episodes.

SODIUM VALPROATE

Sodium valproate is the anticonvulsant most commonly used in bipolar disorder. Some studies suggest equal efficacy with lithium; others note inferior long-term outcomes such its relative paucity of evidence for a reduction in suicide. It

[14] Nasrallah, et al. Carbamazepine and valproate for the treatment of bipolar disorder: a review of the literature. *Journal Affective Dis.* 2006;95 (1-3):69-78.

may be superior to lithium for mixed mood states, rapid cycling and other non-classical forms of bipolar disorder, but less effective for severe mania and classic bipolar I[14]. The combination with lithium is more effective in preventing mood episodes than either agent alone.

Side effects

- Usually better tolerated overall than lithium, with less noncompliance.
- Main serious side effect is hepatic failure. This is rare (1 in 20 000), but a benign elevation in transaminases (up to 3 X normal) is common. Mild elevations warrant regular monitoring, with drug cessation if elevation worsens.
- Less cognitive dulling than lithium
- Tremor (additive with lithium tremor in combination)
- Weight gain often significant.
- Hair thinning and deterioration in hair quality often unacceptable to patients.
- Causes polycystic ovarian syndrome (PCOS) in young women, resulting in weight gain, hirsutism, impaired fertility, impaired glucose metabolism, hyperandrogenism. The incidence of this disorder is controversial. Monitor for menstrual irregularity and weight in young women, and refer to gynaecologist if changes occur.
- Serious risk of teratogenicity. Increases risk of spina bifida to 1-4%.

Commencing and monitoring valproate

Before or at commencement, take baseline LFTs and a ß-HCG if relevant. Warn women about teratogenicity and polycystic ovarian syndrome. Warn about rare hepatic failure and other side effects. Warn manic patients and their families that post-manic depression is common, and is not the result of the mood stabiliser. They should seek treatment for this, if it occurs, and not cease the medication.

Dosing

Gradual (starting with 500mg and increasing to therapeutic dose over 2 or more weeks) or loading (20mg/kg, around 1500mg per day) regimes are safe and generally well tolerated. Loading may provide a faster response in acute mania.

Allow 5 days for steady state to be achieved, then take blood level. Stated therapeutic ranges are for anticonvulsant effect. Levels above 315 mM/L are recommended, but the most effective range in bipolar disorder is unknown – it is best to titrate to clinical effect and side effects.

Dosing usually bid, but can be once daily to improve compliance.

Drug interactions of particular note

- Increases lamotrigine levels, which can result in Stevens-Johnson syndrome
- Carbamazepine reduces valproate level, while valproate increases carbamazepine level
- Mildly increases clozapine levels. Prevents clozapine seizures.

CARBAMAZEPINE

This drug is perhaps underused as a mood stabiliser. Studies suggest equal efficacy with valproate in bipolar disorder, and its long term side effects are often less problematic than those of valproate[15,16].

Side effects

- Rash (in 5-15%), which requires cessation, as rarely this can progress to dangerous rash such as Stevens-Johnson syndrome. Rechallenge after a benign rash may be successful.

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15. Post, et al. Thirty years of clinical experience with carbamazepine in the treatment of bipolar illness: principles and practice.CNS Drugs. 2007;21(1):47-71.

16. Nasrallah, et al. Carbamazepine and valproate for the treatment of bipolar disorder: a review of the literature. Journal Affective Dis. 2006;95 (1-3):69-78.

- Transient neutropenia is common, agranulocytosis rare.
- Serious risk of teratogenicity, namely spina bifida (1-3%), craniofacial abnormalities or developmental delay.
- Note less weight gain, hair loss and tremor than lithium or valproate.
- Sedation, dizziness or ataxia.
- Hyponatraemia is common. Monitor severity and cease if a significant reduction occurs.
- Can reduce T4 and T3, without changing TSH. Not clinically significant.
- Benign hepatic enzyme elevation may occur. If progressive, cease drug, as serious hepatic toxicity may rarely occur.

Use and interactions

Warn patients about side effects, especially rash and agranulocytosis, and teratogenicity. If relevant, take a ß-HCG level to exclude pregnancy. Warn manic patients and their families that post-manic depression is common, and is not the result of the mood stabiliser. They should seek treatment for this, and not cease the medication.

Start at 200mg bid and titrate to clinical effect and side effects. Again, stated therapeutic levels are for anticonvulsant action, and the therapeutic range in bipolar disorder is unknown.

Once daily dosing of the slow release form can be used to increase compliance.

Carbamazepine powerfully induces cytochrome p450 3A4. This results in several common, clinically significant interactions:

- Autoinduction of its own metabolism and a drop in carbamazepine levels with time. This effect is maximal at one month after starting treatment.
- Reduction in blood levels of oestrogen from contraceptives, which can result in pregnancy. Use higher dose OCP or other contraceptive methods.
- Reduction in levels of many antidepressants, antipsychotics and anticonvulsants, among other drugs. Always check for interactions and adjust doses if necessary.

LAMOTRIGINE

Studies suggest effectiveness in bipolar depression, either as monotherapy or with an antidepressant, but a relative lack of efficacy in treating or preventing mania. It is therefore often combined with another mood stabiliser to target both mood poles[17]. If rash does not occur, it is generally very well tolerated. Patients find the lack of weight gain or sedation particularly welcome. As is true for the other anticonvulsants, there is little evidence of efficacy in unipolar depression.

Some common interactions

Valproate, often combined with lamotrigine, greatly decreases its metabolism. Conversely, lamotrigine increases valproate metabolism, causing valproate levels to fall by around 25%. Carbamazepine slightly increases lamotrigine metabolism, as does sertraline. There is no interaction with lithium.

Important side effects

- 10% of patients develop rash with lamotrigine. 0.3 – 1% experience serious rash, including Stevens Johnson syndrome, therefore, the drug must be ceased if there is any rash at all.
- A recent large study reports that taking lamotrigine during first trimester is associated with an increased incidence of cleft lip and palate[18].

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[17] Bowden, et al. A placebo controlled 18 month trial of lamotrigineand lithium maintenance treatment recently manic or hypomanic patients with bipolar I disorder. *Arch Gen Psych.* 2003;60:392-400.

[18] Homles, et al. Increased frequency of isolated cleft palate in infants exposed to lamotrigine during pregnancy. *Neurology.* 2008;70:2152-2158.

Use and dosing

Rapid escalation of dose increases the incidence of rash, so adherence to a slow commencement protocol is very important. Start at 25mg per day and increase over 6 weeks to 200mg/day (see MIMS for details). A final dose range of 200 – 400 mg is generally used. If the patient is also taking valproate, the above doses must all be halved.

If a patient ceases the drug for more than 5 days, this dosing regime must be recommenced. There is no useful test for serum lamotrigine level, and no blood monitoring is recommended.

GABAPENTIN, PREGABALIN AND TOPIRAMATE

Despite initial hopes, evidence for the effectiveness of these anticonvulsants in mood disorders has unfortunately failed to materialise[19,20]. They are often of some usefulness in the management of chronic pain, particularly neuropathic pain.

PSYCHOTROPIC DRUGS IN PREGNANCY AND BREASTFEEDING

LEARNING OBJECTIVES

- Describe the various iatrogenic risks of psychotropic agents
- Identify psychotropic treatment regimes which are comparatively safe in pregnancy
- Identify psychotropic agents which are comparatively safe to use in breastfeeding women

INTRODUCTION

As mental illness frequently affects adults in the child-bearing years, the use of psychotropic medications in pregnancy requires closer consideration. This is made difficult by the fact that the information upon which many assumptions are made in this area is based on animal studies and case reports. Moreover, in many instances it is difficult to differentiate a putative teratogenic event related to psychotropic medication and a spontaneous abnormality in an otherwise unremarkable pregnancy, where such instances occur at a rate of 2-3% of all pregnancies carried to term.

It must be noted that information in this area has the potential to change rapidly and deferring to resources including Mothersafe, a free telephone service where up to date information on drugs in pregnancy can be sought, is important.

Mothersafe is based at the Royal Hospital for Women in Randwick and can be reached on;
(Sydney metropolitan area) 9382 6539
(Non metropolitan area) 1 800 647 848

CLASSIFICATIONS OF MEDICATIONS IN PREGNANCY

The Australian Therapeutic Goods Administration (TGA) classification of drugs in pregnancy is shown in Table 1. Medications in Category C, D and X raise the most concerns, with the latter two warranting consideration of pregnancy in all female patients in their child bearing years. It is important to note that Category X implies complete contraindication in pregnancy, with many of the other categories based upon lower levels of evidence.

[19] Maidment, ID. Gabapentin treatment for bipolar disorder. *Ann Pharmacotherapy.* 2001;35(10):1264-9.

[20] Chengappa, et al. The evolving role of topiramate among other mood stabilisers in the management of bipolar disorder. *Bipolar Disorder.* 2001;3:215-32.

Category A – Drugs which have been taken by a large number of pregnant women and women of childbearing age without any proven increase in the frequency of malformations or other direct or indirect harmful effects on the fetus having been observed.
Category B1 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals have not shown evidence of an increased occurrence of fetal damage.
Category B2 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed. Studies in animals are inadequate or may be lacking, but available data show no evidence of an increased occurrence of fetal damage.
Category B3 – Drugs which have been taken by only a limited number of pregnant women and women of childbearing age, without an increase in the frequency of malformation or other direct or indirect harmful effects on the human fetus having been observed.
Category C – Drugs which, owing to their pharmacological effects, have caused or may be suspected of causing, harmful effects on the human fetus or neonate without causing malformations. These effects may be reversible. Accompanying texts should be consulted for further details. Studies in animals have shown evidence of an increased occurrence of fetal damage, the significance of which is considered uncertain in humans.
Category D – Drugs which have caused, are suspected to have caused or may be expected to cause, an increased incidence of human fetal malformations or irreversible damage. These drugs may also have adverse pharmacological effects. Accompanying texts should be consulted for further details.
Category X – Drugs which have such a high risk of causing permanent damage to the fetus that they should not be used in pregnancy or when there is a possibility of pregnancy.

Table 1

TGA CLASSIFICATION FOR SELECTED PSYCHOTROPIC DRUGS

ANTIPSYCHOTICS

Category B1 – pimozide, thiothixene

Category B3 – quetiapine, ziprasidone, aripiprazole, olanzapine, risperidone

Category C – chlorpromazine, fluphenazine, thioridazine, trifluoperazine, clozapine, flupenthixol, droperidol, haloperidol, zuclopenthixol

Paliperidone – limited data – recommend avoiding

* When given in high doses during late pregnancy, related compounds have caused prolonged neurological disturbances in the newborn infant

ANTIDEPRESSANTS

Category B2 – venlafaxine, mianserin, tranylcypromine

Category B3 – Mirtazapine, moclobemide, nefazodone Phenelzine

Category C – citalopram, fluoxetine, fluvoxamine, sertraline, amitriptyline, clomipramine, dothiepin, doxepin, imipramine, nortriptyline,

Category D – Paroxetine

* The use of SSRIs in the third trimester may result in a withdrawal state in the newborn infant.

ANTICHOLINERGICS

Category A – Procyclidine

Category B1 – benzhexol

Category B2 – benztropine,

ANTICONVULSANTS/MOOD STABILISERS

Category B1 – gabapentin

Category B3 – topiramate

Category D – lithium, sodium valproate, carbamazepine, lamotrigine, phenobarbitone, vigabatrin

BENZODIAZEPINES

All category C

PSYCHOTROPIC MEDICATIONS AT HIGH RISK IN PREGNANCY (CATEGORY D)

Lithium

The potential teratogenicity of lithium is well established. The risk ratio of cardiac anomalies following foetal exposure to lithium is estimated between 1.2-7.7[21]. The UK National Teratology Information Service have concluded that lithium increases the risk of all types of malformation of approximately three-fold and with a weighting towards cardiac malformations of around eight-fold. Whilst septal and valvular defects have been described following fetal exposure to lithium, the classic cardiac malformation is Ebstein anomaly. Ebstein anomaly is characterized by apical displacement of the septal and posterior tricuspid valve leaflets, leading to "atrialization" of the right ventricle with a variable degree of malformation and displacement of the anterior leaflet of the valve. The leaflet anomaly leads to tricuspid regurgitation. The severity of regurgitation depends on the extent of leaflet displacement, ranging from mild regurgitation with minimally displaced tricuspid leaflets to severe regurgitation with extreme displacement. Echocardiogram is the criterion standard for diagnosis. In M-mode echocardiography the finding is typically paradoxical septal motion and dilated right ventricle. There is delayed closure of tricuspid valve leaflets more than 65 milliseconds after mitral valve closure. On two-dimensional echocardiography there is apical displacement of the septal leaflet of tricuspid leaflet of greater than 8 mm/m2 – considered the most specific sign of the anomaly. Apart from cardiac malformations following first trimester exposure to lithium there are potential dangers towards the end of the third trimester, related to lithium toxicity in the foetus, with case reports of cardiac arrhythmias, cyanosis and hypertonicity. Some studies have also described congenital goitre and neonatal hypothyroidism[22]. Moreover, the rapid shifts in fluid balance following parturition may predispose to lithium toxicity.

