

## The mental health of people with Prader Willi Syndrome with a specific focus on psychotic illness

Prader-Willi Syndrome (PWS) is a complex genetic condition involving a range of physical, mental health and behavioural characteristics. This factsheet has been prepared for people with PWS, families of people with PWS and for others who provide support. In the factsheet the risks for a specific mental illness, referred to as '*psychosis*' or '*psychotic illness*', and its presentation, course and treatment, are considered. You may wish to share this with your General Practitioner or others.

The problem is often that when an illness develops, it is not identified, and therefore the most appropriate and effective treatments, which can be started once the diagnosis is made, are not offered. In this factsheet some background information is given before the specific relationship between PWS and psychotic illness is considered, as this is necessary to fully understand the relationship between psychotic illness and PWS.

### The genetics of PWS

There are three main genetic causes of PWS: a deletion at a specific site on the copy of chromosome 15 inherited from the father (deletion sub-type); inheritance of both copies of chromosome 15 from the mother, as opposed to one from each parent (the uniparental disomy or UPD sub-type); and a very rare form referred to as an 'imprinting centre defect'. These account for approximately 70%, 25% and less than 5%, respectively of people with PWS.

### The behavioural characteristics of PWS

Whilst people with PWS are all individuals and will vary in the nature and extent of their needs, research has identified specific characteristics that are particularly common in people with PWS. Of these the over-eating behaviour (hyperphagia) is the best recognized, with its origins in early childhood and the risk of severe obesity if access to food is not controlled. A tendency for temper outbursts, repetitive and ritualistic behaviours (sometimes referred to as obsessive compulsive behaviours), and skin picking may also be apparent. To varying degrees, this cluster of problem behaviours commonly affect people with PWS regardless of the exact genetic cause and are referred to as 'the behavioural phenotype' of PWS – the term 'phenotype' meaning the outward manifestation of a syndrome of genetic origin.

### The mental health of people with PWS

In addition to an increased propensity to the above behaviours, people with PWS may experience significant anxiety, particularly at times of change in routine, and may also have periods of low or elevated mood, sometimes presenting with evidence of depression or 'hypomania' or 'mania'. Depression is more than unhappiness and is characterized in general by periods of being low in mood, sometimes tearful and irritable and is usually associated with a deterioration in sleep pattern, sometimes a reduction in appetite (although not common in people with PWS) and a significant loss of interest in things that he/she would normally have enjoyed. Hypomania (a less severe form of mania) is characterised by increased activity and energy, sometimes excessive talking with a tendency to move from one topic to another and to

grandiosity and again to irritability. If these variations in mood between high and low repeat over time this is referred to as a bipolar disorder. Where a person's mood is either elevated or low then this may also increase the likelihood of the above problem behaviours – for example skin picking may become worse with depression.

These 'mood disorders' (also referred to as 'affective disorders') tend to develop in the teens and into adult life and they can also affect people with PWS of all genetic sub-types.

Psychotic illness (or psychosis) refers to illnesses that are characterised by the emergence of abnormal mental beliefs and experiences – for example, delusional ideas that people are going to harm you or to influence you in some way; or hallucinations, such as hearing voices, usually from outside of the head talking to you or commenting on your thoughts. Sometimes hallucinations can be visual or even tactile – seeing objects or people who are not there or feeling things on your skin that don't exist. These are very real to the person experiencing them and often frightening. There are other features that can occur, such as the sense that your thoughts are being influenced, or it may appear to others that the person's thoughts have become muddled – referred to as 'thought disorder'.

In the case of people with PWS there is also sometimes confusion and a sense of bewilderment – those affected may be uncertain as to where they are or the time, day, or month. Some forms of psychotic illness (particularly those that are related to abnormal mood) can fluctuate over time with changes over days or weeks. It is these changes in mood and the onset of abnormal mental beliefs and experiences that is referred to by the term 'mental state' and which are characteristic of psychotic illness. Psychiatric assessment in such circumstances will involve a systematic assessment of a person's mental state by specifically asking about the presence or absence of the above mental phenomena. Sometimes the person may not be willing or able to describe the abnormal mental experiences they are having, but it becomes apparent through odd comments they make or how they behave.

