# Mental health

## Introduction

This tutorial isn't intended to be an in-depth review of mental health disorders and the drugs used to treat them, it's more of a guide to the commoner questions that you may encounter and tips on how to answer them. Because we're focusing on frequently asked questions, this tutorial only discusses antidepressants and antipsychotics; for guidance on drugs used in other disease states such as bipolar disorder, anxiety and insomnia refer to the information sources (below).



One in four people in the UK will experience a mental health problem each year. The frequency of some conditions such as depression is commonly expressed as the number of new cases annually (the incidence). For other conditions, such as schizophrenia, the frequency is given as the risk over a patient's lifetime (their lifetime prevalence). Mixed anxiety and depression is the most common problem affecting nearly 10 people in every 100, each year. Personality disorders are also common, affecting between 3 to 5 people in every 100 over their lifetime. For statistics on other mental health conditions, MIND have a really clear summary and help on interpreting the figures.

To understand the impact of developing a mental health disorder upon patients' lives, you may like to listen to a psychiatric nurse discussing his own depression, or to a patient describing his bipolar disorder and the importance of medicines in managing it. You can also read a mother's experience of postnatal depression.

# 1. Swapping between antidepressants

Swapping between antidepressants is often a difficult balance of minimising the risk of a drug interaction while ensuring that the patient has adequate levels of antidepressant on board during the period of changeover. Interactions may be pharmacodynamic or pharmacokinetic in nature.

- **Pharmacodynamic** interactions may arise if the two antidepressants act upon the same neurotransmitter(s). For example swapping between two agents that increase serotonin levels can lead to 'serotonin syndrome': it is usually rapid in onset, occurring within the first few doses of the second drug. Fatalities have been reported.



- **Pharmacokinetic** interactions may arise through effects on cytochrome p450. For example, some of the SSRIs are potent inhibitors of CYP2D6, which is involved in the metabolism of tricyclic antidepressants. Concomitant use can lead to tricyclic toxicity.

  The inhibition of CYP2D6 can persist for some time after stopping an SSRI, so an interaction with a tricyclic antidepressant is still possible even when an SSRI has been discontinued.

  To avoid such interactions, cross-tapering regimens are sometimes recommended. However these aren't always appropriate – for example if the patient is suffering a severe adverse reaction, then the causative antidepressant should be discontinued immediately.

For further information on swapping between antidepressants, including cross-tapering regimens, refer to the information sources (below).

## 2. Swapping between antipsychotics

Questions about swapping between antipsychotic drugs occur less frequently than for antidepressants, but they present similar problems with regard to interactions and loss of symptom control. Several strategies have been proposed and are outlined clearly in information sources (below) such as Bazire's *Psychotropic Drug Directory* and *The Maudsley Prescribing Guidelines* and so will not be repeated here. Studies comparing these techniques are lacking, so when recommending a strategy consider:

- The **individual patient** concerned (e.g. the indication for switching, ability to manage a complex cross-tapering regime if being treated at home, their clinical condition).

- The **medicines** involved (e.g. risk of interactions, side effect profile, half-life, risk of discontinuation symptoms).



## 3. Stopping psychiatric medicines



Most antidepressants have been reported to cause a 'discontinuation syndrome' when stopped abruptly or if a few doses are missed. It is important to realise that the majority of patients are not affected. However, paroxetine and other drugs with a short half-life seem particularly likely to cause the problem. Note that the term 'withdrawal' is less preferred by some experts due to its association with drugs of abuse.

Symptoms usually appear within a few days of discontinuing therapy and they are often mild and self-limiting. For example, sudden discontinuation of paroxetine can cause dizziness, sensory disturbances (electric shock sensations), sleep disturbance, agitation or anxiety, nausea, tremor, confusion, sweating, headache, diarrhoea, and palpitations. For some patients, these reactions may be severe and long-lasting, making it difficult to stop treatment.

If left untreated, symptoms should resolve within several days to weeks, but may be minimised by slowly tapering the drug over about 4 weeks. An exception to this rule is fluoxetine which when taken at doses of 20mg per day or less may be stopped abruptly, although higher doses require tapering. Regardless of this, all antidepressants should be stopped abruptly if they are suspected of causing a serious side effect (e.g. an arrhythmia).

A discontinuation syndrome may also occur in neonates born to mothers who have been taking antidepressants close to delivery.