Paroxetine

Concerns about the potential teratogenicity of paroxetine are based upon three recent studies. The first, a Danish population based cohort study, found an association between maternal use of SSRIs during the first trimester and an increased risk of both congenital malformations overall (odds ratio 1.4 (95% CI 1.1-1.9)) and congenital cardiac malformations (odds ratio 1.6 (95% CI 1.0-2.6))[23].

The second is a retrospective study conducted by the manufacturer, GlaxoSmithKline (GSK)[24]. The findings suggest that, compared with other antidepressants, paroxetine use during the first trimester is associated with an increased risk of both congenital malformations overall (odds ratio 2.2 (95% CI 1.34-3.63)) and congenital cardiac malformations (odds ratio 2.08 (95% CI 1.0-4.23). The most common abnormality was ventricular-septal defects, although others were described.

Most recently preliminary information about the results of a new study examining data from a Swedish Medical Birth Registry have been made available[25]. This study suggests that babies born to mothers who have taken paroxetine in the first trimester of pregnancy are at an approximately 2 fold higher risk of congenital cardiac malformations compared with the equivalent frequency in the population (odds ratio 2.22 (95% CI 1.39-3.55)). This study also suggests that the other SSRIs

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21. Cohen L, Freidman J, Jefferson J, et al. A re-evaluation of risk of in-utero exposure to lithium. *Journal of the American Psychiatric Association.* 1994);271:146-150.

22. Williams K, Oke S. Lithium in Pregnancy. *Psychiatric Bulletin.* 2000);24:229-231.

23. Wogelius P, Nørgaard M, Munk EM, Mortensen PB, Lipworth L, Sørensen HT. Maternal use of selective serotonin reuptake inhibitors and risk of adverse pregnancy outcome (Abstract). *Pharmacoepidem Drug Safety.* 2005;14:S72-S73.

24. http://ctr.gsk.co.uk/Summary/paroxetine/studylist.asp.

25. www.janusinfo.org

examined (citalopram, fluoxetine and sertraline) are not associated with an increased risk of congenital malformations.

The results of these studies suggest that women should not take paroxetine in the first trimester, and that this does not appear to be an SSRI class effect.

Anticonvulsants

Sodium Valproate

There is a twenty fold increase in neural tube defects following fetal exposure to valproic acid compounds. A syndrome of specific craniofacial abnormalities and long, thin digits with hyperconvex nails has been described in infants exposed to valproic acid during pregnancy. Valproic acid appears to be associated with a higher risk for major congenital malformations as well as developmental delay and decreased verbal intelligence. These appear to be dose-related.

Carbamazepine

Prenatal exposure to carbamazepine increases the risk of neural tube defects ten-fold. A syndrome of craniofacial abnormalities, intellectual impairment and hypoplastic nails is described in infants exposed to carbamazepine in utero, Carbamazepine is also associated with a risk of cardiac anomalies.

EFFECTS OF UNTREATED PSYCHIATRIC DISORDER IN PREGNANCY

Any treatment decision must be weighed against the deleterious impact of untreated or suboptimally treated psychiatric disorder. Untreated psychiatric disorder imperils the fetus or infant through a variety of risks including poor antenatal care, propensity to nutritional neglect or exposure to toxins or trauma. Moreover, infants under the care of a mentally ill parent are more likely to manifest non- organic failure to thrive or developmental delay, particular cognitive development.

GUIDELINES FOR BREAST-FEEDING

Information comes from small case series and single case reports[26]. This limited dataset indicates that all psychotropic drugs are excreted into breast milk and that the infant is therefore exposed to them. In recent decades sufficient data have accumulated to allow psychiatrists to confidently prescribe tricyclic antidepressants, selective serotonin reuptake inhibitors, conventional antipsychotics, carbamazepine and sodium valproate to breast-feeding mothers. There are not sufficient data on newer antipsychotic medications to allow women to breast-feed safely. Clozapine or lithium should not be used in breast-feeding women. Recommended practice is that breast- feeding mothers requiring psychotropic medication be on a low dose of one single drug.

ELECTROCONVULSIVE THERAPY (ECT)

LEARNING OBJECTIVES

- To understand the indications, work up , legislative issues, administration techniques and anticipated complications of ECT.

INTRODUCTION

ECT has been part of psychiatry's treatment mix for almost eighty years and remains an effective management option for a range of psychiatric disorders. However, we now have an evidence base supporting its efficacy, particularly in major depressive disorder, but also bipolar depression as well as mania, clozapine resistant schizophrenia, the neuroleptic malignant syndrome and some types of catatonia.

[26] Kohen D. Psychotropic medication and breast-feeding. *Advances in Psychiatric Treatment.* 2005);11:371-379.

With modern anaesthesia, EEG monitoring, dose titration, empirically robust approaches to seizure adequacy, the introduction of novel forms of electrical stimulus, particularly ultra brief pulse ECT, and the adoption of bifrontal stimulus placement, there has been a substantial improvement in safety, patient acceptance and efficacy.

Despite these undoubted advances, the mechanism of action of ECT remains elusive, though neuroendocrine changes involving corticosteroids and prolactin, changes to neurotransmitter function including GABA, dopamine & serotonin and changes to prefrontal blood flow have all been postulated. The reported observation that ECT stimulates the production of brain derived neurotrophic factor (BDNF) and, in animals, promotes hippocampal neuronal growth, offers possible areas of future research to help understand why ECT is one of psychiatry's most effective treatments.

INDICATIONS FOR ECT

The following are disorders where ECT can be considered an option.

A major depressive episode (MDE) associated with both major depressive and bipolar disorders. While usually reserved for patients who have failed to respond to an adequate trial of pharmacotherapy, ECT can be considered a front line option when a depressed person is not drinking & eating adequately, is highly suicidal or is profoundly psychomotor retarded or agitated. The use of ECT for a major depressive episode associated with a borderline personality disorder should not be approached with optimism.

A manic episode of a bipolar disorder which has failed to respond to appropriate pharmacotherapy or is of such severity that the person's health or safety is at risk would be another situation where ECT could be considered.

Recent evidence supports ECT as an effective treatment option for patients with schizophrenia who have failed to respond to clozapine, with around half responding to a combination of both treatments.

While catatonia is often said to be an indication for ECT, the efficacy is better for catatonia associated with mood disorders, autism & brief psychotic & schizophreniform disorders as against chronic schizophrenia.

Apart from the neuroleptic malignant syndrome, the efficacy and safety of ECT has yet to be demonstrated for other forms of "malignant" catatonia including the toxic serotonin syndrome.

HIGHER RISK SCENARIOS & ECT

Serious morbidity & mortality associated with ECT administration is most commonly cardiac in origin, not infrequently an arrhythmia in the postictal phase.

While there are no absolute contraindications for ECT & the clinician always considers the risk, benefit balance, the following are seen as high risk situations: a recent myocardial infarction or stroke, raised intracranial pressure, severe cardiac valve disease, poorly controlled congestive cardiac failure, unstable angina, aortic & cerebral aneurysms & significant respiratory pathology.

With appropriate precautions and treatment, the presence of hypertension, diabetes, glaucoma, retinal detachment, osteoporosis, dementia and HIV do not preclude ECT administration. Likewise ECT can be administered during pregnancy with appropriate precautions.

PRE ECT WORK UP

The key part of such a work up is a thorough history and physical examination focussing on the respiratory, cardiovascular & central nervous

systems. People with chronic mental illness often have poor dentition which poses the risk of a broken tooth being aspirated.

Key investigations include electrolytes, particularly sodium & potassium, and an ECG. A routine biochemistry profile and a full blood count are also regularly performed. Chest X-rays are usually only necessary in the presence of respiratory disease & brain imaging only if there is the suspicion of raised intracranial pressure.

A baseline depression rating scale like the Montgomery–Åsberg Depression Rating Scale (MADRS), and a baseline test of cognition like the Folstein Mini Mental State Examination (MMSE), or more usefully, the Addenbrooke's Cognitive Examination (ACE-R), are mandatory to provide an evidenced based standard to measure changes in mood and cognition as the ECT course progresses.

An anaesthetic consult is mandatory & other consults ordered as appropriate.

As the elderly often have medical problems & often are suffering from melancholic depression, they need a thorough and thoughtful work up as they can easily become dehydrated, hypotensive, and at risk for deep vein thrombosis, chest infections, acute renal failure and electrolyte disturbances. While cognitive impairment does not preclude ECT, consideration should be given to using a right unilateral stimulus electrode placement & twice weekly treatments. Females make up the majority of elderly people referred for ECT & many are osteoporotic, demanding appropriate work up, consultation and anaesthetic precautions.

MEDICATIONS AND ECT

Medications which lower ECT risk are usually given first thing in the morning of treatment with a sip of water; these include antihypertensives, bronchodilators, corticosteroids, antiglaucoma eye drops, antireflux agents and antiarrhythmics.

Use of psychotropics should be rationalised & minimised. Benzodiazepines should be withdrawn prior to ECT with an appropriate wash out period, both lithium and mood stabilising anticonvulsants are usually withheld both the evening before & the morning of ECT, if ECT is being administered because of a failed antidepressant, then it is logical to switch to an antidepressant of another class during ECT. Antipsychotics including clozapine & antidepressants can usually be safely maintained during an ECT course.

INFORMED CONSENT & THE MENTAL HEALTH ACT

The *Mental Health Act* regulates the administration of both voluntary and involuntary ECT in NSW and the ECT referrer and practitioner must have a good working knowledge of the relevant sections and adhere to its requirements.

ADMINISTRATION OF ECT

ECT is administered in stand-alone ECT suites, day only surgery facilities, recovery areas and operating theatres.

It is a requirement of both the RANZCP and the NSW Ministry of Health that trainees are at all times supervised by an accredited psychiatrist when administering ECT.

Familiarity with EEG monitoring & interpretation, dose titration, use of both brief and ultrabrief pulse width stimuli, correct right unilateral, bitemporal and bifrontal stimulus electrode placements and management of events like prolonged and inadequate seizures and an inability to achieve correct impedance are key competencies for a trainee to achieve.

Duration of the ECT course is often a question of clinical judgment informed by careful clinical assessment and the use of appropriate instruments

like the MADRS. Evidence that one of the strongest predictors of relapse following completion of an index episode course of ECT for a major depressive episode is stopping before complete remission has been achieved should also inform decision making.

The references included below offer a concise & practical description of modern ECT administration techniques.

COMPLICATIONS

The side effect which causes most patient concern with ECT is cognitive impairment, particularly retrograde amnesia. This needs to be discussed with patients at the time of consent and honest, understandable and accurate information conveyed.

In summary, cognitive impairment is most likely with a bitemporal stimulus electrode placement, the use of stimuli which are unnecessarily above seizure threshold and prolonged seizures.

The elderly are more vulnerable and there is evidence concurrent use of lithium, particularly at higher serum levels, and benzodiazepines increase the risk of confusion.

On the other hand, right unilateral stimulus electrode placement, adhering to an evidenced based dosing protocol & use of an ultrabrief pulse stimulus are less likely to cause cognitive impairment.

Retrograde amnesia is usually reversible over the weeks following the completion of an ECT course.

Other complications include jaw & muscle pain, usually worse after the first treatment, & due to a combination of suxamethonium & the motor seizure, dental complications associated with spasm of the master and temporalis muscles from the electrical stimulus, a manic switch and postictal delirium.

RELAPSE PREVENTION

While an index episode course of ECT often achieves a meaningful clinical response, there is a considerable risk of relapse in the weeks and months following without appropriate prophylaxis.

The most frequent approach is continuation then maintenance pharmacotherapy often involving an antidepressant, sometimes augmented with a mood stabiliser. A lithium-nortriptyline combination has the most robust evidence for post ECT relapse prevention in a major depressive disorder.

However, in some patients, relapse cannot be prevented with pharmacotherapy alone & consideration can then be given for continuation/ maintenance ECT.

While there is evidence supporting its efficacy in both mood disorders and schizophrenia, there are few evidence based data to guide frequency of ECT administration and duration of treatment, which is often a matter of clinical judgment in collaboration with the wishes of the patient and family.

A reasonable approach would be to move from weekly to fortnightly to three weekly and possibly even a monthly schedule with a reduction in frequency every couple of months, monitoring for signs of relapse.

References

Electroconvulsive Therapy : an Australasian guide, edited by J.W.G. Tiller, R.W. Lyndon, Australian Postgraduate Medicine, Fitzroy, Vic. 2003.

Electroconvulsive Therapy: ECT Minimum Standard of Practice in NSW www1.health.nsw.gov.au/pds/ActivePDSDocuments/PD2011_003.pdf

PRO RE NATA (PRN) MEDICATION

LEARNING OBJECTIVES

- To develop an organised and structured approach to prescribing PRN medication for both the oral and intramuscular route

INTRODUCTION

Patients in Acute treatment settings may experience distress, agitation or behavioural disturbance which necessitates after non pharmacological interventions the use of "PRN" medication.

