Emerging psychosis in young people – Part 1

Key issues for detection and assessment

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BACKGROUND
A delay in the recognition of first episode psychosis is common and is often associated with psychological distress, social decline, and as recent evidence suggests, lasting brain changes. It is increasingly evident that early intervention potentially alters the course of these serious mental illnesses. General practitioners are ideally placed to identify early changes that may herald an emergent psychotic illness and to bridge the existing gap between patients, their families and specialist mental health services.

OBJECTIVE
This article summarises the rationale and importance of early detection of emerging psychotic illness in young people, and provides practical tips regarding its assessment and detection.

DISCUSSION
Early warning signs of emerging psychotic illnesses include behavioural, emotional and cognitive disturbances. Risk factors include a combination of a family history of a psychotic illness coupled with a decline in functioning, or a history of a brief self limiting psychotic episode (even if triggered by drugs such as cannabis or amphetamines). It is important that those working in primary care recognise these features in order to facilitate a speedy referral to specialist youth friendly mental health services, or if such services are not available, to initiate treatment and provide appropriate ongoing management.

One in 5 adult Australians experience a mental disorder in any 12 month period.[1] In adolescents and young adults, the rate increases to one in 4 accounting for about 70% of the burden of disease in young people across all medical illnesses.[2,3] Like most mental disorders, psychotic illnesses usually emerge when people are young, with 80% of first episodes occurring between 16–30 years of age. While the incidence may be low, it is important to detect all potential new cases of emerging psychotic disorders as early as possible.

Let there be no delay

Patients presenting with a first psychotic episode who meet the criteria for schizophrenia have a mean duration of functional impairment or subthreshold psychotic symptoms of about 5 years and experience psychotic symptoms for about 1 year.[4–6] Most have sought help from health care professionals several times before recognition of their underlying illness, yet only a minority receive appropriate treatment.[7] This delay in detection and treatment causes distress to patients and their families, and often disrupts social[8] and cognitive[9] development as well as brain maturational processes.[10] It appears that untreated psychosis may even have direct neurotoxic effects.[4] Although still under debate, recent evidence provides increasing support that the duration of untreated psychosis is likely to impact on functional and symptomatic outcomes[8,11] implying that this very early stage of illness may be the crucial phase for interventions with major implications for prevention of impairment and disability.[8,12–15]

Protect the brain – a neurobiological rationale for early detection and intervention

Studies have demonstrated that patients suffering from chronic schizophrenia have structural, metabolic and functional brain changes.[10] However, the timing of these brain changes is unclear. Some of the brain changes probably occur early in development pointing toward a – probably nonspecific – neurodevelopmental vulnerability.[16] However, recent studies have also found new brain changes around the onset of the psychotic illness.[17,18] Importantly, longitudinal studies from the first psychotic episode onward suggest that these brain changes mainly progress in the initial couple of years and reach a plateau early in the course of the psychotic

illness[19,20] supporting the idea that the early phase of psychosis may constitute a critical period for treatment.[21,22] Encouragingly, a recent study found that the use of the newer antipsychotic medications prevent these progressive brain changes and may be neuroprotective.[23]

'At risk mental state'

To prevent a mental illness or poor outcomes associated with frequent relapses, we need to predict if someone is at risk of developing an illness or of having a progressive course. This is not always easy. Adolescence and early adulthood is a phase in life where most young people experience 'troubles'. The difficulty for young people, and for those in close proximity such as relatives, teachers and health care professionals, is to differentiate between those having 'troubles in life' from those who are at grave risk of developing a serious mental illness.[24]

The term 'at risk mental state' has recently been coined to identify people at increased risk of psychosis. An 'at risk mental state' is usually characterised by a sustained and clinically important deviation from the premorbid level of experience and behaviour.

Our own research has demonstrated that the presence of low grade (subthreshold) psychotic symptoms, poor functioning, depression, and disorganisation predicted the onset of an overt psychotic episode in up to 40% of 'at risk cases' within 1 year,[26] yet many young people with such presentations often have their issues ignored or trivialised. In other medical conditions such as cancer, we would not risk delaying life saving treatments with similar odds. However, the temptation to ignore the problem or look for alternative explanatory models in psychiatry is much greater, in part because of a lack of understanding of the underlying aetiopathology and the stigma and implications of a diagnosis of mental illness for young people and their families.

