

Guide to Stopping Antidepressants (Symptoms on Stopping Antidepressants)

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Stopping antidepressants

Dependence on and withdrawal from imipramine, the first tricyclic antidepressant was reported in 1959. It had only been introduced in 1958. It now seems highly likely that the effects on stopping imipramine stemmed from its serotonin reuptake inhibiting ability.

As of 2014, close to 10% of the population of most Western countries are on antidepressants more than 50% of whom are likely to be hooked on them.

This guide focuses on SRIs. SRI stands for serotonin reuptake inhibitor. SSRIs are selective SRIs but selective does not mean these drugs are pharmacologically “clean”. It means that they have no effects on the norepinephrine /noradrenaline system.

Over-Potent SRIs	Brand Names
Citalopram	Celexa, Akarin, Celapram, Celius, Ciazil, Cipramil, Cipram, Cimal, Citabax, Ciprapine, Citalec, Citol, Dalsan, Cilift, Recital, Emocal, Sepram, Seropram, Citox, Cital
Desvenlafaxine	Pristiq
Duloxetine	Cymbalta, Ariclam, Xeristar, Yentreve, Duzela, Dulane
Escitalopram	Lexapro, Cipralex, Seroplex, Esertia
Fluoxetine	Prozac, Fluctin, Fludac
Fluvoxamine	Luvox, Fevarin, Faverin, Dumyrox, Favoxil, Movox, Floxyfral
Paroxetine	Paxil, Seroxat, Sereupin, Aropax, Deroxat, Divarius, Rexetin, Xetanor, Paroxat, Loxamine, Deparoc
Sertraline	Zoloft, Lustral, Serlain, Asentra, Tresleen
Venlafaxine	Effexor, Efexor
Vortioxetine	Brintellix

Less Potent SRIs	Brand Names
Amitriptyline, Clomipramine Dosulepin, Doxepin, Imipramine Diphenhydramine Chlorphenamine	Elavil, Tryptixol, Lentizol Anafranil Prothiaden Sinequan, Zonalon Tofranil Benadryl Chlorphen, Actifed

There are other non-SRI antidepressants such as the monoamine oxidase inhibitors (MAOIs) and mirtazapine that also cause dependence and withdrawal. These problems differ from those caused by serotonin reuptake inhibitors. They remain less well characterized at the moment.

There are also a number of norepinephrine reuptake inhibitors like reboxetine, atomoxetine, bupropion, desipramine, nortriptyline, and protriptyline. Any problems these drugs cause are less in focus perhaps primarily because they are used much less often.

Prominent withdrawal symptoms

SRI withdrawal symptoms come in two forms - the unusual:

- Dizziness – “when I turn to look at something I feel my head lags behind”.
- Electric Head - strange “brain” sensations – “it’s almost like the brain is having a version of goose pimples”.
- Electric shock-like sensations – zaps – like being prodded with a cattle prod.
- Strange tingling or painful sensations.
- Muscle spasms/ tremor.
- Nightmares or other vivid dreams.
- Agitation.
- Hallucinations or other visual or auditory disturbances.
- Sensitivity to noises or visual stimuli, temperature, pain or mental stress.

And the all-too-usual that may lead your physician to think this is just the original problem:

- Depressive symptoms & anxiety feelings – the commonest withdrawal symptoms.
- Labile mood – emotions swinging wildly.
- Irritability and stress intolerance.
- Confusion.
- Fatigue/ malaise – flu-like feelings.
- Insomnia or drowsiness.
- Sweating.
- Feelings of unreality.
- Feelings of being hot or cold.
- Change of personality.

Other effects

Most of the serotonin in us is in our gut, blood stream, muscles and bones rather than our brains. So the entire body is affected by both the drugs and their stopping.

Stress effects

Antidepressants and other drugs are also a physical stressor on the brain and body. These stresses cause problems that endure after treatment is withdrawn – such as the tardive dyskinesia after antipsychotic withdrawal – see Page 13. A stress effect is something a person may ultimately bounce back from.

