

# Anti-Psychotic Medication

## Introduction

The first anti-psychotic drug, chlorpromazine (Largactil), was discovered by accident in 1952. A group of drugs, the phenothiazines, were being investigated for their anti-histamine properties when an anaesthetist noticed they had a calming effect and made patients indifferent to what was going on around them. Subsequent testing on psychotic and manic patients showed that these drugs had a marked anti-psychotic effect. There are three main categories of anti-psychotic drugs-the first generation of drugs, the depot injections and the newer atypical drugs.

## First generation of anti-psychotic drugs

These drugs were the mainstay in the treatment of psychotic illness from the mid fifties onwards and were the first type of medication that were effective in the treatment of schizophrenia. Their use led to a revolution in psychiatry allowing the eventual emptying of long stay hospital wards and greatly improving the quality of life for people suffering from schizophrenia and other related illnesses. Although these drugs reduced the symptoms of psychosis they were not effective in every case and have a large number of side-effects which often leads to poor patient compliance.

### The first generation of drugs in use include:

Generic name	Trade name	Usual dosage range
Chlorpromazine	Largactil	75-400mg
Flupenthixol	Depixol	3-10mg
Perphenazine	Fentazin	5-30mg
Sulpiride	Dolmatil	200-1000mg
Trifluoperazine	Stelazine	5-30mg
Haloperidol	Serenace	3-30mg
Pimozide	Orap	2-20mg

Please note that the given dosages are a guide only and psychiatrists may use other dosages.

## Mode of action

There are over 100 different types of neurotransmitters in the brain. Anti-psychotic medications mainly block the receptors for the transmitter dopamine but they also interact with other transmitter systems in the brain. The extent of receptor blockage and the type of receptor blocked varies between the different anti-psychotic drugs. The ability of this type of drug to interact with the dopamine system in the brain led to the dopamine hypothesis of schizophrenia. This theory postulated that schizophrenia was due to overactivity of the dopamine mechanism in the brain but it is now realized that this is a gross oversimplification and many other factors are implicated. Anti-psychotic drugs have the effect of dampening down an overactive brain.

## Uses of anti-psychotic medication

Anti-psychotic drugs are used in the treatment of schizophrenia, schizoaffective disorder and the manic phase of bi-polar disorder. There are three main types of symptoms of schizophrenia. Positive symptoms include hallucinations, delusions and other thought disorders. Negative symptoms that may be present are apathy, lethargy, social withdrawal and poverty of thought, action and speech. Cognitive symptoms affect the ability of a patient to concentrate, solve problems and to tackle complex tasks. The first generation of drugs are effective in reducing positive symptoms in most cases but are not so good at treating negative symptoms. It is claimed that atypical medication is better at tackling the negative aspects of schizophrenia than the traditional drugs. Most patients respond to medication though a few patients will not show any improvement. The drugs are not a cure and often have to be taken for many years.

## Atypical anti-psychotic drugs

The atypical anti-psychotics are listed below.

Generic name	Trade name	Usual dosage range
Clozapine	Clozaril	400-600mg
Amisulpiride	Solian	400-800mg
Olanzapine	Zyprexa	10-30mg
Risperidone	Risperdal	1-6mg
Zotepine	Zoleptil	75-300mg
Quetiapine	Seroquel	400-600mg
Aripiprazole	Abilify	

It should be noted that the given dosages are only a guide.

The atypical anti-psychotics are a fairly recent development. The range of side-effects experienced by patients taking these drugs is often less than with first generation drugs. The first generation drugs can cause movement disorders and stiffness (see side-effects section below) but this not generally the case with atypicals. The atypicals are better tolerated than the older drugs often leading to better patient compliance. Olanzapine has been found to have a mood stabilizing effect and is used in the treatment of bi-polar disorder and schizoaffective disorder. This dual action of olanzapine means that often a separate mood stabilizer does not have to be prescribed for such patients.

The choice of drug depends on the patient and a drug that suits one person may not suit another. It is up to the skill of the psychiatrist to find the most appropriate drug. A newly diagnosed schizophrenic is usually prescribed an atypical drug. A patient on a first generation drug may be considered for transfer to an atypical depending on the side-effects that they are experiencing and their response to their existing medication. Atypicals are expensive drugs and should be used when they will have maximum benefit.

Aripiprazole is the latest drug to be introduced for the treatment of schizophrenia. It has a different mode of action to the existing drugs in so far as it tends to activate dopamine receptors rather than block them. It is too early to evaluate whether aripiprazole is a significant advance in the treatment of psychotic illness.

Clozapine was introduced as a treatment for schizophrenia some years ago but was withdrawn due to its side-effects. It was found to have a detrimental effect on the body's white blood cells and in some cases this proved to be fatal. However, it has now been reintroduced and has been found to be effective, particularly in cases which are resistant to other drugs. It is only prescribed in controlled conditions and regular blood tests are essential - initially every week - so the drug can be withdrawn if the white blood cells are being badly affected.