Questions about stopping antipsychotics completely are less common, but the same principles of tapering apply, to avoid discontinuation symptoms and a relapse or rebound of the patient's symptoms.

## 4. Restarting psychiatric medicines

You might be asked about when and how to restart psychiatric medicines after a temporary discontinuation, such as if the patient has suffered a serious side effect, taken an overdose or been non-compliant.

For some medicines, the product manufacturer gives specific advice (e.g. clozapine) but in most cases such guidance is lacking. In these situations, you will usually need to consider the clinical condition of the patient, the length of time the patient has been without therapy, and the side effect and pharmacokinetic profile of the medicine. A patient who has been without medication for more than a few days may need to be initiated on therapy again 'from scratch'.




For example, you might be asked about a patient with schizophrenia who has forgotten to take their quetiapine for a week. Re-starting the patient on a dose similar to their old maintenance dose seven days ago risks side effects such as postural hypotension because the amount of drug left in the system will be low. However, if you treat the patient with the low doses usually used to initiate therapy it will take longer to control the patient's symptoms. You will need to balance safety (side effects and ability to monitor patient) versus his clinical condition (severity of symptoms, dangers to himself and others). Where you set this balance will be affected by where the patient is being treated (e.g. home *vs* inpatient).

# 5. Choosing psychiatric medicines

You may quite often be asked to help choose the right medicine to treat a mental health illness. The diverse range of unwanted effects that psychiatric drugs can have, and their potential to interact with other medicines, means that the choice is not always straightforward.

Their side effect profile can make treatment choice difficult in many patient groups including those with heart disease and epilepsy, and in women who are pregnant or breastfeeding. The potential drug interactions are many; common scenarios include the use of antidepressants in patients taking serotonergic agents such as the triptans or tramadol, and combining medicines that are known to prolong the QT-interval. As with any long-term treatment, patients need to be aware of the perceived benefits and risks and involved in the decision-making process if they are able. Refer to the Information sources, below, for treatment recommendations in all these special populations.

**Mental Health Case Study**

***Lucy is a 27-year-old woman who suffered a stillbirth 6 months ago after unexpectedly falling pregnant. She sits and weeps for long periods of time and has been unable to talk to anyone about how she feels. Although her mother is alive and well, she lives 200 miles away. She currently lives with her husband.***

***Lucy suffers from epilepsy and currently takes sodium valproate. Investigations suggest that valproate was unlikely to have caused the stillbirth.***

***Her appetite is poor, she has lost 2 stones in weight and she sleeps poorly, often awakening at 4am thinking how cruel the world is and how she might as well end it all. She cannot cope with her job as a nursing assistant and is not looking after her home or doing any cooking. She constantly argues with her husband who thinks that enough time has passed now and she should be able to get back to work.***

1. What do you think might be Lucy's diagnosis?
2. What aspects of her story made you think this was her diagnosis?

***Lucy visits her GP and is prescribed amitriptyline 50mg at night for a month. Four days later she is admitted to an acute psychiatric ward following an attempted overdose. She has no past psychiatric history.***

3. Comment on the appropriateness of the prescription.
4. Which antidepressant would you recommend for Lucy and why?
5. What events in her life may be causing or exacerbating her condition?
6. How might you encourage compliance with a new antidepressant treatment regimen?

***When you've considered answers to these questions, read on to see some suggested answers.***

## Mental Health Case Study Suggested answers

**1. What do you think might be Lucy's diagnosis?**
Depression
Differential diagnosis of postnatal depression.

**2. What aspects of her story made you think this was her diagnosis?**
Low mood
Suicidal ideation
Reduced and interrupted sleep
Not looking after herself
Weight loss
Symptoms for more than two weeks

**3. Comment on the appropriateness of the prescription.**
Not appropriate as Lucy has epilepsy: tricyclics decrease the seizure threshold, amitriptyline being the most convulsive.
Tricyclics are also toxic in large doses, e.g. overdose.
Furthermore, there is an interaction to consider. Amitriptyline levels are increased by valproate, and the pharmacokinetics of valproate can be affected by amitriptyline.

**4. Which antidepressant would you recommend for Lucy, and why?**
You could choose an option such as sertraline or citalopram due to lack of interactions with anticonvulsants, and they are less likely to reduce seizure threshold.
For the same reasons, mirtazapine might be an appropriate second choice should Lucy not respond to sertraline/citalopram or be intolerant of side effects.