Legacy effects

Drugs including antidepressants can also cause damage and leave a legacy afterward. There is an increased risk of bone fractures for instance for years after. There are enduring eye problems. There is a risk of birth defects for months or perhaps longer after stopping.

Catastrophic effects

A small number of people have a severe “toxic” reaction to SSRIs with neurological and other features often starting within days of starting treatment. The after-effects may endure for months or years.

These drugs in the doses they are usually given are grossly overpowered. It’s like a huge articulated truck traveling down a stone-walled country lane.

- Some people have no problems on withdrawing.
- Some have minimal problems that peak after a few days before diminishing.
- Some have problems, which can be helped by the management plan outlined on Page 7.
- Some are unable to stop whatever approach they take.
- Some will have enduring problems after stopping.

For many the biggest problem once they start reducing is finding that there is no going back because a higher dose that worked before no longer works.

Withdrawal can last 6-12 months. If problems endure after this they are more likely to be legacy, or stress effects.

Is this withdrawal?

There are four ways to distinguish antidepressant withdrawal from any problem that might have led to treatment in the first instance.

1. If the problem begins immediately on reducing or halting a dose or begins - within hours, days or weeks - then it is more likely to be a withdrawal problem. If the original difficulties have cleared up and you are doing well, on discontinuing treatment no new problems should show up for several months or indeed years.
 2. If the nervousness or other odd feelings that appear on reducing or halting the SSRI (sometimes after just missing a single dose) clear up quickly when you are put back on the SSRI or the dose is put back up, then this also points to a withdrawal problem rather
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than the original illness. When original illnesses return, they take a long time to respond to treatment. A quick response to the reinstatement of treatment points to a withdrawal problem.

3. While withdrawal may overlap with features of any problem for which you were first treated - both may contain elements of anxiety and of depression. Withdrawal will also often contain new features not in the original state such as pins and needles, tingling sensations, electric shock sensations, pain and a general flu-like feeling.
4. If you are on a treatment and doing well but the treatment then stops working and you need more of the same drug to get the original benefit, you have likely become dependent and are at a greater risk of having withdrawal problems.

How to withdraw

Ideally your doctor will be on board – if not you may need to change doctors.

Many doctors suggest withdrawal by taking a pill every other day for a few weeks and then spacing them out further. There is no basis for this approach and it can make things worse.

In previous protocols, we suggested dropping half the dose at the start and a further half later before taking things more gradually. These jumps are too big.

The first step is to get a liquid formulation of your antidepressant. If need be demand your doctor specifies a liquid prescription. Your local pharmacist can source a liquid form of almost any drug– see Page 18. The problem may be your insurance coverage refusing to pay for a more expensive form of medication.

Two different theories about dependence and withdrawal dictate different approaches.

1. The Half-Life theory says the very short half-life of paroxetine and venlafaxine make these drugs more problematic. This leads to a withdrawal strategy that advocates switching from paroxetine or a long half-life drug like fluoxetine.
2. The Potency theory says paroxetine and venlafaxine are worse because they are more potent SRIs. This leads to a switch to less potent SRIs like imipramine or dosulepin.

Either approach is helped by having access to treatment in liquid form.

Tapering

a) **Simple taper**

Convert to a liquid form of the drug you are on. Reduce by a comfortable amount in weekly steps. This may mean reducing as little as 1 mg per week and being prepared to stop and stabilize if things get too difficult. Another approach is to reduce by 10% each week. For some people depending on the drug and their own physiology, there may be a need to go very slowly, others may be able to go faster.

b) **Reduced potency approach**

Switch to Imipramine or Dosulepin 100mg. Imipramine comes in 25mg and 10 mg tablets and also in liquid form. It is the first SRI. You could also combine half your dose of a potent SRI with 50 mg imipramine or dosulepin and then taper from the potent drug first.

