



Antipsychotics

This Factsheet aims to give an overview of the use of **antipsychotic** drugs as a treatment for mental illness, including the biological explanation for their function, evidence on their effectiveness, and the potential downsides to their use. Words in bold are defined in the glossary, and the worksheet allows the opportunity to practice what you have learned.

The examiner expects you to be able to:

- Name some common antipsychotic drugs,
- Know the difference between conventional and atypical antipsychotics,
- Explain the effects of antipsychotics on the brain,
- Evaluate the use of antipsychotics with regards to their effectiveness,
- Discuss the downsides of their use, including side effects and ethical issues.

Exam Hint: Make sure to check the specification of the exam board you are studying to know exactly what you are required to know. Antipsychotic medication is a required component of the schizophrenia topic for both AQA and WJEC/Eduqas. OCR and Edexcel require knowledge of one “biological treatment” for mental illness, of which antipsychotics would be an appropriate choice.

Antipsychotic medication is primarily used to treat schizophrenia.

A. Introduction

Before the development of antipsychotic medication, treatment options for people diagnosed with **psychosis** and/or **schizophrenia** were limited. People diagnosed with severe mental illness were often locked away in asylums, and treated with **ECT** or even **psychosurgery**. Antipsychotics were first developed in the 1950s, and they started a revolution in the treatment of severe mental illness. Antipsychotics reduced symptoms of psychosis to such a great extent, that patients who were previously classed as incurable could be discharged from hospital.

Since the introduction of the first antipsychotic drug *Chlorpromazine* in 1952, many more antipsychotic drugs have been developed. These drugs can be broadly categorised into two types; conventional and atypical. The differences between the two are detailed later.

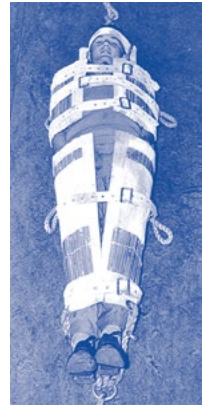
However, it should be noted that antipsychotics are not a one size fits all treatment. Due to reasons that we don't yet fully understand, different types of antipsychotics work better for some people than others. Also, the side effects (that in some cases can be quite severe) likewise vary from individual to individual. This is why there are so many different types of antipsychotics available. Finding the correct combination and dosage is often a case of trial and error. It is also worth noting that none of the antipsychotic drugs provide a cure for mental illness. However, many millions of people rely on antipsychotic medication to allow them to live a normal life.

Exam Hint: Although antipsychotics are not without ethical issues, one positive is the cultural shift they have brought about in the treatment of mental illness. This wider social and cultural effect is a valid point to make in an exam question.

Before antipsychotics, treatment options for people diagnosed with severe mental illness were limited.

B. Conventional (First Generation) Antipsychotics

The first antipsychotic medication widely used was *Chlorpromazine*. This drug was first made in the 1880s as a synthetic dye and then later used as an **antihistamine**. In 1952, it was used for the first time as an antipsychotic in a clinical trial. The initial results were astounding, reducing symptoms enough so that patients could be released from hospital. Chlorpromazine is a low potency drug; in other words, a large quantity of the drug has to be administered in order to gain the desired effect.



Later antipsychotics were generally higher potency, meaning that smaller doses are needed to get the same effect. *Haloperidol* is 50 times more powerful than Chlorpromazine. A higher potency drug means that a lower dose is needed. This will generally result in fewer and less severe side effects.

A final antipsychotic is *Fluphenazine*, which unlike the previous two antipsychotics is administered as an injection rather than pills taken orally. Often, schizophrenia is treated with Fluphenazine when the symptoms have been stabilised using other drugs.

C. Atypical (Second Generation) Antipsychotics

From the 1970s, newer, more effective antipsychotics have been developed. These tend to have fewer side effects, and they also tend to work much quicker than the conventional antipsychotics.

Clozapine was developed in the 1960s, but not widely used until the 1970s. Clozapine is one of the most effective antipsychotics; however, the potential side effects are very serious, and can be fatal. Therefore, it tends to be used as a last resort when other treatment options have failed. *Aripiprazole* is another atypical antipsychotic. This drug works in a slightly different way to the others described here (see section E: “Differences between conventional and atypical antipsychotics”). While generally quite effective, this drug often has the side effect of weight gain or issues with **motor control**.

Exam Hint: Being able to name specific antipsychotics in your answer would signal to the examiner that you have specific rather than general knowledge, and would add to the quality of your answer.