While the presence of a first degree relative with a psychotic illness increases the relative risk of having a mental illness from 1 to 10% in the case of schizophrenia or bipolar affective disorders,[27] this is not sufficient to justify early intervention or premature diagnostic labelling. However, if a positive family history is combined with other features such as a decline in functioning or the emergence of subthreshold psychotic symptoms, in particular during critical developmental periods such as adolescence or postmenopause, then the increase in relative risk to a level of 30–40% justifies at the very least regular assessments and possibly more active psychological treatment to prevent psychosis. General practitioners play a key role in raising awareness in patients that the presence of such symptoms may be an early warning sign that needs special attention (see *Case history*).

How can I detect a psychotic patient or a patient at risk?

The key advantages of the GP is that he/she:

- often has a multi-dimensional view of the patient since early childhood, including some knowledge of their family and living situation
- can provide a low stigma environment in which to assess and treat patients with psychiatric disorders, and
- can reassess the patient over time if symptoms are unclear.

This puts the GP in a strong position to enquire and recognise at risk mental states or overt psychosis at a very early stage and prevent any delays in treatment. The difficulty that a GP faces is that psychotic disorders are low prevalence disorders, and may only see a few cases per year. Furthermore, the clinical presentation of an emerging psychotic illness varies from person-to-person. Many factors such as age, gender, culture, family history of mental illness or a personal history of trauma, as well as current or past history of substance abuse may influence the presentation. The onset of symptoms may be gradual and insidious characterised by withdrawal, lack of motivation and poverty of thinking. In fact, the acute onset of florid psychotic symptoms including hallucinations, thought disorder and delusions without a proceeding at risk mental state is the exception rather than the rule, making early recognition and treatment of psychosis a difficult endeavour.

Furthermore, GPs often have only limited time to explore subtle changes in functioning or presentation associated with emerging psychotic disorders; and the complexity of presentations can make it difficult to differentiate between those with an emerging psychotic illness from other common major mental illnesses. More significantly, there is an imminent danger of 'forgetting to enquire' about psychotic-like experiences once the diagnosis of depression, personality disorder or substance misuse has been made. It is therefore essential that GPs be prepared to consider the possibility of psychosis in any young person presenting with cognitive, emotional or behavioural difficulties.

Something is not quite right – assessment strategies

The most important goal in assessment is the engagement of the patient in a therapeutic alliance.[28] If we cannot engage the patient, we

Case history – John

John, 19 years of age, lives with his parents and two younger brothers. He was always a shy child and did reasonably well in school until year 11 when he lost interest in his studies and left. John began isolating himself increasingly, preferring to play computer games in his room. He smokes cannabis 3–4 times a week. He experienced an episode of depression 3 years ago, when he dropped out of school. He has been 'moody' since then. He has occasionally told his parents that he may be developing a 'sixth sense' and that it sometimes feels like he is 'different' to everyone else. His parents are worried that he is not fulfilling his potential. John seems unconcerned by all this worry, although he did once tell his younger brother that he had heard a voice whispering to him on two occasions when there was no-one else around.

Discussion – John may be experiencing a psychotic at risk state. He has deteriorated in his functioning. Ideally he needs further assessment by a specialist youth mental health service, if available, together with support to deal with his substance abuse. If such services are not available, regular monitoring is advisable. Engagement is likely to be an issue as he does not feel there are any problems at present.

cannot assess the extent of his/her condition nor deliver the best possible treatment. Most potential cases will see their GP for other reasons. The key issue for the GP is to realise that 'something is not quite right' and enquire about possible psychotic symptoms, including subtle ones. *Table 1* provides screening questions to enquire about symptoms that may be indicative for an at risk mental state or overt psychotic state. If changes persist or worsen over time and are associated with an increased functional disability, the GP should take them seriously and consider the possibility of an emerging mental illness[26] (*Table 2*). The danger of normalising changes by family members, individuals or health care professionals is often a lost opportunity to prevent further decline in social, psychological and brain maturational processes.[29]