c) **The half-life approach**

Convert the dose of SSRI you are on to an equivalent dose of fluoxetine liquid. Seroxat/Paxil 20mg, Effexor 75mg, Cipramil/Celexa 20mgs, Lustral/Zoloft 50mgs are equivalent to 20mg of fluoxetine liquid. Fluoxetine's long half-life helps to minimize withdrawal problems. But some people become agitated on switching to fluoxetine. This might be caused by fluoxetine or because the substitution does not cover withdrawal from their original drug. If the agitation improves as fluoxetine is reduced it is more likely to be caused by fluoxetine. You could also combine half the drug you were on with a half dose of fluoxetine. The next step is to reduce gradually the dose of the original drug and after that to reduce the fluoxetine.

Next steps

- a) Stabilize on one of these options for a few weeks or more before proceeding.
- b) If there are minimal problems reducing, it may be possible to go slightly faster than outlined here. If the original drop was difficult, the dose should be reduced by 1 mg amounts weekly or two weekly. A syringe is helpful in reducing the dose evenly.
- c) Withdrawal doesn't always get worse at every step down. There are shelves – points where there are difficulties after which it can be easier again. If things get difficult, wait at that stage for a longer period before reducing further. At times like this, contact with someone else who knows what is involved can be helpful.

Withdrawal complexities

Destabilization

For some people, withdrawal can destabilize systems. If they run into problems on the way down and try to put the dose back up they find that a dose that worked before or an even higher dose no longer works. It can become impossible to get back to equilibrium leaving the person intensely uncomfortable without any way to alleviate their distress.

Psychotherapy

Withdrawal and dependence are physical phenomena. Even totally normal people given SSRIs for 2-3 weeks can have anxiety and depression when they try to stop. This anxiety or depression will not respond to traditional psychotherapy or cognitive therapy – we need a specialized therapy that take the physical reality of withdrawal into account.

But if you become anxious, you will be hyper-vigilant. You might notice you have a bad reaction to some food or other medication and figure you must steer clear of this. Some people get phobic particularly if the experience is literally shocking.

We don't know enough to say that people can't become allergic to food and other things. It is possible you can become both properly allergic and phobically allergic. Hypnosis or NLP may help some; an appropriate cognitive or behavior therapy may help others.

Self-help support groups can be invaluable. Join one. If there is none nearby, consider setting one up. There will be lots of others with a similar problem.

One hazard of withdrawal is becoming emotional again, as the numbing effect of SSRIs lifts. Many people or their partners are very frightened by this.

Detoxification

For some people on treatment for years, their drug may get captured in adipose tissue and leak out slowly over the course of a year or more causing problems as it does.

Leakage like this may contribute to a risk of birth defects even in those off the drug for months. But it is not clear how much of a withdrawal problem it could cause if only because withdrawal can happen after only a few weeks on treatment, and leakage should alleviate withdrawal by smoothing out drops in blood levels.

The idea of a stored drug gives rise to attempts at detoxification. At present there is nothing we know of that reliably detoxifies more speedily than just the passage of time.

Treatments for difficult withdrawal

Rhythm adjustment

We do not know what causes enduring antidepressant withdrawal. It may be nothing to do with serotonin. Similar problems happen on antipsychotics and benzodiazepines

All these drugs affect cell rhythmicity also. They can affect heart rhythms and cause the heart to simply stop. This effect may be linked to calcium channel blocking. No one knows for sure. In this case it might be possible to substitute a calcium channel blocker for an SRI and stop withdrawal happening this way.

The best known calcium channel blocker is verapamil. This has been used successfully in some withdrawal cases but it may just postpone withdrawal until verapamil is stopped. If so, the quality of life on verapamil is better than on an SSRI.

Reducing hyper-vigilance

Many people complain of temperature dysregulation on stopping an SSRI. This might be because of actual temperature dysregulation or because of hyper-vigilance.

People who complain of feeling cold and later hot, when checking their body temperatures against that of a friend often find that both have much the same fluctuations but the person in withdrawal is more aware of the problems.