Most antipsychotics are taken as pills. Others, such as Fluphenazine, are injections

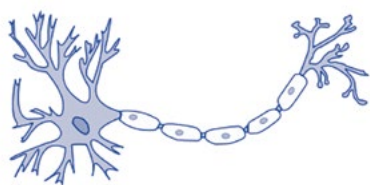


D. How They Work

Initially, the actual mechanism by which antipsychotics worked in the brain was largely a mystery. However, further research and an increased understanding of how the brain works has shed light on how antipsychotics reduce the symptoms of psychosis.

The brain is made of billions of cells called **neurons**. These neurons communicate with each other using chemicals called **neurotransmitters**. The gap between the **axon terminal** of the **presynaptic neuron** and the **dendrite** of the **postsynaptic neuron** is called a **synapse**. Neurotransmitters cross this gap from the axon terminal of one neuron to the dendrite of the receiving neuron. Here, the neurotransmitter attaches to specialised molecules called **receptor molecules**. This causes an electrical signal to be sent down the post-synaptic neuron.

The brain is made up of billions of cells called neurons



There are many types of neurotransmitter in the brain. The one that is important for understanding antipsychotics is **dopamine**. Previous research into schizophrenia has found evidence that the brains of individuals diagnosed with schizophrenia have much higher levels of dopamine than **neurotypical** controls. In broad terms, antipsychotics influence the functioning of the neurotransmitter dopamine in the brain.

Antipsychotics work by attaching to the dopamine receptor molecules on the dendrites of the post-synaptic neuron. This means that dopamine can no longer activate these molecules as the antipsychotic is blocking them. This means that antipsychotics work as a dopamine **antagonist**.

Initially, this blocking of the receptor molecule causes the axon terminal of the presynaptic neuron to release more dopamine into the synapse. However, over time, levels drop as dopamine reserves are exhausted.

There are different types of dopamine receptors in the brain. When discussing antipsychotics, the most important dopamine receptors are the D2 receptors that are found predominantly in the **limbic system**. This is a system of **subcortical** structures that are engaged in many functions, particularly emotions, memory and arousal. When antipsychotics block D2 receptors, it can reduce over-stimulation and may reduce some of the positive symptoms of psychosis such as delusions and hallucinations.

How antipsychotics work at the synapse

E. Differences between Conventional and Atypical Antipsychotics

While both conventional and atypical antipsychotics perform similar functions, there are some differences between them. Nearly all antipsychotics work as dopamine antagonists.



Antagonist drugs reduce the effect of dopamine all over the brain. This works great for areas of the brain where dopamine is too high, but in areas of the brain where dopamine levels are just right, it can reduce the levels of dopamine causing problems with motor control or weight gain.

The atypical antipsychotic Aripiprazole, however, is a partial **agonist**, and therefore works a little differently. In areas of the brain where dopamine is too high, it occupies the receptors, but only gives a partial response so that the result is reduced activity. But in areas of the brain where dopamine is too low, it acts to boost the levels of dopamine activity. This means that Aripiprazole is less likely to lead to weight gain.

Another difference is that while conventional antipsychotics only work by blocking dopamine receptors, atypical antipsychotics also block **serotonin** (specifically the 5-HT_{2A}) receptors in specific parts of the brain too. Blocking these serotonin receptors actually has the effect of increasing dopamine levels in these areas, cancelling out the drop in dopamine caused by the D2 dopamine receptors being blocked. Many of the side effects of antipsychotics are caused by dopamine levels falling in parts of the brain where they need to stay stable. This means that atypical antipsychotics tend to have fewer side effects as levels of dopamine stay relatively stable in much of the brain.

Another key difference is that atypical antipsychotics tend to occupy the dopamine receptors for a shorter time than conventional antipsychotics. This means that the desired effect (reduced dopamine) is achieved, but the blocking of the receptors does not last long enough to cause side effects.

Exam Hint: You need to know about and be able to describe the differences between conventional and atypical antipsychotics. Being able to state that atypical antipsychotics tend to have fewer side effects is good, but being able to explain the neurochemical reasons why is even better.