Table 1. Screening questions for psychotic-like experiences (questions relate to the previous 12 months)

Have you noticed yourself being paranoid or suspicious of others?
Have you worried that somebody has been out to get you? Wanting to harm you?
Do you feel like anyone is watching you, talking about you or laughing at you behind your back?
Have you had the feeling that you have special powers that other people don't have or are especially important in some way?
Have you felt that things around you had a special meaning intended just for you? For example has the TV or radio been sending you messages?
Have you felt that someone or something outside yourself has been controlling your thoughts, feelings, actions or urges? Have you had feelings or impulses that don't seem to come from yourself?
Have you felt that ideas or thoughts have been put into your head or taken out of your head by someone or something else?
Have you felt your thoughts are less private than usual?
Have you thought that your thoughts are broadcast so that everyone can know what you are thinking? Or that people can read your mind?
Have you seen or heard things that other people don't seem to hear or see?
Observations during the interview:
Are you (the interviewer) having any trouble following the patient's answers, understanding what they are trying to say?
Are they pressured in speech?
Do they seem unable to answer questions because of being perplexed or thought blocked?
Do they go off the subject and get lost in their words?
If the patient has answered yes to any of these questions then further investigation of symptomatology and presentation will be required as the possibility of an emerging or active psychotic illness needs to be considered

Source: ORYGEN Youth Health Assessment proforma

Assessment of suicide risk and risk management

In first episode psychosis the suicide rate is particularly high in the early phase of illness. The decision of whether to treat a patient in an in- or out-patient setting is often related to risk issues and needs to be addressed according to presentation, support and available resources. In areas where mobile treatment teams are available, home based treatment is often favourable and can prevent patient trauma by involuntary admissions or restraint. Unfortunately, some adult mental health services have limited resources or little commitment to avoiding coercive practices such as seclusion and forced sedation, in particular after hours or weekends. In areas where a support network is not available, suicide risk is often managed using available resources such as community nurses or GPs. This may result in significant anxiety and distress within the available service providers and needs appropriate support. Telemedicine or phone consultations with specialist mental health services are potential strategies to deal with these difficult situations. However, only few areas across Australia provide such secondary consultation services for GPs.

Assessment of psychiatric comorbidity

Many patients with an emerging psychotic disorder have comorbid substance abuse,[30] depression,[31] comorbid personality traits such as borderline personality features, or a combination of these. Such features need to be recognised and integrated in the formulation and treatment plan as they may interfere with the establishment of a therapeutic alliance and ongoing management.

Up to 80% of adolescents experiment with drugs, with alcohol still the most frequently used.[32] About one in 3 adolescents use cannabis, with about 10–15% using more than twice a week.[32–35] Often more than one illicit drug is used. Recent controlled studies[33,34] confirm that early cannabis use may increase the risk for schizophrenia. General practitioners often have limited support and time in dealing with such complex cases. However, the GP and the patients' families may be able to facilitate the establishment of a support network that addresses the complexity of each individual case and ultimately leads to an early referral to a specialist service before progression of functional decline.

Assessment of medical comorbidity

An increasing body of evidence suggests that psychotic disorders (and their treatment) are associated with factors such as diabetes, lipid abnormalities and cardiovascular disorders.[36,37] A range of investigations are therefore recommended, preferably before initiation of antipsychotic medications, as these may inform us about the choice of the first line treatment (*Table 3*).[36]

Patients with major mental illness may have a greater risk of diabetes and lipid abnormalities, that is not only associated with medication

effects or weight gain, but seems to be present before treatment initiation.[38] Additionally, the newer antipsychotic medications have a high frequency of metabolic side effects such as dyslipidaemias and increased rates of glucose intolerance that are not only related to weight gain.[39] The use of psychotropic medications such as clozapine need additional tests (eg. troponin, echocardiogram).