A hyper-awareness of bodily functions like this comes from the Locus Coeruleus nucleus. This brainstem nucleus is also hyperactive in opiate withdrawal, where it is managed very successfully with clonidine or lofexidine.

Lofexidine in a dose of 0.2mg QDS is used for opiate withdrawal. We are trying a lower dose, 0.2mg BD, in SSRI withdrawal.

Clonidine in a dose of 0.025mg (25 mcg) BD is another option. The side effects of both are a drop in blood pressure with dizziness, a slow heart rate and a dry mouth.

The Locus Coeruleus Nucleus monitors for dangers. When you spot a tiger in the jungle, the LCN primes you to fight or flee. But the LCN is in fact much more attuned to things going on inside you than on the outside. This is why you want to empty your bowel or bladder when you feel anxious even though you just did so a few minutes earlier.

Having said this, SRI dependence and withdrawal does involve real bowel disturbances from diarrhea through to food intolerance that are difficult to see just as a vigilance problem and there is much more serotonin in the gut and muscles than anywhere else.

Stabilizing the histamine system - 1

The SRIs are a group of antihistamine drugs that also inhibit serotonin reuptake. Despite marketing propaganda, they are not selective or clean drugs.

One way to manage withdrawal might be to switch to an SRI antihistamine such as chlorphenamine or diphenhydramine. These are less potent SRIs and switching to them is a way to slowly reduce the dose.

A related option here is to switch to a tricyclic antidepressant such as dosulepin which is also an antihistamine with less potent serotonin reuptake inhibiting properties.

The best way to think about this is that the SSRIs are like sports cars that can pick up pace incredibly quickly but a car like this isn't needed in a town or a city. The amount of serotonin and reuptake inhibition from dosulepin or chlorphenamine is all that is really needed for most situations.

There are other antihistamines that do not inhibit serotonin reuptake such as loratadine or cetirizine that might be useful if withdrawal comes more from histamine than serotonin.

Stabilizing the histamine system - 2

A further option on the antihistamine front is to view serotonin withdrawal as a histamine over-activity (semi- allergic) state brought around by the fact that the person has been on antihistamines chronically.

One of the ways to damp down histamine over activity is to use a mast cell stabiliser such as sodium chromoglycate. Sodium chromoglycate (Nalcrom) is used extensively for people with food intolerance – a complaint that many people with SRI withdrawal have.

The histamine system can be further damped by adding a H2 receptor blocker such as cimetidine or ranitidine.

Cinnarizine is an antihistamine that is also a calcium channel blocker.

Pregnancy

The key group in all of this are women of child-bearing years. Many pregnancies are unplanned and several weeks advanced before the woman is aware of the situation. SSRIs are now clearly linked to an increased frequency of birth defects, of miscarriages, premature birth, low birth weight, and withdrawal and pulmonary hypertension in newborn infants.

SRI may also be linked to increased rates of autistic spectrum disorder, ADHD, and learning disabilities in children born to mothers on them through pregnancy.

One of the biggest problems of SRI dependence involves women who are on treatment and unable to stop who wish to become pregnant. Getting off an SRI at present seems more difficult for women than men, even with the incentive of wishing to become pregnant.

Although more women on antidepressants have perfectly normal babies than have babies with problems, nine months of worrying can have a bad effect on a mother and on the later relationship between mother and child.

Companies have known about these issues for decades. The first reports of problems date to 1972. And for centuries farmers have kept livestock out of fields in which the SRI “weed”, St John’s wort, grows because of the risk of spontaneous abortion.

Physiological basis for SSRI dependence

Many people after stopping SRIs complain that other drugs can trigger a “relapse”. These reports may link to a feature closely related to dependence and withdrawal.

Ketamine has recently been reported as producing dramatic benefits in people with severe depression. There no serious complications reported from giving ketamine to patients with depression or other conditions, but when people with SRI withdrawal are given ketamine it produces bowel problems including vomiting, temperature dysregulation and pain sensitivity.