INDICATIONS FOR PRN MEDICATION

Administration of PRN initiated by the clinician or requested by the consumer. Common circumstances in which PRN medication use is indicated include;

- Distress arising from psychopathological symptoms
- Agitation arising in the course of an episode of severe mental illness
- Anxiety reactions to psychological phenomena or the ward environment
- Suicidal ideation or impulses to self-harm
- Insomnia
- Physical aggression
- Severe disorganisation of behaviour engendering risk of misadventure
- Intoxication or withdrawal from substances

PRECAUTIONS

- Sedation generally aims to titrate to the point of rousable sleep, not unconsciousness
- Patients naive to medications are likely to respond to smaller doses and should be monitored closely. This is also true for elderly patients
- Medically compromised or intoxicated patients should receive smaller doses
- Sedation and its effect on respiratory function should always be considered and managed as appropriate
- Significant caution required in pregnancy

PRINCIPLES OF DOSING

- Oral medications are preferable to parenteral medications in acute situations where PRN medications are required
- Multiple agents increase risk of side effects and unpredictable course of sedations
- Using adequate therapeutic doses that quickly achieve sedation is better than repeated sub therapeutic doses
- Always consider medications given in the previous location of care (ED, community mental health service, ambulance

CONSIDERATIONS FOR PARENTERAL DOSING

- Injectable medication is particularly indicated when individuals are displaying dangerous behaviour
- In mental health settings the intramuscular route is used mostly, and it is atypical for the intravenous route to be required

DRUGS FOR ORAL ADMINISTRATION

		<64YO	MAX DOSE PER 24H	>64YO	MAX DOSE PER 24H
1ST LINE ORAL	**lorazepam**	1-2mg q 2-6h	10mg	0.5-1mg	7.5mg
	diazepam	5-20mg q 2-6h	60mg	do not use	–
	risperidone	0.5-1mg q 2-4h	6mg	0.5-1mg	4 mg
	olanzapine	5-10mg q 2-4h	30mg	2.5-5mg	10 mg
	haloperidol	0.5-2mg q 2h	3-4mg	0.5mg	2mg
2ND LINE ORAL	**quetiapine**	50-200mg tds	800mg		
	chlorpromazine	50-200mg q 2h	800mg	avoid	

- Benzodiazepines are generally the medication of first choice as they are more sedating and have fewer side effects than antipsychotics
- Combinations of benzodiazepines and antipsychotics can be used for more disturbed patients
- Close monitoring of patients is required after last administration of sedating injectable medications, with individual services having protocols for duration of monitoring required. Excessive sedation, hypotension or respiratory depression are particular clinical states that close monitoring.
- Benzodiazepines are best avoided in the elderly where possible. There is an increased risk of cumulative sedative effects.

DRUGS FOR PARENTERAL ADMINISTRATION

		<64YO	REPEAT INTERVAL	MAX DOSE PER 24H	>64YO	MAX DOSE PER 24H
1ST LINE PARENTERAL (IM)	**droperidol**	5-10mg IM	after 20min	repeat to max 15- 20 mg	5mg IM	10mg
	haloperidol	5-10mg IM	after 20min	15mg	0.25-1.5mg IM [3]	
	midazolam	5-10mg IM	q 20min	up to total 20mg /24h	–	–
2ND LINE PARENTERAL	**droperidol + midazolam**	5-10 mg +5-10mg IM	after 20min	up to total 15mg droperidol and 20mg midazolam		
	haloperidol + midazolam	5-10 mg + 5-10mg IM	after 20min	15mg haloperidol, 20mg midazolam		
	olanzapine	5-10mg IM wait 2 hrs if benzo-diazepine has been given	q 2-4 hours	30mg; avoid combination with benzodiazepine	2.5mg IM	10mg
	zuclopen-thixol acetate	50-150mg IM	after 48hours	to max 400mg over a 4 day period. midazolam can be used in combination There is no "Course" of acuphase, and continuing such treatment should form part of a therapeutic plan i.e. if patient being established on zuclopenthixol decanoate		

- Zuclopenthixol acetate IM should NEVER be used in antipsychotic-naïve patients. Should only be administered after specialist psychiatric assessment and consultation with consultant psychiatrist and there is a high likelihood of recurrent agitation and aggression
- Lorazepam injection is not currently available in NSW
- Prophylactic benztropine should not be used routinely. It should be used to treat symptoms only.

DELIRIUM CONSIDERATIONS

- Benzodiazepine should be avoided in delirium (except for cases of alcohol withdrawal associated delirium)
- Give single dose of oral haloperidol 0.5-2.5mg or risperidone 0.5-1mg or olanzapine 2.5-5mg
- In the elderly delirious patient avoid cholinergic medications (eg olanzapine), consider risperidone, haloperidol

PRESCRIBING GUIDE

- In acute psychiatric units it is important to always have considered PRN medication in a management plan, including proactive consideration of the charting of intramuscular medications.
    - Oral and IM benztropine should be available as a PRN order for 'DYSTONIA' whenever a patient has received or is currently being treated with any antipsychotic medication – specify both oral and IM on medication order. It is NOT indicated with the treatment of akathisia and should not be used to treat this.
- Clearly specify indication for use
- Indicate maximum dose per 24 hour period
- include range of dose if appropriate and Frequency of administration
- If multiple medications are listed for same indication, highlight the rank order for usage
- PRN medication use should be reviewed daily by treatment team

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3

MANAGEMENT CHALLENGES

3. MANAGEMENT CHALLENGES

LEARNING OBJECTIVES

- Describe the predictors of physical aggression in psychiatric patients
- Outline non pharmacological management of physical aggression in psychiatric patients

MANAGEMENT OF PHYSICAL AGGRESSION

INTRODUCTION

Physical aggression is an infrequent but problematic feature in psychiatric practice. Incidents can occur in a number of settings, however junior medical staff are usually required to manage them in Emergency Departments and in inpatient settings. Whilst this section outlines general principles of management, each clinical setting may have its own approach to the management of such incidents.

DETERMINANTS OF PHYSICAL AGGRESSION

Table 1 outlines the indicators of acute risk for physical aggression. As was described in the section dealing with formal risk assessment, there are historical or 'static' indicators and dynamic or 'variable' components. Whilst a history of previous aggression heightens the concern about a particular patient's presentation, it is the observable, cross-sectional features of mental state, which determine the immediate likelihood of physical aggression.

GENERAL PRINCIPLES OF MANAGEMENT

Different levels of physical or verbal aggression necessitate different responses. Levels of disturbance can be categorised from 1-3 with appropriate management approaches. In any process of intervention, the medical officer ought to take responsibility for their own safety and the safety of other staff including:

- Wearing appropriate attire (e.g. Breakable name tags)
- Access to duress alarms
- Ensuring the patient and staff have a clear means of escape
- Ensuring there are adequate staff available for assistance

LEVELS OF DISTURBANCE

Consideration of escalating stages of aggression can help provide a framework for responding to developing clinical scenarios.

Level 1 disturbances are characterised by lower levels of physical aggression, reflecting more the patient's subtle experience of distress. In general, such incidents are best managed by providing the patient a lower stimulus environment and the opportunity to ventilate their distress.

Arousal reduction techniques such as deep breathing, mindfulness or progressive muscle relaxation are the best approaches.

Level 2 disturbances are characterised by more significant agitation, menacing behaviour on the part of the patient including verbal aggression and damage to property. The appropriate management of this level of disturbance includes a combination

PAST HISTORY OF PHYSICAL AGGRESSION
Past aggressive behaviour, severity, use/possession of weapons
Past or recent threats
Substance abuse
Impulsivity
Poor psychosocial supports
Recent severe stress, loss or threat of loss
Past infections/diagnosis of antisocial personality disorder
CURRENT SYMPTOMS/MENTAL STATE
Intoxicated
Cognitively impairer
Psychotic and or manic
Delusions or hallucinations focussed on a particular person
Command hallucinations
Preoccupation with violent ideation
Delusions of control, especially with violent themes
Agitation, hostile or suspiciousness
Frustration or anger
Pacing/Shouting/non cooperative
Pain

Table 1

of recruiting appropriate numbers of staff via a so-called 'duress' or emergency call, isolation of the patient from the at risk environment and the appropriate use of oral or parenteral medication to relieve distress

Level 3 disturbances are the most severe, characterised by actual physical aggression or assaultive behaviour. Such patients are often severely distressed by psychotic symptoms or disinhibited by alcohol or other drugs. These instances represent psychiatric emergencies and warrant management including use of physical restraint, seclusion, the administration of parenteral psychotropic medication and the appropriate level of monitoring.

The safe restraint of such patients, to protect both staff and the patient from injury, requires special training. Psychotropic medication administered parenterally, particularly when benzodiazepines are combined with antipsychotic medications, may be unpredictable in their effects. Parenteral psychotropic treatment should only be used when adequate resuscitation facilities are available, and must be followed with close monitoring by nursing

staff for signs of cardiovascular instability, oxygen desaturation and airway protection.

The circumstances of seclusion or administration of emergency parenteral antipsychotic medication require careful documentation in both the patient's chart and a formal 'seclusion register' (a requirement of all Declared Mental Health Facilities).

In May 2017 the New South Wales Government has commenced a review of restrictive practices in mental health units in response to some high profile media articles surrounding seclusion and restraint. However, this review has been initiated on the background of significant positive steps already taken across local health districts to address this issue over the last five years, which have seen a reduction in episodes and durations of restraint and seclusion across most acute psychiatric units during this period. Further improvements must always be worked towards to ensure that the least restrictive approach to the management of a patient is also the safest for the staff managing the situation. This is likely to remain a fine balance.

The psychotropic drug use in the management of aggression is discussed in the Pro Re Nata (PRN) section of this document.

ALCOHOL AND OTHER DRUG ISSUES

ALCOHOL USE

It is clear from Australian population data that use of alcohol and other psychoactive substances is common amongst people with mental disorders. Intoxication and withdrawal may precipitate or accompany presentations with acute psychiatric symptoms.

While many Australians drink alcohol at levels within recommended guidelines, a proportion of people develop problematic alcohol use. This can range from episodic binge alcohol use which results in acute harms (alcohol poisoning, vomiting, injuries, aggression) to chronic daily use which can lead to tolerance and withdrawal, along with longer term harms (liver disease, cardiomyopathy, neurological problems, nutritional deficiencies, cognitive impairment and failure to fulfil occupational or social roles).

ALCOHOL WITHDRAWAL

Alcohol withdrawal symptoms are variable and not always predictable from an alcohol consumption history. Early diagnosis and appropriate management reduces the risk of seizures and prolonged, complicated withdrawal. Untreated, severe withdrawal can progress to delirium and autonomic instability which may require ICU admission, and has, historically, had a ten percent mortality rate.

Acute alcohol withdrawal symptoms include tremor, sweating, diaphoresis, low grade fever, tachycardia, hypertension, and anxiety. Along with sympathetic arousal, there is neuronal excitability which can result in seizures, usually in the first 48 hours after the patient's last alcohol consumption. Disorientation, confusion and fluctuating level of consciousness can develop, along with hallucinations (visual, auditory or tactile) and persecutory delusions, sometimes not emerging until the third or fourth day of a seemingly mild withdrawal. The presence of delirium needs assertive management with benzodiazepines, more intensive nursing care and adequate hydration. Autonomic instability and agitation can also require parenteral alpha-adrenergic agonist treatment (such as dexmedetomidine administered in ICU).

ASSESSMENT AND TREATMENT

Full assessment of alcohol use and withdrawal will include electrolyte status, renal and hepatic function and nutritional status. Electrolyte imbalances and dehydration should be corrected.

Thiamine deficiency is common in chronic alcohol use, and the risk of developing Wernicke's encephalopathy can be significantly reduced by early administration of parenteral thiamine (thiamine 100-300mg IV or IM initially). Wernicke's encephalopathy may present acutely with confusion, ataxia, ophthalmoplegia and nystagmus, and any of these features in the presentation warrant high dose thiamine treatment initially (eg. thiamine 300mg IV tds). Thiamine 100-300mg daily should continue during the admission, and can be administered orally if tolerated and Wernicke's has been excluded. Magnesium is a cofactor in thiamine utilisation, so correcting low magnesium is also helpful. Wernicke's symptoms that do not improve with parenteral thiamine replacement over 7 days are likely to mean that the damage is chronic and Korsakoff's psychosis (Chronic Persistent Amnestic Syndrome due to Alcohol) is present.

A history of previous alcohol withdrawal is useful in planning treatment. If the patient has previously had a seizure, or complicated alcohol withdrawal, early loading with diazepam is indicated. This can be done by giving Diazepam 20mg every 2 hours to a maximum of 80mg or until the patient is lightly sedated. This type of regime is sometimes called "front-end loading". Residual withdrawal symptoms after 80mg Diazepam need further assessment and treatment, likely involving advice from a specialist Drug and Alcohol or Addiction service.