**5. What events in her life may be causing or exacerbating her condition?**
Recent pregnancy.
Loss of baby.
Husband not supportive.
Mother lives over 200 miles away.
? Co-morbidity (epilepsy).
? Social circumstance (needs help at home, feels isolated)

**6. How could you encourage compliance with an appropriate treatment regimen?**
Involve her husband in the treatment plan.
If you have the opportunity to counsel Lucy you could educate her about antidepressant treatment, including: onset of 4 weeks to action; need to continue for at least 6 months after recovery if first episode; possible withdrawal effects if stop suddenly.

# 6. Managing side effects

You may be asked for advice on how to manage side effects in patients taking psychiatric medicines. Compared to other therapeutic areas, the medicines used in mental health are particularly likely to be linked to groups of related adverse effects or syndromes, rather than individual complaints. For example, certain antipsychotics can cause well-established patterns of extrapyramidal side effects. These are characterised by movement disorders such as:

- Acute dystonia (involuntary muscle contraction).
- Akathisia (increased restlessness often in lower limbs, feeling of 'unease' and irritability).
- Parkinsonism (bradykinesia, tremor, rigidity).
- Tardive dyskinesia (involuntary movement including myoclonic jerks, tics, chorea and dystonia).

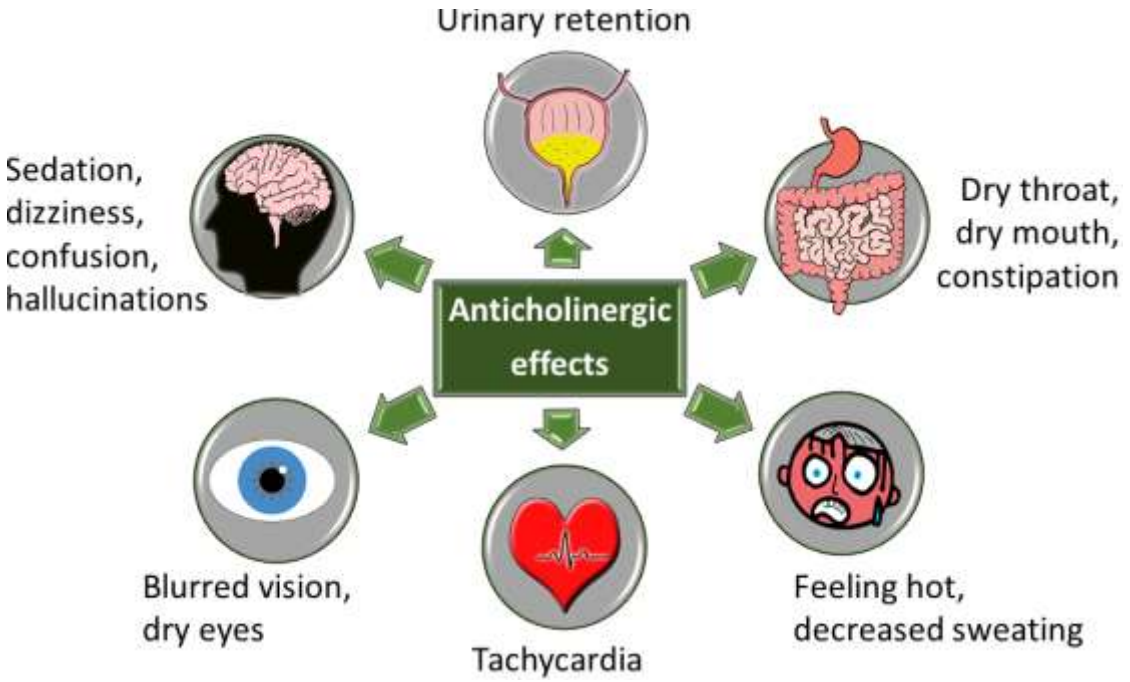
If some of these terms are unfamiliar to you, there are US videos describing **acute dystonia**, **akathisia**, and **tardive dyskinesia** that may help you. They describe the presentation of these conditions, but the treatments and terminology sometimes represent US rather than UK practice.