F. Side Effects

One of the downsides to all antipsychotics is that they often come with side effects. These side effects can range from mild to life threatening. For some individuals, the side effects may be so unbearable that they are worse than the symptoms they were trying to eradicate. Common side effects are:

- Tardive dyskinesia: involuntary repetitive movements of the body, commonly in the mouth and tongue, but also the limbs and eyes.
- Parkinsonism: reduced motor control leading to tremors in the hands, slowness of movement and problems with balance.
- Agranulocytosis: a potentially fatal drop in white blood cells. This is a specific risk of Clozapine; patients on this medication must have regular blood checks.
- Weight gain: an issue particularly with atypical antipsychotics. This weight gain can lead to secondary issues such as high blood pressure and diabetes.

Exam Hint: While the side effects of antipsychotics can be serious, they need to be balanced against the reduction of psychotic symptoms. A discussion of this cost-benefit analysis could be a good evaluation paragraph.

Weight gain is a common side effect of antipsychotics.



G. Effectiveness

A number of studies have been conducted that have investigated the effectiveness of antipsychotics. Most research focused on their use as a treatment for schizophrenia.

- Cole et al. (1964) found that 75% of patients given one of the earliest conventional antipsychotics showed improvement, compared to only 25% of those given a **placebo**. Additionally, of those given the antipsychotic, none showed a worsening of symptoms, compared to 48% of the placebo group who did.
- Ravanic (2009) compared the long-term effectiveness of conventional and atypical antipsychotic medication. He found that the atypical antipsychotics produced much better outcomes for patients, and also produced fewer side effects.

However, while antipsychotics may produce dramatic reductions in psychotic symptoms, the side effects may put patients off the drug, reducing adherence to the medication. There is also the issue that due to the nature of psychosis, without supervision, patients will not take the drugs. Patients diagnosed with schizophrenia may be hospitalised, medicated, and then discharged from hospital. However, there is a risk that the patient stops taking their medication, becomes ill again, and then is readmitted to hospital. This is often referred to as “revolving door psychiatry”.

There may be many reasons why an individual diagnosed with schizophrenia may not adhere to their medication (**non-compliance**): the side effects may be unbearable; they may feel “normal” and no longer sick, so they feel that they no longer need to take their medication; they may be unable to plan their own behaviour and so forget to take their medication; they may be suffering from paranoid or persecutory delusions, and so do not trust the medication or the person issuing it; or they may lack insight into their illness, and not be aware that they are sick

- Lobos (2010) compared Clozapine with a number of other atypical antipsychotics and found that it fared very favourably in reducing the positive symptoms of the illness, but that the risk of serious side effects caused many patients to drop out of the study.
- Valenstein et al. (2004) performed a huge study on over 63,000 patients diagnosed with schizophrenia taking antipsychotic medication, and found that in about 40% of cases, adherence to the regime was poor (meaning that they missed doses, or refused to take their medication). The only drug where this was not a problem was Clozapine that had only 4.6% of patients showing poor adherence. This is possibly because patients on Clozapine have to have weekly blood checks, meaning that they come into regular contact with medical professionals who can encourage adherence.

This means that we need to be careful when drawing conclusions from the results of clinical trials where compliance to medication is strictly regulated. In the real world, the actual level of effectiveness may be hampered by non-compliance.

It should also be noted that the evidence here does not take individual differences into account. Psychosis and schizophrenia are complex and their causes are not fully understood. Some antipsychotics work better for some people than others. The findings from studies into the effectiveness of these drugs can give us an idea of the overall trends in terms of which drugs tend to work, but they tell us little about which drugs will work for a specific individual.

Exam Hint: When presenting research findings into the effectiveness of antipsychotics, it is important to address the issue of non-compliance that can hamper the validity of the findings.

In reality, many people who take antipsychotics have low compliance.



H. Ethical Issues and Social Implications

One of the greatest strengths of antipsychotics comes from the fact that many millions of people rely on them to live relatively normal lives. Before their discovery, many people diagnosed with mental illness had limited options for treatment or care. **Institutionalisation** was common. However, there are millions of people today who are able to live productive lives, raise families, and have careers due to antipsychotic medication. The impact that antipsychotics had on treating psychosis has been compared to the impact that penicillin had on the treatment of infection.

Antipsychotics are not only a benefit to the individuals themselves, but to society. The cost of antipsychotic medication is much lower than the cost of institutionalisation. As the NHS has limited funds, any treatment that provides value for money means that more money is available for other patients. However, it needs to be acknowledged that antipsychotics are not without risk or side effects. For example, patients may gain weight, leading to diabetes; this would then require further treatment that would cost the NHS money.