In situations where the risk of severe withdrawal is lower or not clear, then symptoms can be monitored over the first 24-48 hours with an Alcohol Withdrawal Scale (AWS), every 2 hours. Diazepam is administered in response to scores of 4-5 or above on the AWS, in doses of 10-20mg. This type of regime is called "symptom triggered" and requires staff to have some experience of assessing acute alcohol withdrawal symptomatically. The initial 24 hour Diazepam requirements can then be given as a daily total dose, divided tds or qid, if this is easier to manage.

Nursing care in alcohol withdrawal is focussed on careful monitoring of withdrawal symptoms, rehydration, and a safe, low stimulus and supportive environment, with reorientation as needed.

While diazepam is generally used for managing alcohol withdrawal, decompensated liver failure delays diazepam metabolism and it can accumulate. Shorter acting benzodiazepines such as Oxazepam are safer in such patients. Respiratory failure and advanced age are also relative contraindications for diazepam use and shorter acting benzodiazepines are preferable.

Alcohol withdrawal lasts 5-7 days, in the acute phase, and withdrawal delirium will be prolonged, for up to 10-14 days. Residual, low grade symptoms, such as sleep disturbance, anxiety and cravings, can persist for weeks afterwards. Acute withdrawal may be planned or it may occur in the context of another illness and this provides an opportunity for that person to consider changing their alcohol use pattern. The next step following acute withdrawal, is relapse prevention which may include counselling, rehabilitation and support groups, and pharmacotherapy. Naltrexone, an opioid receptor antagonist, and Acamprosate, which acts on the NMDA and GABA systems, both have some effect in reducing relapse rates.

OTHER DRUG USE AND WITHDRAWAL SYNDROMES

In general, a non-judgemental and thorough approach to patients who use alcohol and other drugs, will assist in appropriately managing

withdrawal and ongoing care. Accurate estimations of drug and alcohol use assist in planning the appropriate treatment and assist the patient to be as comfortable as possible. Most withdrawal syndromes include an element of arousal, and any strategy that reduces arousal in the patient will facilitate better care.

BENZODIAZEPINES

Benzodiazepines are used for their sedative, hypnotic and anxiolytic effects. Higher doses can result in disinhibition and amnesia. They are most useful for the short term management of distress and agitation.

Long term prescribed use can lead to the development of tolerance, and abrupt cessation can lead to withdrawal. Binge use is also seen among patients vulnerable to substance use disorders, and an accurate history of amounts being used can be difficult to elicit. Benzodiazepine withdrawal should be as a possible aetiology in someone who develops delirium without another identified cause.

BENZODIAZEPINE WITHDRAWAL SYMPTOMS

Anxiety	Insomnia
Tremor	Tachycardia
Disorientation	Derealisation
Muscle Tension	Aches
Headaches	Confusion
Perceptual Disturbances	Seizures

Benzodiazepine withdrawal has some similarities with alcohol withdrawal due to their similar actions on GABA and the risk of seizures and delirium complicating withdrawal.

MANAGEMENT OF BENZODIAZEPINE WITHDRAWAL

Withdrawal is best managed with a long acting benzodiazepine such as diazepam. A regular regime of diazepam can be estimated by halving the usual dose reported by the patient, when their regular use is carefully assessed. While an inpatient, this can then be slowly reduced. Ideally benzodiazepine withdrawal, is managed better over weeks to months, rather than days, but this is not feasible for all patients and a shorter withdrawal in hospital still reduces the risk of seizures. Benzodiazepine use disorders can be difficult to manage, especially when they occur in patients with other substance or alcohol use problems.

DOSE EQUIVALENTS OF BENZODIAZEPINES

AGENT	DOSE EQUIVILENT
Diazepam	10mg
Alprazolam	0.5mg
Bromazepam	5mg
Chlordiazepoxide	25mg
Clonazepam	0.5mg
Flunitrazepam	1mg
Lorazelam	1mg
Nitrazepam	10mg
Oxazepam	20mg
Temazepam	10mg

OPIOIDS

Opiates and related drugs have the following effects - analgesia, euphoria, sedation, CNS depression, and pupillary constriction. There are a range of different opioid drugs available in Australia, and illicit, prescribed and over the counter formulations are used regularly by people with opioid use disorders. The half-life of the drug being taken and the route of administration will

influence the timing of the onset of withdrawal and its duration. It is important to get an accurate drug use history in an assessment of someone with opiate withdrawal.

EFFECTS OF OPIATES AND OPIOIDS

CHIEF ACTIONS
Analgesia,
Sedation,
Respiratory depression,
Euphoria
OTHER ACTIONS
Decreased Blood pressure,
Constriction of pupils,
Decreased gastric emptying,
Reduced gastrointestinal motility,
Elevated pyloric sphincter tone,
Elevated sphincter of oddi tone,
Reduced follicle stimulating hormone/leutinising hormone, testosterone,
Elevated prolactin,
Reduced adrenocorticotrophic hormone,
Elevated antidiuretic hormone,
Cough suppression
SIDE EFFECTS
Nausea and vomiting
Constipation
Dry mouth
Sweating
Vasodilation and itching
Menstrual irregularities
Sexual dysfunction

Table 1

Opiate and opioid (synthetic opiates) drugs have a distinctive withdrawal syndrome, characterised by lacrimation, yawning, piloerection, sweating, nausea/vomiting, diarrhoea, hot and cold flushes, aches, pains, cramps, tachycardia and pupillary dilatation. Opiate withdrawal can be managed in an outpatient setting, and does not usually have the risk of seizures.

EXAMPLE OF A BUPRENORPHINE REGIME

DAY	BUPRENORPHINE DOSE (AND SUGGESTED RANGE)
1	6mg (4-8mg) usually 2mg test dose, then further dose if no precipitated withdrawal
2	8mg (4-12mg)
3	10mg (4-16mg)
4	8mg (2-12mg)
5	4mg (0-8mg)
6	0mg (0-4mg)
7	0mg (0-2mg)
8	0mg (0-1mg)

SYMPTOMATIC TREATMENT OF OPIATE WITHDRAWAL

SYMPTOMS	TREATMENT
Anxiety, agitation, insomnia	Diazepam 5-10mg 4-6 hourly PRN Temazepam for insomnia
Nausea and vomiting	Metoclopramide 10mg TDS or PRN orally/IMI OR Prochlorperazine 5mg 4-6 hourly PRN
Abdominal cramps	Hyoscine butylbromide 20mg PRN QID orally or IMI
Diarrhoea	Loperamide 2mg initially, then 1 tablet after each unformed stool, up to 8 tabs per day
Muscle Aches and pains	Paracetamol 1g PRN QID (maximum 4g mg in 24 hours) OR Ibuprofen 400 mg PRN QID
Sweating and agitation	Clonidine 75 µg every 6 hours (be mindful of monitoring needs, avoidance in hypotensive patients and bradycardia)

Opiate substitution treatment is the safest and most effective treatment available for opioid dependence, and acute opiate withdrawal has a relapse rate of up to 90%. Opiate withdrawal managed with Buprenorphine (a long acting high affinity opiate partial agonist) has better retention in treatment, but ongoing abstinence once withdrawal is completed, is difficult to maintain. Opioid substitution treatment (with Methadone or Buprenorphine) assists in reducing the risk of overdose, complications from injecting, crime and other comorbidities.

Initiation of methadone or buprenorphine maintenance treatment, requires a diagnosis of severe opiate use disorder, with the presence of tolerance and/or withdrawal, and then registration on an Opioid Treatment Program. Methadone (a long acting full opiate agonist) is started at a low dose and increased slowly, until drug use has stabilised. The slow titration is necessary as methadone takes 5-7 days to stabilise in the body due to its long half life and tendency to distribute into a wide range of tissues. Buprenorphine is a partial agonist with high receptor affinity, so requires the patient to be in withdrawal prior to commencing the first dose. There is a risk of precipitated withdrawal after the initial dose if there were full agonist medications remaining on the opiate receptors. Daily opiate treatment is administered with the aim of stabilising drug use and reducing the morbidity from injecting illicit drug use.

Since the rates of prescription opioid misuse have increased, there are growing numbers of patients on Opioid Treatment as a result of codeine or oxycodone use, and their complications.

STIMULANTS

Stimulant intoxication is probably more difficult to manage in hospital, than withdrawal. Psychotic symptoms can occur in up to 25% of patients who use methamphetamine regularly, and aggression is also an issue. Management of these symptoms will involve using benzodiazepines, and possibly antipsychotics to reduce the risk of aggression and psychosis.

Withdrawal from stimulants includes an initial “crash” period after use, and then a period of low and irritable mood and poor sleep and reduced concentration. There is little evidence about what helps these symptoms, pharmacologically, although some clinicians use low doses of antipsychotic or antidepressant medications.

CANNABIS

Regular cannabis use is common amongst patients with mental health issues, and cannabis is the most widely used illicit substance in Australia. Cannabis withdrawal occurs in a proportion of patients who cease daily cannabis use, and includes symptoms such as nausea, vomiting, irritability and aggression, anxiety, disturbed sleep, restlessness, anorexia and weight loss.

Management of cannabis withdrawal is best done symptomatically, with the aim of improving sleep, reducing irritability and maintaining nutrition. The evidence for any specific pharmacological treatment is limited.

NICOTINE

While smoking rates are decreasing in Australia, clients with mental health problems and substance and alcohol use problems are still more likely to have a nicotine use disorder than the general population. Initiation of nicotine replacement in hospital can reduce the risk of agitation and aggression, by reducing nicotine withdrawal symptoms.

RECOGNITION AND MANAGEMENT OF DELIRIUM

INTRODUCTION

The Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM 5) gives the diagnostic criteria for delirium as[1]:

- A disturbance in attention (i.e., reduced ability to direct, focus, sustain and shift attention) and awareness (reduced orientation to the environment)
- The disturbance develops over a short period of time (usually hours to a few days), represents a change from baseline attention and awareness, and tends to fluctuate in severity during the course of a day
- An additional disturbance in cognition (e.g. memory deficit disorientation, language, visuospatial ability or perception)
- The disturbances are not better explained by another preexisting established or evolving neurocognitive disorder and do not occur in the context of a severely reduced level of arousal such as coma
- There is evidence from the history, physical examination, or laboratory findings that the disturbance is a direct physiological consequence of another medical condition, substance intoxication or withdrawal or exposure to a toxin or is due to multiple aetiology

Alternative terms include: acute confusional state, acute brain syndrome, toxic psychosis, acute brain failure, postoperative psychosis.

EPIDEMIOLOGY OF DELIRIUM

Studies estimate that between 10-31% of medically ill patients in hospital have features of delirium[2]. This rate may be higher in certain patient groups such as those in Intensive Care Units and in patients following cardiac surgery. In the elderly the rate may be as high as 40%[3]. However, the condition is

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often missed. In one study delirium was missed in up to 67% of cases by physicians[4]. The risk factors for delirium[5] are;

- Advancing age
- Cognitive impairment
- Dehydration
- Alcohol abuse
- Significant medical illness
- Sensory impairment
- Malnutrition
- Polypharmacy

PATHOPHYSIOLOGY

Almost any illness can contribute to the development of delirium. The most likely cause(s) in an individual patient will depend on the patient's age, medical history and on the clinical setting (for example, on a surgical ward it will be important to search for dehydration, electrolyte disturbance and to review post-operative analgesia). Even if a potential medical cause has been found, it is important to pursue other investigations as the aetiology of delirium is commonly multi-factorial.

The medical illnesses commonly associated with the onset of delirium are shown here[6].

CLINICAL FEATURES OF DELIRIUM

When asked to review a patient on the medical wards it is important to consider delirium as a possible differential diagnosis regardless of the nature of the referral. Anxiety, depressed mood and apparent psychomotor retardation, psychotic symptoms as well as aggression and agitation may all be presenting features of delirium.

CENTRAL NERVOUS SYSTEM DISEASES

- Vascular disease
- Neoplasms
- Infections – encephalitis, meningitis
- Trauma
- Epilepsy/postictal states

SYSTEMIC DISEASES

- Cardiovascular – cardiac failure, myocardial infarction
- Respiratory – hypoxia, hypercapnia
- Hepatic – encephalopathy
- Renal – acute/chronic renal failure
- Endocrine (hypo-or hyper-function) – pituitary, adrenal, pancreas (hypo/hyperglycaemia), parathyroid, thyroid
- Metabolic – dehydration, vitamin deficiencies (e.g. thiamine), electrolyte disturbances (Na, K, Ca, Mg, PO4), acidosis/alkalosis, heavy metals, malnutrition, anaemia
- Infection/Sepsis
- Neoplastic disease
- Autoimmune Diseases – vasculitis, SLE

EFFECTS OF MEDICATIONS AND ILLICIT SUBSTANCES

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A useful first step is to carefully read through the patient's medical file. Important information can be gathered regarding current and past medical illnesses and drug and alcohol history. The nursing notes are a particularly useful resource. These entries often give important clues that a patient may be confused or disorientated. Pay close attention to night-shift entries as night is a time when the symptoms of delirium may be most florid. A scan of past medical records may reveal previous episodes of delirium or a history of cognitive impairment. Next review the observation and medication charts. The medication list may suggest an aetiological cause but also consider medications that may have been missed (e.g. Does the patient normally take sleeping tablets? Have these been charted?). Collateral history from family, friends and/or general practitioner is also important. Occasionally, a prodromal phase may be evident characterised by vivid dreams, restlessness, distractibility, irritability and tearfulness. This phase may occur 1-3 days prior to the onset of the full syndrome. Delirium tends have an acute onset over hours to days and a fluctuating course. It may be useful to see patients at different times of the day to detect this. The clinical features of delirium are shown in here 3.