Another example of a group of related adverse effects is the **Syndrome of Inappropriate AntiDiuretic Hormone** secretion (SIADH). Antidepressants, antipsychotics and carbamazepine are amongst the many medicines that can stimulate the over-secretion of antidiuretic hormone which causes significant fluid retention, resulting in hyponatraemia. This triggers symptoms such as weakness, weight gain, cramps, vomiting and anorexia. It can lead to confusions, coma and death so it's important to pick this problem up early.

## Anticholinergic burden

Many medicines have anticholinergic side effects, also known as antimuscarinic effects, which are additive when more than one of these types of drug is taken together. Mental health medicines such as tricyclic antidepressants, many antipsychotics, and procyclidine can all cause these symptoms, as well as medicines used for non-mental health reasons such as hyoscine, oxybutynin, carbamazepine, and older antihistamines like chlorphenamine.

Acetylcholine is a neurotransmitter that mediates activities such as peristalsis, bladder emptying, slowing of the heart, saliva production, control of body temperature, and focusing of the eye. It is also found in the brain where, amongst other actions, acetylcholine helps alertness, concentration, and learning. Given the widespread role of acetylcholine in controlling basic body functions, medicines with anticholinergic properties can cause a broad range of side effects. Many of these anticholinergic side effects are summarised in the infographic below:




As you can see, anticholinergic side effects are numerous and quite diverse, and they may present in ways which make a drug-related cause not immediately obvious. The dizziness and sedation due to these medicines may cause **falls** in the elderly, for example, and dry mouth may contribute to **dental decay**. Importantly, anticholinergic medicines may also contribute to the development of **cognitive impairment** and symptoms of **dementia** in older patients. For these reasons, anticholinergic medicines must be used with care in the elderly and avoided when possible.

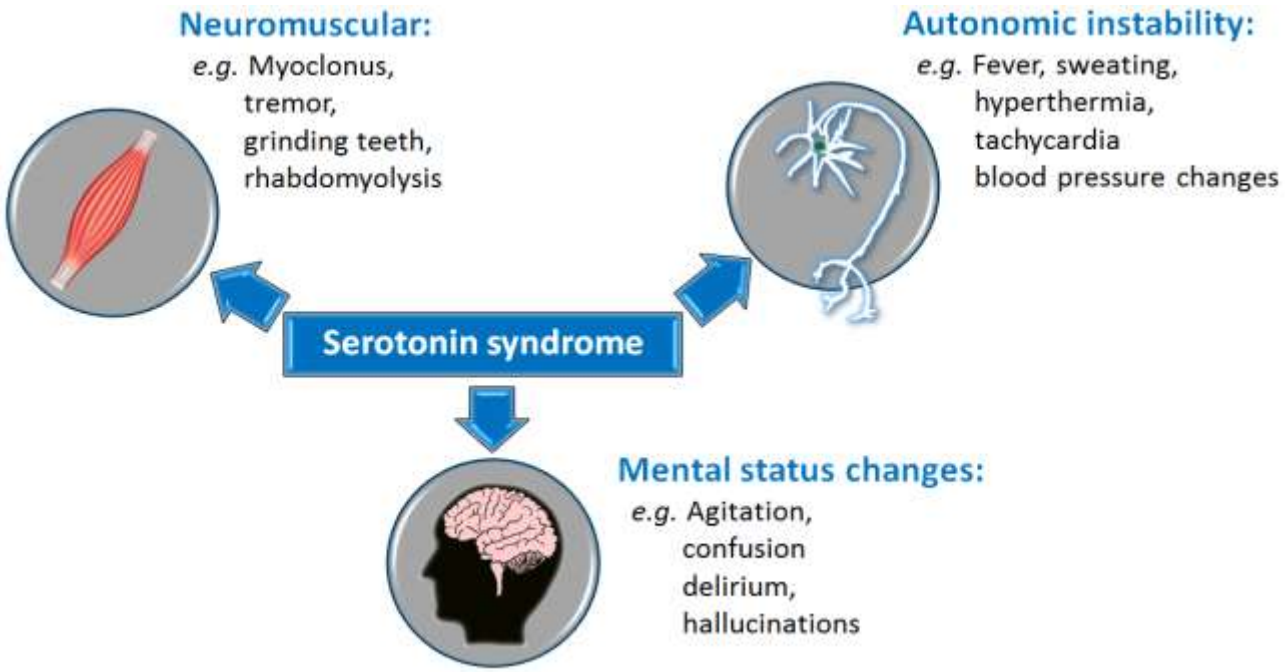
Two UK websites allows you to calculate an **anticholinergic burden score** for individual patients by estimating the ability of all their medicines to block the actions of acetylcholine. Take a look at one or both of these now: ACB Calculator and Medichec.