Organic disorders such as Huntington disease, multiple sclerosis, or other neurological conditions need to be considered in patients presenting with psychotic symptoms, in particular if the presentation is atypical (eg. older age of onset) (*Table 4*). In young people, one should also be cautious not to miss any sexually transmitted infections. HIV infection and mental illness co-occur, being mutual risk and exacerbating factors.[40] AIDS may initially manifest with psychological symptoms such as depression[41] or first episode psychosis.[42]

What to do next

Patients with at risk mental state

It is important to note that the at risk mental state is not sufficient to initiate antipsychotic treatment as not all patients will progress toward a full-blown psychotic episode. However, patients in the at risk mental state phase are at very high (and often imminent) risk of an emerging mental illness. Such patients need close monitoring and need to be engaged in a therapeutic alliance. At this stage, an early referral to a specialist youth friendly mental health service should be considered. This is often a difficult process and patients, as well as their families, may be wary. Furthermore, even if the willingness is there, it is often difficult to access specialist mental health services if no clear-cut symptoms are present. The availability of a good psychiatric history and the description of psychotic-like experiences will facilitate the involvement of mental health services. In the case of a progressive decline, an early initiation of treatment may become warranted so that the duration of untreated psychosis can be reduced to the absolute minimum.

Table 2. Warning signs of emerging psychotic disorders

The key is to enquire, observe and recognise changes in the following domains:

Behaviour

Withdrawal and loss of interest in socialising

Deterioration in role functioning

Bizarre behaviour (eg. talking to him/herself, gesticulation)

Thinking

Thought content (odd or unusual ideas, eg. paranoid, nihilistic, grandiose delusions)

Stream of thought (abnormalities of the amount and speed of thoughts)

Form of thought (abnormalities of the way thoughts are linked together)

Possession of thoughts (disturbance of the awareness that one's thoughts are one's own)

Cognition

Problems with concentrating (eg. during interview easily distracted)

Problems with memory (eg. as shown by deterioration in study or work)

Problems with execution (eg. not able to perform tasks such as cooking)

Perception

Altered perception of the world (hallucinations)

– auditory (eg. hearing a voice(s) or loud thoughts that nobody else hears)

– visual (eg. seeing shadows, faces, people)

– olfactory (eg. smelling gas)

– tactile (eg. feeling spiders crawling on skin)

Affect and emotions

Alterations in nature – high or low (eg. from being overly happy to extremely sad)

Alterations in reactivity (eg. blunted affect, being unable to express or recognise emotions)

Inappropriate (eg. inappropriate laughter)

Self awareness

Unawareness or denial of being ill

Denial of needing treatment (loss of insight)

Physical changes

Changes in sleep architecture

Changes in eating behaviour (eg. no interest in eating or scared of being poisoned)

Changes in activity (eg. loss of energy, reduced drive and motivation)

Motor abnormalities (eg. mannerisms or posturing [rare])

Patients with an overt psychotic disorder

Once the frequency of the psychotic symptoms have crossed the threshold for a first episode psychosis (daily significant psychotic symptoms for more than 1 week), referral to a youth friendly specialist service should take place and antipsychotic treatment initiated without delay.

The complexity of presentation requires an individual approach adapted according to the needs of the patient and their psychosocial context. The quality of this first contact is important as unnecessary trauma (eg. in the context of an involuntary hospital admission or a restraint situation in an emergency department) may jeopardise the ongoing therapeutic alliance with the patient and their family, and impact on retention within specialist services.

In the north western metropolitan area of Victoria, the Early Psychosis Prevention and Intervention Centre (EPPIC) of ORYGEN Youth Health has access to a mobile crisis and assessment team (Youth Access Team) to respond rapidly to referrals from relatives, GPs, school welfare coordinators, the juvenile justice system, and other allied health workers, and to facilitate the engagement of patients in their home environment. Specialist services such as EPPIC endeavour to prevent hospitalisation (or at least reduce hospitalisation time) and avoid involuntary admissions to hospital by providing assertive outreach treatment if necessary. In other states, similar services will be developed in the near future (see *Resources*).

