Important points

- Conditions included under the 'umbrella' term of mental illness are schizophrenia and bipolar disorder (manic depression)
- The genetic basis is an inherited predisposition to develop the condition

The schizophrenias

- The chance that anyone in the population will develop schizophrenia is about 1% (ie. 1 chance in 100)
- Where there is a family history, risks for family members of developing schizophrenia increase with the number of affected relatives and their degree of relatedness
- Symptoms include psychotic episodes; there may also be disorganisation of thoughts and feelings and social withdrawal
- It is likely that several different genes are involved, perhaps causing susceptibility to different forms of schizophrenia. Several genes have been identified to date
- The environmental factors that trigger the condition remain unknown but may include pregnancy complications and problems during delivery, recreational drug use such as cannabis and methamphetamine (also called *speed* or *ice*)

Bipolar disorder

- Formerly called manic depression, it is a disorder of mood and is characterised by major mood swings: generally fluctuating from 'high mood' (mania) to 'low mood' (depression)
- The chance that anyone in the population will develop bipolar disorder is about 2-3% (ie. 2-3 chances in 100)
- Where there is a family history, risks for family members of developing bipolar disorder increase with the number of affected relatives and their degree of relatedness
- There are several forms of bipolar disorder characterised by the severity of the depression and/or mania Several different genes are thought to be associated with bipolar disorder in different families
- The environmental factors that trigger the condition are still largely unidentified
- **Predictive genetic testing is not available to determine if a family member is at risk of developing schizophrenia or bipolar disorder**
- Currrently risks for developing the condition are based on data collected on many families.

A number of conditions that affect the way a person thinks, feels and acts are grouped under the 'umbrella' label of mental illness. Most mental illnesses can be treated.

The conditions include:

- Depression
- Anxiety
- Personality disorders
- Schizophrenia
- Bipolar disorder (manic depression)

The chance that anyone in the population will develop a form of mental illness such as schizophrenia and bipolar disorder during a their lifetime is

- 1 or 2 in100 (1% - 2%)
- The same regardless of socioeconomic level, occupation, ethnicity, culture and intelligence
- Higher than the general population risk where there is a family history of these mental illnesses

Recent research has highlighted the genetic basis of some forms of schizophrenia and manic depression.

This Fact Sheet deals only with the genetic basis of these two forms of mental illness.

The schizophrenias

Just as the term mental illness is an 'umbrella' for a number of different conditions, the term 'schizophrenias' is used because there is likely to be a number of different conditions under this 'umbrella'.

There is a wide variety of symptoms and not all people diagnosed with the condition always exhibit all the symptoms which usually first appear in late adolescence or early adult life.

Symptoms always include a psychotic episode(s) that include losing touch with reality, hallucinations, delusions, and paranoia. They may also include disorganisation of thoughts and feelings and social withdrawal.

Clues to the genetic basis of schizophrenia

Many studies have demonstrated that schizophrenia can run in families.

The evidence that heredity plays a role in the development of some forms of schizophrenia has come from studying identical twins and other family situations.

- If an identical twin (monozygotic twin) develops schizophrenia, then the chance that the other twin will also develop it is 1 chance in 2 ie. 50% (see *Table 58.1)*
- This genetic involvement has been confirmed by studying identical twins who were raised separately (therefore not sharing the same environment) as well as studying adopted children of mothers with schizophrenia
- Risks for family members of developing schizophrenia increase with the number of affected relatives and their degree of relatedness (see *Table 58.1*)

Inherited predisposition and schizophrenia

Our genes, that are part of chromosomes, provide the information for our bodies to grow and develop, and to work properly throughout our life (see Genetics Fact Sheet 1). When the information in the genes is changed in some way, the information sent to the cells may be different.

Inherited predisposition means that a person has inherited from a parent one or more gene copies containing variations in the information that do not cause a problem directly.