There is a striking uniformity to these responses which suggests these subjects are in a physiologically different state to other people – that they are sensitized in some way. The subjects in question appeared to have an intensified and dramatic withdrawal process that shows many of the features of previous SSRI withdrawal.

This seems a striking demonstration that there is enduring dysregulation of some sort but also suggests there must be something that can be done to relieve the problem.

Enduring withdrawal

SSRI withdrawal may not be a problem for some. For others it can last years. Enduring problems can follow either abrupt or tapered discontinuation of treatment. We do not know how common these states are. Many people presenting to their doctors are told they have a recurrent mood disorder and are put back on an antidepressant because the problems look “depressive”, and most doctors do not think that problems of this sort could persist this long.

An enduring problem is likely to be underpinned by physical changes in the body that physical and mental activity will bypass. Regular exercise and social activity rather than withdrawal is important. It is also important, if possible, not to get defined by the problem.

If it is impossible to stop meds, it is probably best to stabilize on a less potent SSRI like desvenlafaxine.

Legacy or stress related mood disturbances

When dependence on and withdrawal from antipsychotics was first outlined in the 1960s, in addition to classic states such as tardive dyskinesia, a variety of stress syndromes that have since been termed tardive dysthymia, and tardive akathisia were described.

The initial withdrawal problems often center on “electric zaps”, and “electric head”, but later these recede into the background and are replaced by depression or anxiety. As these sometimes intense depressions come to the fore they may seem like new illnesses, and be hard to distinguish from an original depression.

The management of these depressions or tardive dysthymia is different to managing severe withdrawal. At present it is not clear what helps the difficulties some people face 6 months or more into the discontinuation period.

Faced with ongoing problems, people commonly ask whether they should go back on the original antidepressant and start a new and even more gradual taper.

Going back on something that has caused such difficulties seems risky and in many cases a return to the original medication does not alleviate the problem.

Generally the longer the interval off the drug, the less likely it has been that restarting treatment will help.

There is a trend to considering leaving people on treatment indefinitely. There are several drawbacks to this.

Ongoing treatment may increase the risk of premature mortality. The risks of fractures or hemorrhages are increased, and substantially increased if combined with other treatments like aspirin.

Because of blunting effects on emotions and libido, SSRIs impair the quality of life.

A better option may be to turn to an antihistamine, or a tricyclic antidepressant, such as dosulepin. The rationale here is that a small amount of SRI may be all that is needed to produce a helpful anxiolytic effect in those suited to drugs of this type. Potent SSRIs are in fact almost grotesquely overpowered for this purpose.

A third option is to turn to a completely different therapeutic principle. Among the options are drugs active on the cholinergic system, calcium channel blockers or dopamine agonists.

Choline-esterase inhibitors and calcium channel blockers have been reported to benefit some individuals with enduring problems after antipsychotic withdrawal.

Dopamine agonists or stimulants are used in restless legs and related syndromes, and restlessness is often present after stopping antidepressants. This seems like a risky option.

Based on the precedent of tardive dyskinesia, it seems that these new dysphorias may last for years. In older individuals they may last indefinitely. In younger individuals, they are more likely to clear up in a 12-36 month timeframe.

There is no clear understanding of what happens in the brain to trigger such problems but it may be that with extended exposure to an antidepressant, some of us lose receptors from nerve terminals and when the drug is stopped these receptors just do not return to normal.

If the explanation offered above is partly correct, with time the condition should resolve but this resolution may take months or years. It would seem intuitively sensible to suggest that activity, which helps to refashion nerve endings, would help and you should therefore be physically active and try to live life as fully as possible and avoid shutting down or withdrawing from activities.

Activities such as walking or swimming may be helpful especially if undertaken in a graded program that ensures there is daily activity and over time builds the activity levels up.

It is not clear at the moment how great the overlap might be between the tardive dysthymia linked to antidepressant, antipsychotic or benzodiazepine withdrawals.