Changes in consciousness level
Altered cognition
Behavioural disturbance
Mood and affect changes including irritability, apathy
Perceptual disturbances including visual and auditory hallucinations

Some authors divide delirium into two groups – hypoactive and hyperactive[7]:

- *Hypoactive Delirium: d*ecreased activity, decreased alertness, somnolence, lethargy, apathy, EEG slowing, e.g. hepatic encephalopathy
- *Hyperactive Delirium:* increased activity and alertness, hypervigilance, fast or loud speech, irritability, wandering, EEG may be normal, possibly more likely to have hallucinations and delusions, e.g. alcohol withdrawal, anticholinergic toxicity

There are rating scales available for screening (e.g. Clinical Assessment of Confusion-A[8]), diagnosis (e.g. Confusion Assessment Method[9]) and severity (e.g. Delirium Rating Scale[10]).

DIFFERENTIAL DIAGNOSES OF DELIRIUM

Dementia: will have a more chronic, insidious course; fluctuations in cognition are less marked; attention less affected; consciousness is clear until the late stages; psychotic symptoms are less common. However, dementia will make individual patients more susceptible to delirium and delirium may be superimposed onto dementia – consider if acute deterioration and fluctuating symptoms.

Collateral history may be needed to clarify the patient's baseline cognition. Consider Lewy Body Dementia that may be associated with a fluctuating cognition and visual hallucinations.

Depression: hypoactive delirium may be misdiagnosed as depression. Depression will be associated with diurnal variation, a more subacute onset but with no clouding of consciousness or disorientation.

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Manic episode: the agitated and irritable delirious patient may appear manic. In mania there will be more goal directed behaviour and less cognitive impairment.

Psychotic illness: hallucinations and delusions more constant and systematised than in delirium, and there is usually no clouding of consciousness or disorientation.

Substance intoxication or withdrawal: the patient who is affected by a substance may be somnolent or agitated but will not be considered delirious unless the cognitive impairment is out of proportion to what would be normally expected from the implicated substance.

Investigations

The investigations performed will depend on the clinical situation but may include;

Bloods – UEC, Ca/Mg/PO4, LFT, FBC, glucose, TFT, CRP, blood cultures, B12, folate

Urine – urinalysis and MSU

ECG

EEG

Cerebral imaging with CT or MRI

CXR

ABG

LP

MANAGEMENT OF DELIRIUM

Risk management

An important aim of treatment is to maintain the safety of the patient, other patients and staff. Patients' with delirium are at risk of suicide, falls, wandering and medical complications. They may be aggressive and try to defend themselves in the face of perceived persecution.

Consideration should be given for the patient to be treated in a single room with 1:1 nursing care. 'Chemical restraint' may be needed (see below) to reduce behavioural disturbance. It should be remembered that the least restrictive option should be used for the shortest amount of time. Ensure adequate hydration, food intake and toileting. Monitor for the development of pressure areas, venous stasis and pneumonia. Access to open windows, balconies, stairwells and other potential environmental dangers should be prevented.

Medicolegal Cconsiderations

Patients with delirium are likely to have impaired capacity to make decisions about their medical treatment. As delirium is a medical emergency most patients may be detained in hospital and provided with medical treatment under 'Duty of Care'. An application to the Guardianship Board may also be considered.

Environmental changes/reorientation

Environmental changes that may help the delirious patient feel less distressed and minimise behavioural disturbance include: having a family member or close friend present, or place photos of loved ones in their room; trying to maintain consistency of staff; providing a room close to the nursing station; having easily sighted clocks and calendars and encouraging staff to repeatedly reorientate the patient; the use of a single room, if possible, to avoid over-stimulation but avoiding too little stimulation by the use of soft lighting and gentle background music. Making sure the patient has glasses or hearing aids, if these are required, will help reduce misperceptions. Education and reassurance to the family and to the patient, if possible, is also important.

Pharmacological treatment

The evidence for the use of psychotropic medications in the setting of delirium is limited. Consideration for medication should be given when the patient is agitated, distressed, sleepless or has psychotic symptoms. In patients who have hypoactive delirium, there is some evidence that medications may reduce the duration of the delirium and decrease distress. Like with all decisions regarding treatment the benefits must be weighed against the risks. Psychotropic medication may result in falls, may impair the patients ability to understand and comply with treatment, and sedative medication may worsen cognitive impairment.

The most studied medication for the treatment of delirium is haloperidol. Haloperidol may be used in doses from 0.5mg to 10mg and has the benefit of oral and parental administration. The dose and frequency of administration will depend on the clinical situation. It has few anticholinergic or hypotensive effects. It may result in a prolonged QT interval on ECG and, therefore, potentially result in an increased risk of Torsades de Pointes. The patient must also be monitored for extrapyramidal side effects but, in the setting of delirium treated with haloperidol, the incidence of these effects is low[11]. Olanzapine (up to 20mg/day) and risperidone (up to 4mg/day). Olanzapine may be better tolerated than haloperidol and can be given intramuscularly. The evidence for these medications is limited. It has been suggested that antipsychotic medication be continued for several days following a resolution of symptoms[12]. Benzodiazepines may worsen confusion or cause disinhibition in the elderly, or in patients with pre-existing organic brain syndromes, and should be avoided in most cases. The exceptions to this rule are the setting of alcohol or benzodiazepine withdrawal and postictal delirium.

Identify and treat the underlying cause(s)

This will depend upon the clinical situation.

PROGNOSIS OF DELIRIUM

There may be a rapid improvement in symptoms once the underlying cause has been found and adequately treated. Delirium often subsides over several days but can last several weeks (1) and maybe more prolonged in the elderly[13].

Delirium has been associated with:[14,15]

- Prolonged hospitalisation
- High frequency of complications e.g. falls, infections, pressure sores
- Increased need for care in institutions
- Increased risk of death

The mortality rate for patients who have had delirium is between 14-36% at 6 months[16].

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11. Kerr IB, Taylor D. Acute disturbed or violent behaviour: principles of treatment. *Journal Psychopharmacol.* 1997;11:271-9.
12. Schwartz TL, Masand PS. The Role of Atypical Antipsychotics in the Treatment of Delirium. *Psychosomatics.* 2002;43:171- 174.
13. Koponen H, Stenback U, Mattila E, et al. Delirium among elderly persons admitted to a psychiatric hospital: Clinical course during the acute stage and one-year follow-up. *Acta Psychiatr Scand.* 79:579-585.
14. Meagher DJ. Delirium: optimising management. *British Medical Journal.* 2001;vol. 322:20; p144-148.
15. Liptzin B. Delirium. In J Sadavoy, LW Lazarus, LF Jarvik, et al (Eds). *Comprehensive Review of Geriatric Psychiatry* (second edition). Washington DC: American Psychiatric Press, 1996.
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NEUROLEPTIC MALIGNANT SYNDROME

LEARNING OBJECTIVES

- Describe the clinical features of neuroleptic malignant syndrome
- Outline the process of diagnosis of the neuroleptic malignant syndrome
- Describe the treatment of the neuroleptic malignant syndrome

INTRODUCTION

The neuroleptic malignant syndrome (NMS) is a rare but potentially lethal complication of antipsychotic treatment. NMS is estimated to have an incidence of between 0.02 to 3.23% of psychiatric inpatients receiving antipsychotic medication[17]. NMS is twice as common in men and all D2 blocking agents, including antiemetics such as metoclopramide and prochlorperazine are implicated. It has been described with use of all classes of antidepressants, and with abrupt discontinuation of anti-parkinsonian medication. There have also been reports of NMS occurring spontaneously in neurological conditions and schizophrenic illnesses. The pathophysiology is largely unknown, although sudden disruption of dopaminergic activity in the striatum and hypothalamus appear to produce diffuse muscle rigidity leading to raised core body temperature, rhabdomyolysis and accompanying disturbances in physiology[18]. The risks for NMS are shown in Table 1.

High doses of neuroleptics
Rapid escalation of dose
Dehydration
Past history of NMS
Affective illness
Organic brain syndrome

Table 1

CLINICAL FEATURES OF NMS

The clinical features of NMS are shown in Table 2. In essence, any patient taking antipsychotic medication who exhibits fever, rigidity or confusion should have NMS excluded.

Hyperthermia
Rigidity or other EPSE
Autonimic dysregulation
Tachypnoea
Confusion or delirium
Rhabdomyolysis and myoglobinurea
Leukocytosis
Elevation of serum creatinine kinase (marked)

Table 2

LABORATORY INVESTIGATIONS

The critical investigation is the serum levels MM fraction of creatine phosphokinase (CPK). Levels are often markedly elevated. CPK levels may be altered by IM injection and physical trauma during an episode of psychosis. In addition to

[17] Lazarus A, Mann SC, Caroff SN. *The Neuroleptic Malignant Syndrome and Related Conditions.* Washington, DC, American Psychiatric Press, 1989.

[18] Stoudemire A, Luther JS. Neuroleptic malignant syndrome and neuroleptic-induced catatonia: differential diagnosis and treatment. *International Journal of Psychiatry in Medicine.* 1984;14:57-63.

raised CPK, the patients white cell count is often significantly raised. Given dehydration and sepsis may be comorbidly present, serum electrolytes and screening for infection are often required. Myoglobin may be present in the urine, warranting closer monitoring of renal function and fluid balance.

DIFFERENTIAL DIAGNOSIS OF NMS

The differential diagnosis of NMS is shown in Table 3.

Serotonin sydndrome
Malignant hyperthermia
Catatonia
Sepsis
Anticholinergic agent intoxication
Overdose of CNS stimulants including MDMA, amphetamine, cocaine
Delirium of other cause

Table 3

Malignant hyperthermia is a hypermetabolic state of skeletal muscle most frequently associated with the administration of halogenated inhalation anaesthetic agents and succinylcholine. It is heritable, and whilst originally thought to be transmitted via an autosomal dominant trait, it is now considered to have a multifactorial pattern of inheritance. The clinical presentation of malignant hyperthermia is identical NMS. The main clinical differentiation is the context of general anaesthesia via halogenated inhaled anaesthetics. The diagnosis of malignant hyperthermia (or of the latent trait) is reliably established by exposing biopsied muscle tissue to caffeine or halothane in vitro, which results in a hypercontractile response when compared with normal muscle. Treatment of malignant hyperthermia is through the use of dantrolene sodium. Muscle tissue from patients with neuroleptic malignant syndrome does not demonstrate a hypercontractile response to caffeine or halothane.

Family histories of patients with malignant hyperthermia have not been documented in patients with neuroleptic malignant syndrome, and the conditions do not seem to be related. Lethal catatonia is a syndrome in which mutism, extreme motor excitement, clouding of consciousness, and fever may progress to severe autonomic disturbances, stupor and coma, and death. It may be a condition related to NMS.

CLINICAL COURSE

NMS is usually present for 2 –14 days. Mortality from the condition is reducing with improved critical care. Prior to 1984 the mortality rate for NMS was 25%. Since 1984 it is 11.6%[19]. NMS may be complicated by contractures, renal failure, hypostatic complications such as deep venous thrombosis or pneumonia. There is evidence that prolonged hyperthermia may lead to cerebellar damage[20].

TREATMENT OF NMS

Treatment of NMS is based upon prompt recognition of the syndrome, the cessation of antipsychotic treatments agent and lithium (if co-administered). Supportive care is usually provided

[19] Shalev A, Hermesh H, Munitz H. Mortality from neuroleptic malignant syndrome. *Journal of Clinical Psychiatry.* 1989;50:18-25.

[20] Lee S, Merriam A, Kim TS, et al. Cerebellar degeneration in neuroleptic malignant syndrome: neuropathologic findings and review of the literature concerning heat-related nervous system injury. *Journal of Neurology, Neurosurgery, and Psychiatry.* 1989;52:387–391.

in critical care setting, with monitoring of fluid balance, renal function and the use of antipyretic agents. ECT has proven efficacy in the treatment of NMS and may be used in severe or refractory cases, particularly where NMS may be related to the use of long acting injectable antipsychotic medication. Anitcholinergic agents, intravenous dantrolene and dopamine agonists such as bromocriptine, amantadine, and apomorphine have anecdotal benefits. If clinically indicated, patients who suffer NMS may be rechallenged with antipsychotic medication, ideally of a different class. The likelihood of recurrence of NMS is substantially lower if the antipsychotic rechallenge is >5 days[21]. Patients should only be rechallenged with antipsychotic medications under close medical supervision with regular monitoring of vital signs, serum CPK and frequent neurological investigation.