Affected relative	Risk for developing the condition (%)	
	Schizophrenia	Bipolar disorder
No close relative (general population risk)	1	2-3
Identical twin (monozygotic)	40-50	70
Both parents	45	50
Brother/sister and one parent	15	20
Parent	13	15
Non-identical twin (dizygotic)	10	20
Brother/sister	9	13
Second-degree relative	3	5
First cousin	1-2	2-3

Table 58.1: *Approximate familial risks in schizophrenia and bipolar disorder for close blood relatives of an affected person (not related by marriage). [Second degree relatives: aunts, uncles, nephews, nieces or grandparents]*

However, it makes them more susceptible ie. at increased risk, for developing the condition later in life when particular environmental factors that trigger the condition are present (see Genetics Fact Sheet 11).

Genes

Research is continuing and some progress is being made into identifying gene(s) in which changes may increase an individual's risk of developing schizophrenia.

- It is likely that several different genes are involved, perhaps causing susceptibility to different forms of schizophrenia
- In some families, there may be genes that have a major effect on the risk of development of schizophrenia. For example, changes in the following genes have been associated with the development of schizophrenia
  - A gene that contains the information for a protein called *dysbindin*, located on the short arm of chromosome 6 (6p)
  - A gene that contains the information for a protein linked to neurotransmitters called *neuroregulin*, located on the short arm of chromosome 8 (8p)
  - A gene that contains the information for a protein designated as G72, located on the long arm of chromosome 13 (13q)
  - Genes in an area on the long (q) arm of chromosome 22 (22q)

It appears that there is also an increased risk for having a child affected by schizophrenia at some time in their life if their father was aged over 50 when they were born.

Environmental factors

Twin studies show that genes are not the only factor influencing the development of schizophrenia.

- Where one twin of a non-identical twin pair (dizygotic twins; fraternal twins) develops schizophrenia, there is only about a 15% chance or 15 chances in 100 that the other twin will also develop the condition
- While this is higher than for the general population who have about 1 chance in 100 (1%) of developing the condition (see *Table 58.1*), it suggests that environmental factors are involved and interact with a genetic susceptibility

The environmental factors are still largely unidentified but research suggests that they may include pregnancy complications and problems during delivery and recreational drug use such as cannabis and methamphetamine (also called *speed* or *ice*).

Bipolar disorder

Bipolar disorder, which used to be referred to as manic depression, is a disorder of mood and is characterised by major mood swings.

- A person with the condition will experience periods of intense activity (termed *mania*) and other periods of feelings of hopelessness (termed *depression*)
- The mood swings appear to occur spontaneously, without any obvious external cause. The pattern of 'highs' and 'lows' can occur repeatedly with little or no breaks between each episode or may occur periodically between long periods when the person shows no symptoms There are several forms of bipolar disorder including:
- *Bipolar disorder type 1* (classical form of the condition) in which affected individuals develop extreme forms of mania, lose touch with reality, often become psychotic and have delusions and hallucinations. This condition is quite severe and often leads to hospitalisation
- *Bipolar disorder type 2* is characterised by a milder form of mania (termed *hypomania*). While the individual with this condition can have periods of extreme excitability, have excessive energy, often lose their inhibitions and have impaired judgment, they do not experience hallucinations nor do they become psychotic

There are not such major differences in the symptoms of depression between the two types of the condition but it is important to note that it is estimated that about 10% of people with the disorder do not experience the depression and just express the mania.

As for schizophrenia, many studies have shown that bipolar disorder can run in families.

Clues to the genetic basis of bipolar disorder

The evidence that heredity plays a role in the development of some forms of bipolar disorder has come from studying identical twins and other family situations.

- If an identical twin develops bipolar disorder, then the chance that the other twin will also develop it is 40%-70% or approximately a 1 chance in 2 (see *Table 58.1*)
- This genetic involvement has been confirmed by studying identical twins who were raised separately (therefore not sharing the same environment) as well as studying adopted children of mothers with schizophrenia

Genes, inherited predisposition and bipolar disorder

The genetic contribution is likely to interact with other factors such as environmental influences to trigger the condition.