While it cannot be denied that antipsychotics have revolutionised the treatment of people diagnosed with severe mental illness, they are not without ethical issues. One issue is that of consent. People diagnosed with psychosis can often not give fully informed consent to taking antipsychotics due to the nature of their illness. This decision may be made for them by next of kin, or medical professionals. This denial of bodily autonomy for people diagnosed with psychosis is an issue as it could be argued that they are being denied free will. On the other hand, perhaps the benefits to the patients outweigh this violation of free will, and to do nothing to reduce their symptoms could be argued to be worse.

Another issue is that of control. The antipsychiatry movement of the 1960s argued that antipsychotic medication was not being used to ease the suffering of people diagnosed with mental illness, but to make them easier to control and conform to society's view of normality. What if the patient was not actually suffering due to their schizophrenia? Would it be right to force them to take medication against their will?

Compliance to medication may be a prerequisite of release from a psychiatric institution. This means that a patient may be readmitted to hospital against their will if they stop taking their medication. This, again, is an issue of free will. Bearing in mind the serious side effects, it could be argued to be unethical to force people to take medication that they do not want to.

A final issue is that antipsychotics only provide a treatment, not a cure. Since antipsychotics have been hugely successful in reducing the symptoms of psychosis, it could be argued that there is less of an interest in finding a cure for illnesses such as schizophrenia. Individuals diagnosed with schizophrenia will usually have to stay on antipsychotics for the rest of their lives without any hope of a cure. Bearing in mind the potential side effects, is this ethical?

Exam Hint: Any evaluation of the ethics of antipsychotics should include both positive and negatives. While there are many ethical issues with their use, the huge social change they have brought about cannot be denied, and this should be reflected in your answer.

Are antipsychotics used to ease the suffering of people diagnosed with psychosis, or to make them fit in with society?



Glossary

Agonist: A drug that blocks the receptor molecule, and activates it in place of the usual neurotransmitter.

Antagonist: A drug that blocks the receptor molecules, preventing the neurotransmitters from binding to them.

Antipsychotic drug: A family of drugs first developed in the 1960s as a treatment for psychosis, particularly schizophrenia. **Antihistamine:** A medication used to treat allergic reactions.

Axon terminal: The end of the long axon of a neuron where neurotransmitters are released.

Dendrite: The short, branch-like extensions of a neuron that receive chemical messages from other neurons. It is where you will find receptor molecules.

Dopamine: A neurotransmitter found in the brain. It has many functions and uses.

ECT: Electroconvulsive shock therapy – a therapy where a low electric current is applied to the brain in order to create an epileptic-like seizure.

Institutionalisation: Enforced hospitalisation for severe mental illness. Sometimes done without the consent of the patient in extreme cases.

Limbic system: A system of interconnected structures in the brain. Primarily involved with the processing of emotion and memory.

Motor control: The ability of the brain to be able to control the movement of the body.

Neuron: Cells that make up the brain, spinal cord, and nervous system.

Neurotransmitter: A chemical in the brain that allows neurons to communicate with each other.

Neurotypical: Individuals with no sign of mental illness or impairment.

Non-compliance: The failure of a patient to adhere to a medication regime.

Placebo: A fake drug given in clinical trials.

Psychosis: A severe mental disorder where an individual loses touch with reality.

Psychosurgery: A therapy that involves the destruction of organically healthy brain matter in order to treat a mental illness.

Receptor Molecule: A protein molecule that receives chemical messages in the form of neurotransmitters from outside of the cell.

Presynaptic neuron: The cell before the synapse.

Postsynaptic neuron: The cell after the synapse.

Schizophrenia: A mental illness characterised by hallucinations, delusions and a variety of other symptoms. Typically, the individual has lost touch with reality.

Serotonin: A neurotransmitter found in the brain. It has many functions and uses.

Subcortical: Regions in the brain that are found underneath the top layer of cortex.

Synapse: The gap between the axon terminal of one neuron, and the dendrite of another.

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Worksheet: Antipsychotics

Name _____

1. Explain two differences between conventional and atypical antipsychotic medication.

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2. Write a paragraph to explain how antagonist antipsychotics work in the brain. Use the following terms in your description:

- a. Receptor molecule
- b. Dopamine
- c. Dendrite
- d. Axon terminal
- e. Synapse

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3. One big issue with the use of antipsychotics is that of non-compliance.

Explain what this means and why this may be an issue when assessing how effective antipsychotics are.

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4. Explain one benefit and one drawback to the NHS of using antipsychotics to treat schizophrenia.

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5. Explain why the lack of free will is an issue when using antipsychotics to treat people with severe mental illness.

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