THE SEROTONIN SYNDROME

INTRODUCTION

The serotonin syndrome is the result of overstimulation of 5-HT1A and 5-HT2 receptors in central grey nuclei and the medulla. The syndrome is potentially fatal and has increased in significance since the introduction of newer antidepressant and antipsychotic drugs which affect the serotonin neurotransmitter systems[22].

PATHOGENESIS OF THE SEROTONIN SYNDROME

The circumstances in which the serotonin syndrome emerges are shown in Table 1.

DIAGNOSIS OF THE SEROTONIN SYNDROME

The diagnostic criteria of the serotonin syndrome are shown in Table 2[23].

Introduction or addition of a serotonergic agent, or increase in dosage, and manifestation of at least 4 major symptoms or 3 major plus 2 minor ones:

MENTAL (COGNITIVE AND BEHAVIOURAL SYMPTOMS

Major – confusion, elevated mood, coma, reduced GCS Minor – agitation, nervousness, insomnia

AUTONOMIC SYMPTOMS

Major symptoms – fever, hyperhidrosis

Minor – tachycardia, tachypnoea, dyspnoea, diarrhoea, altered BP

NEUROLOGICAL SYMPTOMS

Major – myoclonus, tremors, chills, rigidity, hyperreflexia

Minor – impaired coordination, mydriasis, akathisia

Table 2

MECHANISM	AGENTS
• Excess of precursors of serotonin or its agonists	Buspirone, L-dopa, lithium, LSD
• Increased release of serotonin	Amphetamines, cocaine, MDMS
• Slowing down of serotonin metabolism	MAOI drugs
• Reduced reuptake of serotonin	SSRI, TCA
• Ectopic production of serotonin	Carcinoid syndrome

Table 1

[21] Wells AJ, Sommi RW, Crismon ML. Neuroleptic rechallenge after neuroleptic malignant syndrome: case report and literature review. *Drug Intelligence and Clinical Pharmacy.* 1988;22:475-480.

[22] Boyer E et al, The Serotonin syndrome, *New England Journal of Medicine* 2005; 352:1112-20.

[23] Radomski JW, Dursun SM, Revely MA, Kutcher SP. An exploratory approach to the serotonin syndrome; an update of clinical phenomenology and revised diagnostic criteria. *Med Hypotheses.* 2000;55:218-24.

DIFFERENTIAL DIAGNOSIS OF SEROTONIN SYNDROME

The differential diagnosis of the serotonin syndrome is shown in Table 3.

Neuroleptic malignant syndrome
CNS or other systemic infections causes
Toxic encephalopathy
Heat stroke
Delirium tremens
Anticholinergic delirium

Table 3

MANAGEMENT AND OUTCOME OF SEROTONIN SYNDROME

There should be a low threshold for discussing medical concerns with medical teams, as serotonin syndrome will often require management in a medical setting. Management may include serotonin antagonists. Care overall is is directed at supporting the patient through there symptoms. This may include assisting in reducing body temperature, addressing agitation, addressing severe autonomic disturbance, while ensuring care takes place in the appropriate setting.

Most presentations of serotonin syndrome will significantly improve within 24-48 hours of ceasing the precipitating agent.

NOTES

4

COMPLICATIONS

4. COMPLICATIONS

LEARNING OBJECTIVES

- Identify the metabolic complications of antipsychotic treatment
- Describe the prevalence and features of the metabolic syndrome in psychiatric populations
- Outline the principles of management of the metabolic syndrome in psychiatric populations

METABOLIC COMPLICATIONS OF ANTIPSYCHOTIC TREATMENT

SCHIZOPHRENIA AND METABOLIC COMPLICATIONS

Up to 51% of males and 64% of females suffering from schizophrenia are obese (defined as BMI > 90th percentile). This is in contrast to 33% of individuals with other psychiatric diagnoses[1]. Ischaemic Heart Disease (IHD) is a greater cause of mortality in psychiatric patients than suicide. Moreover, the IHD mortality rate amongst people suffering schizophrenia has not trended down as it has in the general population[2]. People with mental illness had a higher prevalence of cardiovascular risk factors such as smoking, obesity, lack of exercise, alcohol consumption and salt intake when compared with control subjects from a community-based sample[3]. It is a sad paradox that patients whose psychiatric symptoms respond best are also those most likely to gain weight as a consequence of treatment with antipsychotic medication[4]. Being female, younger, and with a lower pre-treatment BMI and non-Anglo-Celtic ethnicity appear to elevate risk[5].

Clozapine and olanzapine are associated with the greatest risk of clinically significant weight gain, with other agents producing relatively lower levels of risk. Risperidone, quetiapine and amisulpride generally show low to moderate levels of mean weight gain and a modest risk of clinically significant increases in weight. Ziprasidone and aripiprazole treatment are generally associated with minimal mean weight gain[6]. One study found 32% of olanzapine-treated patients possessed the 'atherogenic' metabolic triad comprising hyperinsulinaemia, increased apolipoprotein B

1. Dinan TG (ed.). Schizophrenia and diabetes 2003: an expert consensus meeting. *British Journal Psych.* 2004;184:(suppl 7):S53-S114.
2. Lawrence DM, Holman CDJ, Jablensky AV, et al. Death rate from ischaemic heart disease in Western Australian psychiatric patients 1980-1998. *British Journal Psychiatry.* 2003;182:31-6.
3. Davidson S, Judd F, Jolley D, et al. Cardiovascular risk factors for people with mental illness. *Australian New Zealand Journal Psychiatry.* 2001;35:196-202.
4. Czobor P, Volavka J, Sheitman B, et al. Antipsychotic – induced weight gain and therapeutic response: a differential association. *Journal Clinical Psychopharmacol.* 2002;22:244-51.
5. McIntyre RS, Mancini DA, Basile VS, et al. Antipsychotic-induced weight gain: bipolar disorder and leptin. *Journal Clinical Psychopharmacol.* 2003;23:323-7.
6. Newcomer J W. 2005. "Second-generation (atypical) antipsychotics and metabolic effects: a comprehensive literature review." *CNS Drugs.* 19(Suppl 1):1-93.

concentration, and small, dense LDL, compared with a figure of 5% in risperidone-treated patients[7].

Data from the National Institute of Mental Health-sponsored Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE)[8] found a prevalence of metabolic syndrome of 42.7%. The mean BMI of the subjects was 29.7 (SD=7.0). Among fasting subjects, 44.4% met criteria for the metabolic syndrome The risk of metabolic syndrome in people suffering schizophrenia is 2–3 times that of the general population.

PUTATIVE MECHANISMS OF METABOLIC CONSEQUENCES OF ANTIPSYCHOTIC TREATMENT

There are a variety of theoretical models of the mechanism of weight gain related to antipsychotic therapy. Apart from the effects of illness on lifestyle there is the possibility of an intrinsic propensity to weight gain in schizophrenia. Stimulation of Histamine 1 receptors may trigger hunger or impair satiety in people taking medications such as clozapine or olanzapine. Insulin resistance, and a propensity to glucose intolerance can occur as a consequence of multiple intercurrent effects of the antipsychotics including the effects of increased body mass and direct interference by of the antipsychotics in the glucose metabolism[9], in particular interference with hepatic glycogen synthesis through alteration of hepatocyte 5HT receptors[10]. The induction of peripheral insulin resistance and the direct influence on pancreatic beta-cell function by 5-HT1A/2A/2C receptor antagonism, or by inhibitory effects via alpha 2-adrenergic receptor is a postulated mechanism[11].

There has been interest in, three identified cytokines which play crucial roles in the regulation of energy balance and glucose metabolism – ghrelin, adiponectin and leptin[12]. Adipocyte expression or secretion of adiponectin an insulin-sensitizing cytokine is affected by olanzapine[13].

The criteria proposed by the National Cholesterol Education Program (NCEP) Adult Treatment Panel III (ATP III), with minor modifications, are currently recommended and widely used[14]. The American Heart Association and the National Heart, Lung, and Blood Institute recommend that the metabolic syndrome be identified as the presence of three or more of these components. The metabolic syndrome is characterized by a group of metabolic risk factors in one person (Table1).

Abdominal obesity
Atherogenic dyslipidaemia
Elevated blood pressure
Insulin resistance or glucose intolerence
Prothrombotic state
Proinflammatory state
Elevated waist circumference

Table 1

7. Bouchard RH, Demers M, Simoneau I, et al. Atypical antipsychotics and Cardiovascular Risk in Schizophrenic patients. *Journal Clinical Psychopharmacol.* 2001;21:110-11.

8. McEvoy JP, Meyer JM, Goff DC, Nasrallah HA, Davis SM, Sullivan L, Meltzer HY, Hsiao J, Scott Stroup T, Lieberman JA. Prevalence of the metabolic syndrome in patients with schizophrenia: baseline results from the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) schizophrenia trial and comparison with national estimates from NHANES III. *Schizophr Res.* 2005;80:19-32.

9. Filakovic P, Koic O, et al 2007. "Second generation antipsychotics and risk of diabetes type II – comparison between olanzapine and risperidone." *Coll Antropol.* 31(4):1105-9.

10. Hampson LJ, Mackin P, et al 2007. "Stimulation of glycogen synthesis and inactivation of phosphorylase in hepatocytes by serotonergic mechanisms, and counter-regulation by atypical antipsychotic drugs." *Diabetologia.* 50(8):1743-51.

11. Schwenkreis P, Assion HJ, 2004. "Atypical antipsychotics and diabetes mellitus." *World Journal Biol Psychiatry.* 5(2):73-82.

12. Hosojima H, Togo T, et al 2006. "Early effects of olanzapine on serum levels of ghrelin, adiponectin and leptin in patients with schizophrenia." *Journal Psychopharmacol.* 20(1):75-9.

13. Richards A A, Hickman IJ, et al 2006. "Olanzapine treatment is associated with reduced high molecular weight adiponectin in serum: a potential mechanism for olanzapine-induced insulin resistance in patients with schizophrenia." *Journal Clinical Psychopharmacol.* 26(3):232-7.

14. National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (final report). *Circulation.* 2002;106:3143- 421.

GLUCOSE REGULATION, DIABETES, ADIPOSITY, AND DYSLIPIDEMIA

Type I diabetes, which accounts for less than 10% of diabetes cases, often begins in childhood and is usually the result of autoimmune destruction of the insulin-secreting pancreatic beta cells. Type II diabetes, which usually begins after age 45, is characterized by two pathological processes: inadequate insulin secretion and impaired insulin action at the insulin receptor, or insulin resistance. Early in the course of type 2 diabetes, insulin resistance, caused by genetic and/or environmental factors, evokes a compensatory increase in pancreatic insulin secretion so that glycaemic control is maintained; insulin levels are elevated, but random and fasting plasma glucose levels remain normal. Insulin resistance and compensatory hyperinsulinaemia are typically associated with elevated fasting triglyceride levels, low levels of high-density lipoprotein (HDL) cholesterol, and elevated levels of atherogenic low-density lipoprotein (LDL) cholesterol particles. Over a period of 7 to 10 years on average, increasing insulin resistance and/or deteriorating beta cell function leads to a state in which pancreatic compensatory capacity is overwhelmed[15].

Insulin insufficiency is first evident as postprandial hyperglycaemia (or an abnormal glucose tolerance test) due to impaired uptake of glucose into muscle. Later in the course of the disease, with progressive loss of insulin secretion, liver glucose production becomes dysregulated, resulting in fasting hyperglycaemia. At this relatively advanced illness stage, an elevated fasting plasma glucose level allows detection of "prediabetes" or type II diabetes. Type 2 diabetes is diagnosed by measurement of fasting plasma glucose level using thresholds for diabetes (>125 mg/dl) and prediabetes (100–125 mg/dl) defined by the American Diabetes Association[15].

With progressive beta cell failure, disinhibition of inhibition of lipolysis increases, further reducing control over free fatty acid release and worsening the characteristic dyslipidemia associated with diabetes. Physiological stress, such as intercurrent illness in the presence of marked impairment in insulin secretory functioning and insulin resistance, can result in severe hyperglycaemia, which can acutely inhibit beta cell function, a state known as glucose toxicity. Under these circumstances, acute glycaemic decompensation may result in diabetic coma and death due to extreme hyperglycaemia with excessive fatty acid and ketone formation (diabetic ketoacidosis) or non-ketotic hyperosmolar states.

Insulin resistance and type II diabetes occur most often in the context of overweight and obesity, particularly excess abdominal adiposity. Adiposity and fitness are each thought to contribute about 30% of the individual variance in insulin resistance, with genetic factors accounting for the remainder. Thus, while excessive abdominal adiposity is significantly related to risk of insulin resistance and diabetes, type II diabetes can also occur in the absence of overweight or obesity.