Genes

The evidence for the exact role of genetics in bipolar disorder is still accumulating. Genes thought to be associated with bipolar disorder in different families are located on several different chromosomes.

- A gene called *Fat,* located on chromosome 4, which has an important role in the brain. People with a variation in this gene appear to be at twice the risk of developing bipolar disorder, though it is not yet clear exactly why
- Variations in a gene called *Slynar*, located on chromosome 12, which is also active in the brain but of unknown function
- Variations in a gene located on the long (q) arm of chromosome 18 (18q) have also been linked to bipolar disorder type 2

Environmental factors

Heredity is not the only factor influencing the development of bipolar disorder.

- Where one twin of a non-identical twin pair (fraternal twins) develops bipolar disorder, there is only about a 20% chance or 20 chances in 100 that the other twin will also develop the condition
- While this is higher than for anyone in the general population who has about 2-3 chances in 100 of developing the condition (see *Table 58.1*), it suggests that other environmental factors are involved, and interact with a genetic predisposition

These environmental factors however, are still largely unidentified.

Is predictive genetic testing possible to determine if a family member is at risk of developing schizophrenia or bipolar disorder?

Genetic testing is not available.

It will still be some years before it is possible to translate these findings into being able to predict who in a family is at increased risk for developing these forms of mental illness, when one or more family members have the condition.

Currently risks for developing the condition are based on data collected on many families (see *Table 58.1*).

Genetic counselling can assist in providing current information about the genetic basis of the condition to the family so that risks for the condition in other family members can be estimated correctly (see Genetics Fact Sheet 3).

Other Genetics Fact Sheets referred to in this Fact Sheet: 1, 3, 11

Information in this Fact Sheet is sourced from:

Austin J. (2005). Schizophrenia: an update and review. *Journal of genetic counselling* 14; 329-340

Barlow-Stewart K, Emery J, Metcalfe S. (2007). Psychiatric conditions. In: *Genetics in Family Medicine: the Australian Handbook for General Practitioners.* NHMRC Available from http://www.nhmrc.gov.au/your-health/egenetics/health-practitioners/genetics-family medicine-australian-handbook-general-prac [Accessed Nov 2012].

Crow TJ. (2007). How and why genetic linkage has not solved the problem of psychosis: review and hypothesis. *American Journal of Psychiatry*, 164: 13-22

Marcheco-Teruel B, Flint TJ, Wikman FP, Torralbas M, et al. (2006). A genome-wide linkage search for bipolar disorder susceptibility loci in a large and complex pedigree from the eastern Part of Cuba. *Am J Med Genet*, 141B:833-843

McMahon, F. J. et al. (2001). Linkage of Bipolar Disorder to Chromosome 18q and the Validity of Bipolar II Disorder. *Arch. Gen. Psychiat*. 58: 1025-1031

Mental Illness Fellowship of Australia. Fact Sheets [online]. Available from: http://www.mifa.org.au/fact-sheets [Accessed Oct 2012]

National Organisation for Rare Disorders (NORD) [online]. Available from: http://www.rarediseases.org/. [Accessed Nov 2012]

Online Mendelian Inheritance in Man, OMIM. McKusick-Nathans Institute for Genetic Medicine, Johns Hopkins University (Baltimore, MD) and National Center for Biotechnology Information, National Library of Medicine (Bethesda, MD) [online]. Available from:http://www.ncbi.nlm.nih.gov/omim/. [Accessed Oct 2012]

Owens MJ (2012) Implications of Genetic Findings for Understanding Schizophrenia *Schizophrenia Bulletin 38:904-907.*

Edit history

November 2012
Author/s: A/Prof Kristine Barlow-Stewart
Previous editions: 2007, 2004, 2002, 2000, 1998, 1996, 1994
Acknowledgements previous editions: Bronwyn Butler; Prof John Emery; A/Prof John MacMillan ; A/Prof Sylvia Metcalfe; Prof Phillip Mitchell; Gayathri Parasivam; Mona Saleh