Managing new affective episodes

Another issue that needs to be addressed is the emergence of a new affective episode rather than a flare-up of tardive dysthymia. In this case, it seems likely that if someone got well on a serotonergic agent in the first instance, they are more likely to show a better initial response to another SSRI than they are to respond to an agent from a different class. This raises the question of whether the short term benefit is worth taking given the likely longer term problems. To some extent this issue depends on what the alternatives are.

First if this is truly is a depressive disorder that has responded to an SSRI in the first instance, this means it is not a particularly severe mood disorder and as such the need to bring about a quick response with drugs because of risks like suicide is not high.

It would seem best to take a less potent serotonin reuptake inhibitor – such as imipramine.

Second, not intervening pharmacologically is often a reasonable option for two reasons. One is that the natural history of such disorders is that they will resolve on average within 12 to 16 weeks. Another is that there is considerable evidence to suggest that those who respond without pharmacological or other interventions are less likely to relapse in future.

Third, there are a number of things affected individuals can do for themselves. Exercising, particularly in a routine, is likely to be helpful, as is physical work generally. Diet, especially avoiding alcohol, is likely to be of some importance.

There are other more esoteric steps a person can take. One is sleep deprivation, which is undertaken regularly as an antidepressant treatment in many European countries.

Finally, CBT or other psychotherapeutic procedures may be of benefit, where these would seem to be less likely to be helpful in tardive dysthymic states.

RxISK terminator algorithm

On the Rxisk.org site we ask and score a series of questions to see if your problem might be linked to stopping a drug. These are the questions.

- 1 Are there previous reports of withdrawal effects from this drug in the manufacturer's literature, FDA database, or RxISK database?
- 2 Did you reduce the dose of the drug?
Did the problem start before or after reducing?
- 3 Was the problem different to your original condition?
- 4 Did you stop the drug?
Did the problem start after stopping?
- 5 Did you restart the drug?
Did the problem clear up?
- 6 Did you increase the dose of the drug?
Did the problem improve?
- 7 How soon after restarting the drug or increasing the dose did the problem improve?
- 8 Did you try a related drug?
Did the problem clear up?
- 9 Have you ever had withdrawal effects before on another drug?
Was it on the same type of drug?
- 10 Have you had other drugs of the same type as this?
Did you have a similar withdrawal effect on them?
- 11 Could anything else be causing this event?

Report your experience on RxISK.org, get a free RxISK Report, and check your RxISK score.

- 9+ points strongly to a linkage
- 4-8 points to a linkage
- 1-4 suggests not enough information to confirm a linkage
- 0 unlikely to be a withdrawal effect

Other treatments considered

When preparing this protocol, we have considered the following treatments which many people suffering from antidepressant withdrawal are likely to hear about or access:

Low dose Naltrexone.

This seems to have some merit but we have no data on it.

Choline-esterase inhibitors viz Donepezil

These might be helpful but evidence not in.

Metformin

Metformin re-sensitizes desensitized receptors; no evidence it helps SRI problems yet.

CoQ10 and Ubiquinol

Potentially useful in general but not clearly specific to antidepressant issues.

SRI Dependence problems caused by excess cortisol

Not at present a useful lead.

SSRI Dependence problems caused by adrenal insufficiency

Not at present a useful lead.

Dietary manipulation of serotonin

Serotonin is normal in depression. No-one knows what's wrong in withdrawal. Trying to manage withdrawal by dietary manipulation is not at present a convincing option.

SSRI Dependence problems caused by mitochondrial toxicity

Interesting idea but has offered no useful leads at present.

Liquids

Liquid formulations of SRIs are available but may require persistence to source them. You should demand a liquid form of your drug because “you are worth it”. Making your does up from a combination of liquids and meds may help reduce the cost.

In the UK

Rosemont Pharmaceuticals (Tel 0113 244 1999)
Cardinal Health, Martindale (Tel 0800 137 627)
Large chain pharmacies like Boots.

In the US, Canada & elsewhere

Action Pharmacy, Toronto (Tel 416 766 2401).

Please help us with details of others.