## Depot injections

These are long acting formulations of anti-psychotic drugs, which are administered every 1-4 weeks by intramuscularly injection. These injections are useful for patients who do not like taking oral medication or for other patients who have a history of non compliance with oral medication and may therefore suffer a relapse into psychosis. As a community psychiatric nurse usually gives the depot, it provides an opportunity for the nurse to regularly monitor the patient's progress. As of yet no atypical drug has been formulated as a depot and all the drugs that are used in depots are first generation.

The following are the main depot injections that are available:

Generic name	Trade name	Usual dosage range
Flupenthixol	Depixol	50-300mg 1-4 weekly
Zuclopenthixol	Clopixol	100-600mg 1-4 weekly
Haloperidol	Haldol	50-200mg 4 weekly
Fluphenazine	Modecate	12.5-100mg 2-4 weekly
Pipothiazine	Piportil	50-200mg 4 weekly

It should be noted that the given dosages are only a guide.

A short acting formulation of zuclopenthixol (Acuphase) is available as an injection and is given to patients in the acute stages of a psychosis. Its effect lasts 48-72 hours and it often speeds up recovery.

## Good practice in the prescription of anti-psychotic medication

In the past there has been a tendency to prescribe high dosages of anti-psychotics: so called mega doses. However, there is no evidence that high dosages are any more effective as once a certain level of medication is reached it will have no further therapeutic action and often leads to extremely unpleasant side-effects. There is usually no need to prescribe more than one anti-psychotic at any one time (polypharmacy). The aim should be to prescribe the minimum dosage that will have a therapeutic effect and guard against any relapse into psychosis. With moderate medication patient compliance tends to be much better.

## Side-effects of anti-psychotic medication

Anti-psychotics have a wide range of side-effects although most of them are uncommon and often a patient will only experience one or two of these side-effects.

## Movement disorders

These may occur with first generation anti-psychotics but are far less common with atypicals:

- Akinesia manifests itself as stiffness and difficulty in movement.
- Dyskinesias include tremor and abnormal movements, such as 'treading grapes', which used to be a common sight in psychiatric wards.
- Dystonia gives rise to abnormal muscle tone and spasms of the muscles of the jaw, face and eyes.
- Tardive dyskinesia is a long term side-effect of the first generation drugs and involves repetitive and involuntary movements of the tongue and mouth. It is often irreversible and is a serious side-effect.
- Akathisia is a restlessness which may make it impossible for a patient to stay in one place for very long. It may also take the form of nervousness and extreme agitation and it is often difficult to distinguish from the symptoms of the illness.

These movement disorders respond to treatment with an anti-cholinergic drug such as procyclidine (Kemadrin) or orphenadrine (Disipal), which are routinely prescribed with first generation anti-psychotics. There is some evidence that anti-cholinergics may make tardive dyskinesia worse once it has started. It is not routine to give a patient taking an atypical anti-psychotic an anti-cholinergic drug.

### **Common side-effects**

Most anti-psychotics cause some sedation though this will vary from drug to drug. Weight gain often occurs and in the case of olanzapine and clozapine this gain may be quite marked: in the region of 5kg or more. It is important to monitor the weight, to eat a sensible diet and to take regular exercise. Other side-effects include dry mouth, constipation and blurred vision particularly with high dosages.

### **Other side-effects**

These drugs can cause hormonal changes and there may be changes in the periods of female patients. Olanzapine causes changes in carbohydrate metabolism and this may also occur with some of the other drugs. There may also be minor changes of the rhythm of the heart though they are not clinically significant. Sexual dysfunction and skin rashes have also been reported.

Photosensitization is a very common side-effect with chlorpromazine and great care has to be taken to avoid unprotected exposure of the skin to strong sunlight. It may help to use a sunscreen. Unprotected skin will quickly burn and give rise to a very unpleasant sensation similar to prickly heat.

### **Interactions and precautions**

Alcohol, barbiturates, pethidine, morphine and benzodiazepines increase the sedative side-effects of anti-psychotics. Co-administration of lithium and chlorpromazine may significantly reduce the blood levels of chlorpromazine. When anti-psychotics are taken with anti-depressants the blood levels of both drugs will be increased. Oral contraceptives can increase the movement disorders caused by first generation anti-psychotics.

It is not clear the effect that these drugs have on the foetus during pregnancy but great care needs to be taken and the risks to the developing foetus balanced with the mental stability of the mother. The drugs may be present in breast milk. Great care also needs to be taken in the operation of machinery and when driving as anti-psychotics can impair alertness and reaction times.

### **Conclusions**

Anti-psychotic drugs are effective in the treatment of schizophrenia, schizo-affective disorder and bi-polar disorder. However, they don't always eliminate all the symptoms and in a few cases the patient response to medication may be very poor. Atypicals tend to be better tolerated than the first generation of drugs and this usually improves patient compliance. Atypicals have fewer side-effects and are better at treating the negative symptoms of schizophrenia. There are drugs in development with different modes of action to the currently used drug and the coming years may see their introduction.

It is not advisable to suddenly stop taking anti-psychotic medication, as a relapse into illness is a high probability. If medication is to be withdrawn it should be gradual and under medical supervision. It may be necessary to take these drugs for a long period, possibly years.