*[Last updated: 09 January 2020]*

We have also written a short, separate tutorial on managing the side effects of anticholinergics medicines. It's intended for clinicians in primary care setting, but it's a good way to refresh your knowledge of this important topic.

## Serotonin syndrome

Medicines that boost the activity of serotonin can cause this syndrome, often when two or more are taken together but sometimes when large doses of a single serotonergic medicine are taken. The medicines causing serotonin syndrome include most antidepressants, St John's Wort, tramadol, triptans, pethidine, and lithium. The resulting excess of serotonin causes a range of symptoms affecting muscles, mental state, and the autonomic nervous system as illustrated below:




Serotonin syndrome shares many symptoms in common with the **neuroleptic malignant syndrome** which, as its name suggests is caused by neuroleptic medicines. Whilst the serotonin syndrome is caused by pro-serotonin medicines, the neuroleptic malignant syndrome is caused by dopamine antagonists. This can be an important way of differentiating between the two syndromes as they both can cause symptoms such as sweating, tachycardia, and changes in mental state. Another important difference is that serotonin syndrome tends to cause muscle spasms (clonus), whilst neuroleptic malignant syndrome typically presents with extreme muscle rigidity.

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At this stage of your career, you're not expected to remember all the details of the various syndromes that we've presented in these pages, but it is important to be aware that they may occur and to be on the alert for patterns of side effects when caring for patients who take medicines for mental health.

*[Last updated: 09 January 2020]*

# Suggested questions

The diverse range of clinical problems in patients with mental health conditions means that it's not possible to provide a shortlist of suitable questions to ask when problem solving. However, if you are being asked to recommend the preferred choice of therapy for an individual patient, then two particularly helpful questions are:

- Ask the prescriber what he or she would usually use.
- Find out whether the patient has tried anything before, and if it was successful and/or tolerated.

This will give you a starting point for problem-solving and help to rule out less clinically appropriate options.

Other tutorials on this site such as the questions sections on Adverse reactions or Interactions may help you in certain circumstances. Of course, you'll want to check the patient's drug history and medical history, and if you're being asked about use of a specific medicine you'll need the indication, dose, frequency, route of administration and expected duration of treatment. So, our guide to general questions to ask when problem solving may also help you.

# Information sources

The Maudsley Prescribing Guidelines and Bazire's Psychotropic Drug Directory are both excellent reference handbooks that cover the most commonly asked questions (e.g. swapping and stopping antidepressants, drug choice in special patient groups). Updated frequently, they are normally amongst the first resources to check if you're not sure where to look. You may have access to the e-book of the The Maudsley Guidelines at your hospital, but the Psychotropic Drug Directory is not available online or in electronic form. They both have lots of practical tips.



NICE Evidence Search will signpost you to specialist psychiatry resources such as the Royal College of Psychiatrists and the British Association of Psychopharmacology, as well as more general guidance from NICE and SIGN. Use the Clinical Knowledge Summaries for evidence-based reviews of how to manage common mental health conditions such as depression, insomnia, and obsessive-compulsive disorder.

There are some UKMi **Medicines Q&As** on commonly encountered scenarios (e.g. depression in mothers who are breastfeeding, and using antidepressants in patients with epilepsy). Access them through the SPS website.

Check whether you have any local guidelines or speak to your clinical experts.

# Next steps in learning...

If you have an interest in mental health and caring for patients who suffer from psychiatric illness, then consider joining the College of Mental Health Pharmacy. It's an opportunity to make contact with colleagues with similar interests, share expert resources, receive training, and keep up-to-date.

BMJ Learning has a range of e-learning around mental health. Click on the 'Browse by speciality' tab then select 'Psychiatry'.

The MHRA has a series of e-learning modules on psychiatry drugs including antipsychotic drugs, SSRIs and benzodiazepines.

CPPE has a number of resources to support your learning and practise in mental health that you can find by entering 'mental health' into the search box on any page of the CPPE website.

In collaboration with the Royal Pharmaceutical Society, the CPPE have also written several medicines optimisation briefings and articles, including: Schizophrenia medicines optimisation briefing and article; Depression medicines optimisation briefing and article