The two main psychotic illnesses affecting the general population are schizophrenia or bipolar disorder – in the case of the latter the disturbance of mood, as described in the earlier paragraph, is also associated with the presence of abnormal mental beliefs and experiences. In the case of people with PWS the manifestations of psychotic illness do not quite fit the recognized characteristics of either of these two disorders, although it is generally considered to be closer to the mood related form of psychotic illness than it is to schizophrenia.

Psychotic illness can affect people with the deletion form of PWS, but it most commonly affects people with the UPD or the imprinting centre defect form of PWS. Approximately 60% of people with PWS due to UPD may develop a psychotic illness by early adult life. There is some uncertainty about the most likely age of onset, with research in one country suggesting that the main risk is in the teenage years and research in the UK suggesting it is in the late teens and early adult life. It is clear, however, that psychotic illness can develop as early as the teenage years.

## **Diagnosis of psychotic illness in people with PWS**

Psychotic illness develops during life and it is the observation of marked changes in a person's behaviour and their 'mental state' that should alert you to the possibility that such an illness may be developing. There is limited research at present, but in general it would appear that the onset of the psychotic illness can be fairly rapid and in some cases over a matter of hours, although this will vary and, for some, the onset may be more insidious. Families have reported that it may be triggered by stress, which could, for example, be due to some a change in routine (change in accommodation, admission to hospital) or a minor infection - but this is not always the case.

Previous and perhaps longstanding behaviours common in people with PWS, such as temper outbursts, skin picking or repetitive and ritualistic behaviours, may become more frequent or change in severity when someone with PWS becomes mentally unwell.

Fully characterizing the likely presenting features of psychotic illness in people with PWS still needs more research but these early features may include a more rapidly fluctuating mood; the development of erratic and bizarre behaviours; and the presence for the first time of abnormal mental beliefs or experiences, which are apparent in the content of the person's speech. Sometimes the person may appear confused and unaware of his/her surroundings. If someone with PWS develops such problems a detailed assessment by the General Practitioner is indicated and referral to a psychiatrist. This is likely to be a specialist psychiatrist in the local learning disability services but could also be to general psychiatric services. The process that then should follow is a detailed history from those people (usually family) that have observed the changes and an assessment of the person him or herself as to the characteristics of the changes that have been observed and whether there is evidence of abnormal mental beliefs or experiences, which would indicate the possible presence of a psychotic illness. One important and, at times, difficult aspect of assessment is checking whether the person with PWS is feeling like harming or killing him/herself. This is of greatest concern where a person has depression and, in that context, is feeling hopeless and he/she may feel others are better off without him or her. If the person has made specific plans as to how he/she might harm him/herself action needs to be taken to ensure that cannot happen. This may include continuous supervision and/or admission to hospital.

Particularly if confusion or disorientation is present, it is important to consider whether or not the mental changes might be due to physical illness that has caused a confessional state (sometimes referred to as delirium). If, for example, there were physical symptoms such as a complaint of pain or a history of recent vomiting, then urgent physical assessment is required as such complaints are rare in people with PWS and are most commonly due to a physical illness. This initial process of assessment leads to what is often described by the term 'differential diagnosis' - i.e. developing a list of possible causes which are then narrowed down through further history taking and examination and, if necessary, investigations. It is arriving at the diagnosis and an understanding of all other relevant factors that informs the final formulation and treatment plan.

### Key Points

1. Psychotic illness is a form of mental illness that may develop in late childhood or early adult life.
2. Psychotic illness more commonly affects people with PWS due to UPD or those with PWS who have an imprinting centre defect.
3. Psychotic illness not uncommonly presents rapidly but can develop more insidiously with a marked deterioration in mood and behaviour and the emergence of abnormal mental beliefs and experiences such as hallucinations and delusions, and sometimes confusion.
4. The onset of such changes in a person's mental state and behaviour requires assessment to eliminate other possible causes. If the development of a psychotic illness is confirmed, effective treatments are available.

## Treatment of psychotic illness in a person with PWS

Treatment can be divided into the immediate, short-term, and longer term. In the immediate situation urgent advice from the General Practitioner and the specialist learning disabilities or general psychiatric services is indicated. Once a diagnosis of psychotic illness has been arrived at, it is important to ensure that the person is safe – is their behaviour putting themselves or others at risk? Might they harm themselves? Are they eating and drinking sufficiently?