Table 3. Recommended medical investigations in first episode psychosis

Investigations	Sequence	Comments
Full blood examination	Baseline and yearly	Signs of infection, red blood cell anomalies (macrocytosis in chronic alcoholism)
Urea and electrolytes	Baseline and yearly	Severe dehydration
Liver function	Baseline and yearly	Liver infections, intoxication
Thyroid function	Baseline and yearly	Thyroid dysfunction is often associated with many psychiatric symptoms
B12 and folate	Baseline and yearly	Alcoholism, malnutrition
Random glucose	Baseline, 3 months after commencing antipsychotic medication and yearly	Higher diabetes risk in psychotic illness
Lipid profile	Baseline and yearly	Lipid abnormalities are major side effect of antipsychotic medication
Urinalysis	Baseline	
Creatinine clearance	As clinically indicated	In young patients only if patients have a history of kidney problems prior treatment initiation
Urine drug screen	As clinically indicated	If suspected drug use
Electrocardiogram	Baseline and yearly	If possible prior treatment initiation, thereafter annually or as clinically indicated (in particular exclude QTc prolongation)
Brain scan	Baseline	Suspicions of organic reason for psychosis (eg. Huntington disorder or multiple sclerosis, encephalopathy)
Weight and waist circumference	Baseline and as clinically indicated	Monthly measures important for initial 2 months, at least quarterly thereafter
Electroencephalogram	As clinically indicated	If atypical presentation or history of seizures or 'blackouts'

Support networks based on the patient's needs are vital. However, in many areas the establishment of such support networks is difficult, as specialist youth services are rarely available and adult mental health services, due to under-resourcing or inappropriate priorities, may not always accept referrals of patients with emerging mental disorders, or have limited capacity to monitor or prevent the progression of disease. General practitioners often have no choice than to find other ways of managing such patients, in particular if patients refuse a referral to a private psychiatrist or a specialist mental health service. Management is discussed in Part 2 of this series.

Conclusion

Psychosis can derail psychosocial development and is potentially toxic to the developing brain. A reduction in the duration of untreated psychosis is therefore a key goal of management. General practitioners play a crucial role in the assessment and early detection of emerging

Table 4. Medical conditions often associated with psychotic symptoms

Delirium (eg. alcohol psychosis)
Epilepsy (eg. temporal lobe epilepsy)
Central nervous system (CNS) infections (+/- intracerebral lesions)
- HIV infection (early manifestation of AIDS)
- Neurosyphilis
- Other viral encephalitis

Neurodegenerative disorders
- Huntington disease (psychotic symptoms are very common)

Autoimmune disorders
- Systemic lupus erythematosus
- Multiple sclerosis

Endocrine disorders
- Thyroid or parathyroid dysfunction
- Cushing disease, Addison disease, phaeochromocytoma

Metabolic disorders
- B12 or folate deficiency (chronic alcohol abuse)
- Porphyrias
- Wilson disease
- Chronic hypoglycaemia

CNS trauma (eg. frontal lobe syndrome)
CNS neoplasma

psychotic illnesses. They are often the first point of contact for young people with mental health difficulties and have the advantage of a multi-dimensional view of the patient which may enable them to detect change in behaviour or functioning suggestive of psychosis at a very early stage. The presence of such changes combined with a family history of mental illness or an early onset of regular cannabis use, requires close monitoring of the patient's mental state and possible referral to specialist psychiatric services. The daily presence of psychotic symptoms that interfere with daily functioning for more then 1 week needs immediate attention and usually requires the initiation of antipsychotic medication. It is important to explore and monitor suicide risk and/or risk to others, as well as psychiatric and medical comorbidity. The engagement of the patient in this early phase of illness is crucial for the outcome of what may be an enduring illness and important for the future referral for specialist assessment and ongoing involvement with specialist mental health services. A close working relationship between specialist mental health services and primary care is therefore essential.