MANAGEMENT OF METABOLIC SYNDROME

The Adult Treatment Panel III treatment guidelines[16] recommend therapeutic life style changes, including reduced intake of saturated fats and cholesterol, increased fibre intake, weight reduction, and increased physical activity as the first-line therapeutic approach to the risk of cardiovascular disease. LDL-lowering drugs, including HMG-CoA reductase inhibitors (statins), bile acid sequestrants,

[15] American Diabetes Association: Diagnosis and classification of diabetes mellitus. *Diabetes Care.* 2004;27(suppl 1):S5-S10.

[16] Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Executive Summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *JAMA.* 2001;285:2486-2497.

nicotinic acid, and fibric acids, are prescribed as needed to achieve target LDL levels.

The metabolic syndrome increases the risk of cardiovascular disease at any given level of LDL and is considered a secondary target of risk-reduction therapy after lowering LDL cholesterol. The Adult Treatment Panel III guidelines identify obesity as the primary target of treatment of the metabolic syndrome and weight loss and increased physical activity as the first-line treatment approaches. Weight loss lowers LDL cholesterol and triglycerides, increases HDL cholesterol, lowers blood pressure, and reduces insulin resistance. Metformin reduces insulin resistance, reduces new-onset coronary heart disease in obese patients with diabetes, and prevents or delays type II diabetes in patients with impaired glucose tolerance. Insulin sensitizers also prevent or delay type 2 diabetes in at-risk patients. Antipsychotics and meet criteria for the metabolic syndrome should be treated with therapeutic life style changes and medications in accordance with hypertension guidelines. Finally, low-dose aspirin may be indicated to mitigate the prothrombotic state in patients with metabolic syndrome at elevated risk of coronary heart disease.

QTC ABNORMALITIES AND PSYCHOTROPIC TREATMENT

LEARNING OBJECTIVES

- Understand the importance of abnormalities of QTc interval
- List psychotropic treatments which can alter the QTc interval
- Describe the risk of sudden death in patients with severe mental illness

INTRODUCTION

The QT interval is an ECG measure that includes both depolarization and repolarization. It begins with the onset of ventricular depolarization (Q wave) and ends with completion of repolarization (T wave). Because the QT interval shortens with increasing heart rates, it is usually corrected for heart rate (QTc). QTc intervals are usually around 400 msec in duration, and values lower than 440 are considered normal (Fig 1). A QTc >500 msec has frequently been used as a cutoff because longer QTc interval measures are associated with substantially higher risk of cardiac arrhythmias.

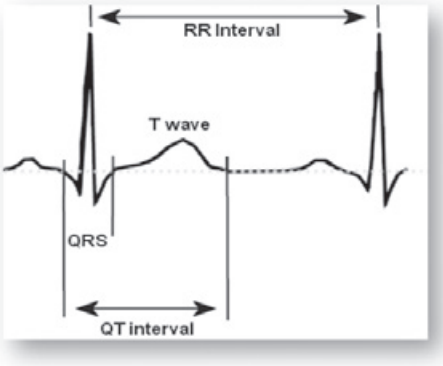

Figure 1 – The normal ECG complex from the P-T waves

Depolarization of ventricular myocardial cells is the result of a rapid influx of Na^+ ions through selective Na^+ channels. Repolarization occurs via cationic inflows through Ca^{++}, Na^+, and several K^+ channels.

This process is reflected on the ECG by the QRS interval. There are 10 described heritable forms of the Long QT Syndrome (LQTS). Drugs can prolong the QTc interval and can induce life threatening cardiac arrhythmias, the most significant of which is 'torsade de pointes'. Sudden death in apparently healthy adults can occur as a result of drug induced QTc prolongation. Prolonged QTc intervals are associated with the risk of sudden death after myocardial infarction and the LQTS. In some forms

of inherited LQTS, sudden death can occur as a consequence of exercise, sleep or emotional shock. QTc interval prolongation is the "clinical red flag" that warns of the possibility of torsade de pointes and sudden death.

TORSADE DE POINTES

Torsade de pointes meaning "twisting around the point" (a reference to a ballet movement) refers to an uncommon variant of ventricular tachycardia (VT) in which the QRS complexes twist about the isoelectric axis of the ECG. The morphology of the QRS complexes varies from beat to beat. The ventricular rate can range from 150-250 beats per minute (Fig 2).

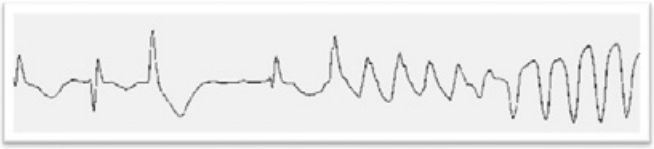

Figure 2

The QTc interval is a modest predictor of torsade de pointes. The underlying basis for the arrhythmia is delay in phase III of the myocardial action potential mediated by the I_{Kr} potassium channel.

This prolonged period of repolarization and the irregularity of repolarization times among different myocardial fibres create re-entrant phenomena or ectopic electrical activity to occur, producing the arrhythmia. As the underlying aetiology and management of torsade are, in general, quite different from VT, the management of torsade with group IA antiarrhythmic drugs can be lethal.

Psychotropic medications associated with prolonged QTc and torsade de points are shown in Table 1.

PROLONGED QTC AND TORSADES DE POINTES
Ziprasidone, Amisulpiride, Droperidol
PROLONGED QTC
Olanzapine, Quetiapine, Risperidone, Chlorpromazine, Clozapine, Haloperidol, Zuclopenthizol

Table 1

SUDDEN DEATH IN MENTALLY ILL POPULATIONS

There is considerable evidence in the scientific literature that people suffering schizophrenia are at higher risk for sudden death. This is both related to antipsychotic treatment, and independent of this variable. Cardiovascular risk factors are covered in a separate section, however it is important to note that chronic mental illness is associated with the lifestyle risk factors for ischaemic heart disease. It is also evident that people with chronic mental illnesses have, for a variety of reasons, less access to early intervention in physical disease.

ACUTE DYSTONIC AND AKATHISIA IN THE ACUTE SETTING

AKATHISIA

"Akathisia" is a drug-induced movement disorder, which presents as a syndrome of motor restlessness, usually in the lower extremities, often accompanied by a subjective sense of inner restlessness, and dysphoria[17]

[17] Barnes TR, Braude WM. Akathisia variants and tardive dyskinesia. *Arch Gen Psychiatry.* 1985;42:874-878.

Akathisia exists in acute, chronic (duration >3 months) and tardive forms (with onset (>3 months). A form of withdrawal akathisia may occur as a consequence of a reduction in the dose of antipsychotic medication[18].

A syndrome resembling akathisia is seen following the initiation of treatment with aripiprazole, although this is an "activation" syndrome arising from partial D_2 receptor agonism in the striatum.

The incidence of acute akathisia of amongst patients taking antipsychotic medication is 31%[19] and the prevalence rate ranges up to 41%[20].

In the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) study, there were no significant differences between first and second-generation antipsychotics in the incidence of extrapyramidal symptoms

There is no parallel between the concurrent severity of akathisia and other extrapyrimadal side-effects of antipsychotic medication, implying that akathisia is a different phenomenon from the other recognised extrapyramidal side-effects of neuroleptic medication.

Akathisia has been described in patients taking SSRI antidepressants. Moreover, the lower propensity or serotonin blocking Second Generation Antipsychotics implies a serotonergic mechanism involved in the genesis of akathisia. Cholinergic and adrenergic pathways are also implicated.

ASSESSMENT OF AKATHISIA

The diagnosis of akathisia is primarily clinical. Observations of motor restlessness in a patient taking antipsychotic or SSRI medication are the commonest clinical sign, although akathisia can present as a primarily subjective sense of restlessness, variably described by the patient as agitation, dysphoria or anxiety.

The Barnes Akathisia Rating Scale can also be used to formally assess akathisia.

Akathisia should be differentiated from psychotic agitation or psychomotor agitation in severe melancholic depression.

Anxiety can be mistaken for akathisia. Some features of tardive dyskinesia, particularly trunk or limb movement, can be confounded for akathisia. Other neurological disorders producing choreo-athetoid movements can resemble akathisia. There is a possible relationship between akathisia and the "Restless Legs Syndrome". This condition is characterized by lower body movement similar to those seen in akathisia, although the symptoms usually occur only during rest, relaxation or sleep, and tend to follow a circadian pattern.

TREATMENT OF AKATHISIA

Akathisia is a sinister symptom, and strongly correlates with medication noncompliance[21], worsening of psychotic symptoms, impulsive behaviour, increased liability for aggression, deliberate self-harm and completed suicide[22]. Reduction of dose of the patient's neuroleptic medication, or changing the patient's treatment to a different agent with a lower propensity for such side effects are the first line measures for treatment. If this is not appropriate, benzodiazepines, propranolol, or anticholinergic medications may be of some help in treating acute akathisia.

18. Sachdev P. Research diagnostic criteria for drug-induced akathisia: conceptualization, rationale, and proposal. *Psychopharmacology.* 1994;114:181-186.

19. Sachdev P. *Akathisia and Restless Legs.* New York, Cambridge University Press, 1995.

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21. Van Putten T. Why do schizophrenic patients refuse to take their drugs? *Arch Gen Psychiatry.* 1975;31:67-72.

22. Van Putten T, Mutalipassi LR, Malkin MD. Phenothiazine-induced decompensation. Arch Gen Psychiatry. 1974;30:13-19. patients 1980-1998. *British Journal Psychiatry.* 2003;182:31-6.

ACUTE DYSTONIA

Acute dystonia should be treated as a medical emergency due to its potential to be life threatening.

The presentation of acute dystonia can include severe, debilitating and often sustained spasms of muscle.

This even can take place up to several days after the medication has been given typically an antipsychotic medication from the "typical" group.

Such events can be unpredictable in their occurrence, but particular attention should be made to any past history of such events in a patient, or of a family history of such events.

Presentations can include dystonia of the neck, tongue and jaw. Body arching may occur. An occulogyric crisis can present where the eyes roll up and become "fixed" - often referred to as the "look ups".

Treatment is to administer immediately intramuscular benztropine 2mg. The offending agent should be ceased. If the presentation is believed to compromise the airway of the consumer then a full emergency response should be initiated.

Oral benztropine should be continued in the aftermath for 2-3 days.

HYPERPROLACTINAEMIA

LEARNING OBJECTIVES

- Understand the normal physiology of prolactin
- Describe the sequelae of raised levels of serum prolactin
- Identify the propensity for different psychotropic agents to raise serum prolactin

INTRODUCTION

Elevation of prolactin levels in patients is a frequent and problematic side-effect of the use of psychotropic medication. Hyperprolactinaemia produces undesirable side effects in the short term, affecting medication tolerability and treatment compliance. Longer-term morbidity chronic iatrogenic hyperprolactinaemia is also of concern.

THE PHYSIOLOGY OF PROLACTIN

Prolactin is released form the anterior pituitary gland in a pulsatile manner with up to 15 peaks per 24 hours. The normal physiological range of serum prolactin levels is between 10-25µg/L. Serum prolactin levels exhibit a circadian pattern and usually peak after 4 hours of a sleep cycle. Prolactin

MEDICATION		HYPERPROLACTINAEMIA
• FGAs – especially haloperidol, zuclopenthixol, flupenthixol, fluphenazine • Risperidone		Significant potential ("prolactin raising")
• Ziprasidone	• SSRI antidepressants	Moderate potential
• Olanzapine • Quetiapine	• Clozapine • Tricyclic	Lower potential ("prolactin sparing")
• Aripiprazole • Amantadine	• Bromocriptine	May reverse

Table 1

has the primary function of lactogenesis via the stimulation of breast tissue and milk synthesis. It suppresses gonadotropin function and likely plays a role in mediating attachment behaviours in humans.

Studies indicate the prevalence of hyperprolactinaemia is 34% in men and75% in women[23]. Traditionally, hyperprolactinaemia is considered to be present at levels > 100µ/L, however clinically significant side-effects can emerge at lower levels. Women, particularly in the post-partum period and pubescent children are particularly vulnerable to iatrogenic hyperprolactinaemia. There is some evidence of menstrual irregularities in women with schizophrenia which predate treatment with antipsychotic medication[24].

Short term

Females – Reduced libido, amenorrhoea, galactorrhoea, mastodynia, anovulation, virilising effects, weight gain

Males – Gynaecomastia, reduced spermatogenesis, reduced libido, erectile dysfunction, weight gain

Longer term

Many of the longer term consequences of iatrogenic hyperprolactinaemia are speculative and established with variable certainty. There is some evidence to suggest that chronic antipsychotic exposure may be associated with reduced bone density through suppression of sex-steroid function. A recent study found a 16% increase in the risk of breast cancer in women chronically exposed to D2 antagonists[25]. Analysis of the FDA database indicates a possible risk of development of pituitary tumours, particularly with risperidone[26].

ANTIPSYCHOTIC MEDICATION AND HYPERPROLACINAEMIA

Any medication that effects some blockade at the D2 tuberoinfundibular neuronal cluster has the capacity to elevate serum prolactin.