How such situations are managed will critically depend on the support network and the nature and extent of a person's problem behaviours.

Occasionally, if there is only very limited support available where the person is living and the person has self-harmed or is expressing ideas of self-harm, admission to hospital may be necessary. The immediate response is therefore to ensure the person's safety through support and supervision and to start medication that is known to be helpful in the case of psychotic illness.

Where the diagnosis is psychotic illness, hypomania or mania, medications referred to as antipsychotic medications or major tranquillizers have been shown, in people without PWS, to improve mood and reduce the distressing abnormal mental state that the illness has given rise to. These medications appropriately used for treating such illnesses are effective and help to 'normalize' the person's mental state, reducing the nature and extent of the hallucinations and delusions and improving any confusion. Systematic evaluations of such treatments for psychotic illness in the general population are considerable, but for people with PWS, who have developed a psychotic illness, the research is limited. However, what research there is suggests that the outcome of treatment for psychotic illness is good.

There is an increasing range of medications available and, as with any form of treatment, the potential benefits need to be balanced against possible risks of side effects. These medications are not for treating 'behaviour', rather they are for treating a diagnosed psychotic illness, and as the psychotic illness improves with treatment so will any associated deterioration in typical PWS behaviours return to how they were prior to the onset of mental illness. Behaviours (such as temper outbursts) that existed before the onset of the psychotic illness will not go away – these will require the types of approaches described in other guidance. Because of atypical brain development there are uncertainties in people with PWS about their sensitivity to medications whose action is on the brain (psychiatric medications act on chemical or neurotransmitter systems and their receptors in the brain), so the advice is to start these medications at a lower than normal dose and build the dose up carefully over time depending on the clinical response. Certain medications in this group, such as olanzapine, are to be avoided as they can increase appetite and in the general population are associated with weight gain. It would be for the General Practitioner or psychiatrist to determine which medication to use. At present risperidone and aripiprazole are among the commonest of the antipsychotic medications to be used.

Where there is evidence of a low mood and clear evidence of depression, antidepressants, especially those in the SSRI group that also help treat anxiety, may be appropriate. Again, they should be used cautiously starting with lower than normal doses and increasing carefully. Where there is evidence of mood fluctuations and/or psychotic experiences, a combination of antipsychotic and anti-depressant medications, or medications that have been shown to stabilise the mood (such as lithium, carbamazepine, sodium valproate) may be indicated.

## Key Points

1. Treatment of psychotic illness should be preceded by a detailed history and examination leading to an understanding and an accurate diagnosis, eliminating other possible causes of the deterioration.
2. In an immediate situation, assessment and support should focus on ensuring that the person is safe, and if feeling suicidal he/she is supported and possible risks identified and managed.
3. Psychiatric medications (particularly the class of drugs referred to as anti-psychotics or major tranquillizers) will need to be given to treat the person's abnormal mental state. The exact medications chosen will depend primarily on the diagnosis.
4. Once the mental state is stabilised and the person is returning to his/her normal state, the medication regime should be regularly re-evaluated to ensure that benefits of the treatment are being maintained and that any side effects are minimised.
5. In the longer term, it is important to maintain food security, and to provide structured and meaningful opportunities for the person with PWS, and to ensure that those providing support are aware of his/her previous illness, so if it occurs again it will be recognised and treatment started.

## Final points

The development of a mental illness such as a psychotic illness is difficult for all concerned. Not uncommonly the person affected doesn't understand that they have developed an illness and may therefore be unwilling to accept treatment. Sometimes, where someone is very mentally unwell, and particularly if there are concerns about risks to themselves or to others, the Mental Health Act is used to bring someone into hospital without his/her consent in order to provide close supervision and to ensure that he/she takes treatment in the form of medication. Once a person's abnormal mental state begins to improve he/she may gain some insight and accept the help that is being offered, and it becomes easier, and concerns about risk and about the person's behaviour diminish.

Mental illnesses can take different forms, and how such illnesses present and their subsequent course may vary. It is important to work closely with local services to gain knowledge about what is right for the particular person with PWS, and through observation and support, to determine over time whether on-going psychiatric medication is needed and, if so, what the optimum dose is; and also to ensure that the right support plan is in place to make certain there is a full recovery and a return to a good quality of life.

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