Resources

- GPs needing more information about the detection and management of early psychosis are encouraged to contact the early psychosis worker at their local area mental health service. GPs in Victoria may contact the ORYGEN Youth Health Service
- ORYGEN (www.ORYGEN.org) provides up-to-date contact information for consumers, carers and doctors
- Mental Illness Fellowship Australia may assist GPs in identifying local services specialised in supporting young people with emerging psychotic illnesses or facilitate a referral to a private psychiatrist specialised in early intervention
- The GP Psych Support service provides GPs with online or telephone psychiatrist support via their website at www.psychsupport.com.au
- The Royal Australian & New Zealand College of Psychiatrists (RANZCP) Private Psychiatrists Referral Directory is available to all VR GPs via the RACGP website at www.racgp.org.au/psychiatristdatabase

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References

1. Taylor AW, Wilson DH, Dal Grande E, et al. Mental health status of the South Australian population. Aust N Z J Public Health 2000;24:29–34.
2. Jablensky A. Schizophrenia: epidemiology. Curr Opin Psychiatr 1999;12:19–28.
3. Beumont P. The mental health of young people in Australia: report by the National Mental Health Strategy. Aust N Z J Psychiatry 2002;36:141; author reply 141.
4. McGlashan TH. Duration of untreated psychosis in first episode schizophrenia: marker or determinant of course? Biol Psychiatry 1999;46:899–907.
5. Hafner H, an der Heiden W. The course of schizophrenia in the light of modern follow-up studies: the ABC and WHO studies. Eur Arch Psychiatry Clin Neurosci 1999;249(Suppl 4):14–26.
6. Hafner H, Maurer K, Loffler W, an der Heiden W, Hambrecht M, Schultze-Lutter F. Modeling the early course of schizophrenia. Schizophr Bull 2003;29:325–40.
7. McGorry PD. 'A stitch in time'... the scope for preventive strategies in early psychosis. Eur Arch Psychiatry Clin Neurosci 1998;248:22–31.
8. Edwards J, Harrigan SM, McGorry PD, Amminger PG. Duration of untreated psychosis (DUP) and outcome in schizophrenia. Psychol Med 2002;32:563–4.
9. Amminger GP, Edwards J, Brewer WJ, Harrigan S, McGorry PD. Duration of untreated psychosis and cognitive deterioration in first episode schizophrenia. Schizophr Res 2002;54:223–30.
10. Keshavan M, Berger GE, Zipursky R, Wood SJ, Pantelis C. Neurobiology of early psychosis. Br J Psychiatry 2005;187:8–18.
11. Harrigan SM, McGorry PD, Krstev H. Does treatment delay in first episode psychosis really matter? Psychol Med 2003;33:97–110.
12. Wyatt RJ, Henter I. Rationale for the study of early intervention. Schizophr Res 2001;51:69–76.
13. Linszen D, Dingemans P, Lenior M. Early intervention and a five year follow up in young adults with a short duration of untreated psychosis: ethical implications. Schizophr Res 2001;51:55–61.
14. Malla AK, Norman RM, Manchanda R, et al. One year outcome in first episode psychosis: influence of DUP and other predictors. Schizophrenia Research 2002;54:231–42.
15. McGorry PD, Warner R. Consensus on early intervention in schizophrenia. Schizophr Bull 2002;28:543–4.
16. Weinberger DR. Implications of normal brain development for the pathogenesis of schizophrenia. Arch Gen Psychiatry 1987;44:660–9.
17. Berger GE, Wood SJ, Wellard RM, et al. Incipient neurovulnerability and neuroprotection in early psychosis: A proton spectroscopy study of the anterior hippocampus at 3Tesla. Schizo Res 2003;60:(Suppl 1):238.
18. Pantelis C, Velakoulis D, McGorry PD, et al. Neuroanatomical abnormalities before and after onset of psychosis: a cross-sectional and longitudinal MRI comparison. Lancet 2003;361:281–8.