First generation antipsychotic medications, particularly high potency agents, have the greatest potential to increase serum prolactin, whereas some second generation antipsychotics have little propensity, or in the case of aripiprazole may reduce prolactin levels – Table 1 (opposite page).

POSSIBLE TREATMENT OF HYPERPROLACINAEMIA

Once it is established that the cause of hyperprolactinaemia is related to psychotropic use, the treatment of iatrogenic hyperprolactinaemia is based primarily upon clinical considerations. Patients who are concerned about reduced fertility or problematic endocrine related side-effects may warrant consideration of medication change to a prolactin sparing antipsychotic medication, although the strategy of changing agents may be associated with increased risk of relapse[27]. Female patients may benefit from the oral contraceptive pill. The administration of dopaminergic agonists such as bromocriptine is ill-advised due to the potential to worsen psychotic symptoms. Some anecdotal evidence suggests that there is potential benefit to the addition of aripiprazole to existing antipsychotic.

23. Smith S, O'Keane V, Murray R, et al. Sexual dysfunction in patients taking conventional antipsychotic medication. *British Journal Psychiatry.* 2002;181:49-55.

24. Wieck A, Haddad PM. Antipsychotic-induced hyperprolactinaemia in women: pathophysiology, severity and consequences: selective literature review. *British Journal Psychiatry.* 2003;182:199-204.

25. Wang PS, Walker AM, Tsuang MT, et al. Dopamine antagonists and the development of breast cancer. *Arch Gen Psychiatry.* 2002;59:1147-1154.

26. Szarfman A, Tonning J, Levine G, et al. Atypical antipsychotics and pituitary tumors: a pharmacovigilance study. *Pharmotherapy 200.* 2006;26:748-5.

27. Kim KS, Pae CU, Chae JH, et al. Effects of olanzapine on prolactin levels of female patients with schizophrenia treated with risperidone. *Journal Clinical Psychiatry.* 2002;63:408-13.

NOTES

5

IMPORTANT LEGISLATION

5. IMPORTANT LEGISLATION

LEARNING OBJECTIVES

- Outline the rationale for the Mental Health Act
- Describe the processes of referral to Declared Mental Health Facilities
- Understand the provisions for involuntary psychiatric treatment in NSW

THE *MENTAL HEALTH ACT 2007*

THE RATIONALE FOR MENTAL HEALTH ACT

The NSW *Mental Health Act 2007* (MHA or Act) provides "for the care and treatment of, and to promote the recovery of, persons who are mentally ill or mentally disordered".[1] The Act exists to strike a balance. On the one hand, it permits doctors, acting as agents of the state, to contain, and provide treatment to, people in the midst of mental illness or emotional crisis, who are thought to require protection from serious harm. On the other hand though, it places tight restrictions around when doctors may use this power.

WHAT CRITERIA MUST BE MET TO PLACE A PERSON UNDER THE ACT?

The Act defines two broad classes of people who may be detained and involuntarily treated – "mentally ill persons" and "mentally disordered persons". Each class of person is defined by a set of three different, but over-lapping, criteria.

MENTALLY ILL PERSONS

A patient may be detained as a mentally ill person if all three of the following apply:

1. The person must suffer a "mental illness". This is not a mental illness as ordinarily understood, but a "mental illness" as defined by the Act. The definition of a mental illness appears with other definitions in section 4 of the Act. Mental illness means a condition characterised by the presence of any one or more of delusions, hallucinations, serious disorder of thought form, a severe disturbance of mood, or irrational behaviour indicating those symptoms. Note that the terms used here are intended to be understood by their ordinary English meaning. So that for example, while psychiatrists would be unlikely to call the ideation exhibited by a person with anorexia nervosa a delusion, the same symptoms may be regarded as a "delusion" by a layperson and therefore a person with that symptom may meet this criterion.
2. Because of the person's mental illness, he or she must need "care, treatment or control" for their "own protection from serious harm", or "the protection of others from serious harm".[2] Again the term "harm" here has its ordinary meaning and the range of possible serious harms a wide. They include not only the possibility of suicide or deliberate self-harm, as long as the latter is serious, but also serious harm

[1] *Mental Health Act 2007* (NSW) s 3.
[2] *Mental Health Act 2007* (NSW) s 14.

to a person's finances, serious harm to their relationships and, probably most common of all, serious psychological harm the person may suffer through the experience of severe delusions or incessant, unpleasant hallucinations.When considering these harms one may consider any likely deterioration that the person may suffer.

This criterion may also include serious harm to a person's reputation, but there is some doubt over this.[3] In practice the doubt is of little consequence since few people may come to serious reputational harm without also needing protection from the range of other possible harms envisaged.

Note that the wording of the protection from harm criterion says nothing about "risk", though people often wrongly abbreviate it in that way. "Risk" is a forward-looking concept that would require a doctor to make some sort of prediction about the future. The protection from serious harm criterion though may usually be met simply by examining the person's current circumstances. if someone is already suffering serious psychological harm, or their health is seriously deteriorating all their relationship with their family is being seriously adversely affected, then if that is due to the effects of the mental illness, it can be said that the person needs protection from serious harm.

The protection from serious harm criterion sets a very low bar in day-to-day clinical work. It will very rarely be the case a registrar or psychiatrist will see a patient in crisis and consider that they may benefit from involuntary admission, but be prohibited from enforcing that admission because the person does not meet the serious harm criterion.

3. It must be the case that involuntary treatment represents the least restrictive avenue of treatment "that is consistent with safe and effective care, is appropriate and reasonably available to the person".[4]

This least restrictive criterion is the criterion that, at the coalface, most often determines whether or not a person can be detained under the Act. As soon as a doctor comes to believe that involuntary treatment no longer represents the least restrictive alternative consistent with safe and effective care, he or she is required to discharge the patient. When a doctor decides that a person, whom people might consider detainable under the Act cannot be, he or she should carefully justify their opinion and the matter will usually hinge on this criterion. (The bar set by the protection from serious harm criterion is so low, that will rarely be a relevant consideration in practice).

MENTALLY DISORDERED PATIENTS

A patient may be detained as a mentally disordered person if three similar criteria apply. The least restrictive criterion applies just as it does in mentally ill people and similarly is frequently the determinative criterion. The other two criteria though are slightly different and are both housed within the following provision: A person is a mentally disordered person if the person's behaviour for the time being is so irrational as to justify a conclusion on reasonable grounds that temporary care, treatment or control of the person is necessary for either for the person's own protection from serious physical harm, or for the protection of others from serious physical harm.[5]

Note that now the mental illness criterion of the mentally ill person has been replaced by the notion of "behaviour that is for the time being

3. *Re J* (no. 2) [2011] NSWSC 1224.
4. *Mental Health Act 2007* (NSW) s 12.
5. *Mental Health Act 2007* (NSW) s 15.

so irrational", and that the protection from harm serious criterion has been altered so that it applies only in the case of serious physical harm. It is easy to see what lawmakers done here. In targeting irrational behaviour they have extended a protective envelope to people who may temporarily fall short of a mental illness, people who are for example extremely upset after a relationship breakdown. However, having lowered that threshold, they have raised the serious harm threshold, so will only apply in cases where the serious harm envisaged is physical. Psychological harm, relationship harm and harm to one's finances, no matter how serious, cannot be used in the context of a mentally disordered person.

THE IMPORTANCE OF A PERSON'S DECISION-MAKING CAPACITY

The criteria set out above for both mentally disordered and mentally ill people are interesting in that they lack an element that is normally considered crucial if a person is to be treated without consent. In general medicine, a competent person may refuse treatment even if that treatment is required to protect them from serious harm or even death. Generally speaking, the only occasions, in general medicine where a doctor can deliver a treatment without a person's consent, is when that person lacks decision-making capacity. The absence of a decision-making capacity criterion in the involuntary treatment criteria listed above is unsettling.

In recent years other Australian states, such as Tasmania, South Australia, Queensland, and Western Australia have all altered their involuntary treatment criteria so as to include a requirement that a person must lack decision-making capacity if they are be subject to involuntary treatment. In New South Wales, the government decided not to include decision-making capacity as one of the involuntary treatment criteria, but instead made it clear in the mental health principles that govern the whole act,[6] the doctors are required to assess a person's decision-making capacity and then make every effort reasonably practicable to respect a person's competent decision.

In practice, this means that unlike the other states listed above, a mentally ill or mentally disordered person in New South Wales, who retains decision-making capacity, can nonetheless be forced to have treatment, but that this should occur only in extraordinary circumstances. Therefore, when determining whether a person can be detained under the MHA, doctors should assess not only the three criteria above, but also the person's decision-making capacity. In the rare circumstance that the doctor believes that the person should be treated despite a competent refusal, he or she should provide a detailed rationale for that decision.[7]

Instructions on how to assess decision-making capacity are beyond the scope of this volume, but in the simplest terms, all adults are presumed to have decision-making capacity, but the presumption can be overturned if it is shown that the person either lacks the ability to understand or retain the information relevant to the decision, or is unable to use and weigh that information to come to a decision.[8]

PATHWAYS TO ADMISSION

A person can be conveyed to a Declared Mental Health Facility (DMHF) by police, ambulance, medical officers, the courts or a primary carer in consultation with a mental health service. Most emergency departments in NSW are DMHFs.

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6. *Mental Health Act 2007* (NSW) s 68.

7. Ryan CJ, Callaghan S. *The impact on clinical practice of the 2015 reforms to the NSW Mental Health Act. Australasian Psychiatry 2017;* 25: 43-47.

8. Ryan CJ, Callaghan S, Peisah C. The capacity to refuse psychiatric treatment – a guide to the law for clinicians and tribunal members. *Australian & New Zealand Journal of Psychiatry* 2015; 49: 324-333.

Once the patient is conveyed to a DMHF they become and 'assessable person'. The person is then assessed by two other clinicians, one of whom must be a psychiatrist, under s 27 of the *Act* and is either further detained, discharged or offered treatment as a voluntary patient. If the person is further detained as mentally disordered they must be released within 3 working days (though this can be re-considered in unusual cases). If the person is further detained as mentally ill, they must be presented to the Mental Health Review Tribunal within short period. At that hearing, the treating team should explain why they believe the person is a 'mentally ill person' in terms in of the Act and why no other least restrictive form of care is appropriate. They must also comment on the person's decision-making capacity. The patient has a legal representative present at the hearing, and Tribunal makes a legal determination as to whether the person can continue to be subject to the Act and if so it may:

- Defer the patient's discharge from the DMHF;
- Make a treatment order for involuntary treatment in a DMHF for a specified period;
- Make a Community Treatment Order.

COMMUNITY TREATMENT ORDERS

One of the main principles of the Act is the requirement to provide treatment under the 'least restrictive option'. In many instances, the patient will be able to safely and effectively receive psychiatric treatment in a community setting. Involuntary treatment in the community is provided under the provisions of Community Treatment Orders (CTOs). If a patient, subject to a CTO, is in breach of its conditions (e.g. consistent non-attendance to appointments) an application can be made for a breach of CTO (s 58)). This may result in the patient being taken to the community health centre or detained in a DMHF.

Though it is likely that CTOs are useful for patients who lack decision-making capacity around their need for treatment, but who are well enough to leave hospital, the nature and strength of their efficacy remain uncertain, and they should be used sparingly.

THE *GUARDIANSHIP ACT 1987*

LEARNING OBJECTIVES

- Describe the basic provisions of the Guardianship Act
- Understand the role of the psychiatrist in Guardianship proceedings

INTRODUCTION

Whilst the *Mental Health Act* provides for involuntary detention and treatment of patients affected by psychiatric illness, the NSW *Guardianship Act 1987* protects the interests and legal rights of people who have lost the capacity to make decisions by reason of a disability or medical illness. The most relevant parts of the *Guardianship Act* for the audience of this work are those referring to medical and dental treatment set out in part 5. These set out the procedures to be followed when a person who lacks decision-making refuses medical treatment.

In an emergency situation, if patients lack decision-making capacity and they are not able to consent to treatment that would save their life or protect them from serious harm, then assuming no regular substitute decision maker is available and there is no reason to believe the person would have refused the treatment when competent, a doctor may give a person necessary treatment without consent.[9]

In less urgent situations the *Guardianship Act* provides a mechanism of appointing substitute decision makers, be they persons responsible, who, generally speaking, may not consent to treatment over a patient's voice objection or guardians who have may do so if authorised to do so by Guardianship Division of the New South Wales Civil and Administrative Tribunal. Applications can be made to this tribunal in a manner that is similar to that described for the Mental Health Review Tribunal above.

Note that in circumstances where both the *Mental Health Act* and the *Guardianship Act* apply, the *Mental Health Act* "trumps" the *Guardianship Act* to the extent that the two are inconsistent.[10]

The role of the psychiatrist in these hearings is usually to provide evidence about the person's decision-making capacity, including at times, why the person was not able to understand, retain or use and weigh the relevant information, despite being offered as much support as possible to do so.

[9] *Guardianship Act 1987* (NSW) s 37; Hunter and New England Area Health Service v A [2009] NSWSC 761.

[10] *Guardianship Act 1987* (NSW) s 3C.

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