19. Carpenter WT, Strauss JS. The prediction of outcome in schizophrenia. IV: Eleven year follow up of the Washington IPSS cohort. J Nerv Ment Dis 1991;179:517–25.
20. Harrison G, Hopper K, Craig T, et al. Recovery from psychotic illness: a 15 and 25 year international follow up study. Br J Psychiatry 2001;178:506–17.
21. Cahn W, Hulshoff Pol HE, Lems EB, et al. Brain volume changes in first episode schizophrenia: a 1 year follow up study. Arch Gen Psychiatry 2002;59:1002–10.
22. van Haren NE, Cahn W, Hulshoff Pol HE, et al. Brain volumes as predictor of outcome in recent onset schizophrenia: a multicenter MRI study. Schizophr Res 2003;64:41–52.
23. Lieberman J, Chakos M, Wu H, et al. Longitudinal study of brain morphology in first episode schizophrenia. Biol Psychiatry 2001;49:487–99.
24. Sullivan H. The onset of schizophrenia. Am J Psychiatry 1927;6:105–34.
25. McGorry P, GROUP IEPAW. International clinical practice guidelines for early psychosis. Br J Psychiatry 2005;187:120–4.
26. Yung AR, Phillips LJ, Yuen HP, et al. Psychosis prediction: 12 month follow up of a high risk ('prodromal') group. Schizophr Res 2003;60:21–32.
27. Gottesman, II, Erlenmeyer-Kimling L. Family and twin strategies as a head start in defining prodromes and endophenotypes for hypothetical early interventions in schizophrenia. Schizophr Res 2001;51:93–102.
28. Day JC, Bentall RP, Roberts C, et al. Attitudes toward antipsychotic medication: the impact of clinical variables and relationships with health professionals. Arch Gen Psychiatry 2005;62:717–24.
29. Lieberman JA, Tollefson GD, Charles C, et al. Antipsychotic drug effects on brain morphology in first episode psychosis. Arch Gen Psychiatry 2005;62:361–70.
30. Mendlowicz MV, Braga RJ, Marrocos RP, Figueira I. Comorbidity and disability in outpatients with schizophrenia. Am J Psychiatry 2005;162:400 author reply 400–1.
31. Hickie IB, Davenport TA, Scott EM, Hadzi-Pavlovic D, Naismith SL, Koschera A. Unmet need for recognition of common mental disorders in Australian general practice. Med J Aust 2001;175(Suppl):S18–24.
32. Pedersen W, Skrondal A. Ecstasy and new patterns of drug use: a normal population study. Addiction 1999;94:1695–706.
33. Arseneault L, Cannon M, Poulton R, Murray R, Caspi A, Moffitt TE. Cannabis use in adolescence and risk for adult psychosis: longitudinal prospective study. BMJ 2002;325:1212–3.
34. van Os J, Bak M, Hanssen M, Bijl RV, de Graaf R, Verdoux H. Cannabis use and psychosis: a longitudinal population based study. Am J Epidemiol 2002;156:319–27.
35. Caspi A, Moffitt TE, Cannon M, et al. Moderation of the effect of adolescent-onset cannabis use on adult psychosis by a functional polymorphism in the catechol-O-methyltransferase gene: longitudinal evidence of a gene X environment interaction. Biol Psychiatry 2005;57:1117–27.
36. Lambert TJ, Chapman LH. Diabetes, psychotic disorders and antipsychotic therapy: a consensus statement. Med J Aust 2004;181:544–8.
37. Henderson DC. Diabetes mellitus and other metabolic disturbances induced by atypical antipsychotic agents. Curr Diab Rep 2002;2:135–40.
38. Ryan MC, Collins P, Thakore JH. Impaired fasting glucose tolerance in first episode, drug naive patients with schizophrenia. Am J Psychiatry 2003;160:284–9.
39. Lambert TJ, Velakoulis D, Pantelis C. Medical comorbidity in schizophrenia. Med J Aust 2003;178(9 Suppl):S67–70.
40. Sewell DD. Schizophrenia and HIV. Schizophr Bull 1996;22:465–73.
41. Cruess DG, Douglas SD, Petitto JM, et al. Association of depression, CD8+ T lymphocytes, and natural killer cell activity: implications for morbidity and mortality in Human immunodeficiency virus disease. Curr Psychiatry Rep 2003;5:445–50.
42. Mason SE, Miller R. Safe sex and first episode schizophrenia. Bull Menninger Clin 2001;65:179–93.

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