Many people living with chronic pain are daunted by the prospect of long term or even permanent drug therapy. What are these drugs, are they safe and how do they work? Concerns such as these can stop people persevering with medicines that may offer a real, life-enhancing solution to their condition. Dr Mick Serpell explains how amitriptyline works and gives reassurance about the side effects that you might experience, especially in the early stages.

The main aims in managing chronic pain are to relieve or to reduce the pain and, just as importantly, to improve your quality of life and get you doing more. There are four approaches to pain management:

1) physical therapy (physiotherapy, acupuncture, TENS (transcutaneous electrical nerve stimulation), etc.;  
2) drug therapy;  
3) regional analgesia (injection of drugs around nerves or other tissues);  
4) psychological therapies (techniques which improve coping with pain).

Two types of pain

Doctors describe pain as either nociceptive, neuropathic, or a combination of the two. It is important to distinguish between the two types of pain, as they need different medicines. Nociceptive pain is pain that starts off as a response to tissue damage or a painful stimulus like a hot surface. Examples include mechanical low back pain and degenerative or inflammatory joint pain, and so it is easy to understand why nociceptive pain is the most common form of chronic pain. Although these pains may begin as purely nociceptive, over time there may be changes within the nervous system that may result in neuropathic pain. Neuropathic pain may also be the result of nerve damage that makes the nerve overactive. Therefore the drugs used for neuropathic pain are aimed at stabilisation or “calming” of the overactive nerves. Perhaps it should be no surprise that drugs used in other conditions where nervous tissue is overactive or “excited”, such as epilepsy or depression, have turned out to be useful medicines for chronic pain where the nerves have become overactive.

Drug therapy

Conventional painkillers such as codeine and ibuprofen are used for nociceptive pain. They are often not effective for neuropathic pain. Most of the drugs used for the relief of neuropathic pain were

originally developed to treat different conditions. For instance, amitriptyline is an antidepressant drug but is now probably used more commonly for pain than for its original use. The situation is the same for some anticonvulsant drugs, which are used more frequently for neuropathic pain than epilepsy.

Change your lifestyle

Always remember that the medicine alone will not be enough. While drug therapy can play a major role in the management of pain, changing your lifestyle (such as building up your fitness and getting more exercise), as well as learning to manage and cope with your pain better, are also vital to the successful outcome.

General principles of drug therapy

Your doctor will start you off at a low dose of your medicine and this is increased up to a suitable dosage and taken for sufficient duration until you obtain noticeable pain relief (or experience severe side effects). This procedure of increasing the dose step by step while monitoring the effect is called “titrating the dose”. If there is no relief the drug will be stopped. Your doctor is likely to gradually wean you off the medication over one to two weeks, to avoid potential side effects from sudden withdrawal. If you get partial, but inadequate pain relief, a second different drug can be prescribed in addition.

Once you are on the right dose and drug combination for you then you may continue on the medication indefinitely. You and your doctor may decide that you should wean yourself off the medicines gradually every six months or so to ensure they are still necessary for you.

Most doctors agree that medication for chronic pain should be taken “round the clock” rather than “as required”. It is easier to keep pain at bay rather than trying to control it after it has been allowed to resurface.

Antidepressants

The tricyclic antidepressants, such as amitriptyline, are the “gold standard” for neuropathic pain as they are the most effective and best-known drugs for this condition.\(^4\) They can also be useful for chronic nociceptive pain, especially if there is a neuropathic component to it. They appear to work in the nervous system by reducing the nerve cell’s ability to re-absorb chemicals such as serotonin and noradrenaline.\(^5\) These chemicals are called neural transmitters. If they are not reabsorbed they accumulate outside the nerve cell and the result is suppression of pain messages in the spinal cord.

All in the mind?

The way antidepressants give pain relief is completely separate from the anti-depressant effect. The dose required for treating depression is much higher (often over 150 milligrams (mg) a day) than the


http://www.medicine.ox.ac.uk/bandolier/booth/painpag/wisdom/adbmj2.html.
doses used for pain relief. Also, there are many different antidepressant drugs available that are effective for treating depression, but only a small number are also effective pain killers.

It is important that the patient is given a full explanation of the rationale for antidepressant therapy. It is not that the doctor believes your pain is due to depression. So do not think that you are not being taken seriously and that the pain is “all in the mind”. Of course, depression can occur with chronic pain, but it is usually an understandable reaction to the pain and improves as the chronic pain improves. However, if severe, it too may require treatment with an antidepressant drug.

**Starting amitriptyline**

One in four people will get significant pain relief with amitriptyline, which is regarded as an excellent result for chronic pain conditions.\(^6\) It is started at a low dose (10 or 25 mg a day) and gradually increased in 10 or 25 mg increments each week up towards 75 mg if any side effects are tolerable.\(^7\) Your doctor may advise you to go higher than this dose. The tablets are small and difficult to cut in half, and will often produce numbness of the tongue due to a local anaesthetic effect, but it is available as a syrup. It is better to use the syrup if small increases of dose are required during the titration (dose build-up) phase.

**Keep taking it!**

You may notice pain relief as soon as two weeks after starting, but often it requires amitriptyline to be taken for six to eight weeks at the best dose level before one can say the drug has been given a fair trial. Many people stop taking the medicine because they experience side effects early on but do not feel any benefit. However, if you can persevere, you will often get tolerant to most of the side effects after a few days to weeks and you may then start noticing the benefits of the medicine.

Although there are a number of side effects associated with amitriptyline most of them are extremely uncommon. The most common ones, experienced by only 5-15% of people, include dizziness, drowsiness, dry mouth, nausea and constipation.\(^8\) These side effects are generally harmless and, provided you do not exceed the dose, will not cause any damage. Most people find they adapt to these and eventually they go away. Amitriptyline is not addictive but if discontinued, it should be withdrawn slowly over two to three weeks in order to avoid withdrawal symptoms of headache and malaise.

**Not for everyone**

Your doctor will not prescribe this drug for you if you have had an allergic reaction to amitriptyline or related drugs; a recent heart attack; or recent administration of drugs that can interact with amitriptyline.

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When should I take it?

Amitriptyline is long acting, so only needs to be taken once a day. As one of the most common side effects is drowsiness, it is best to take it a couple of hours before bedtime. This effect can be particularly useful if you suffer lack of sleep from your pain. Sometimes there is a “morning after” type of hangover feeling, but this usually wears off with time. Occasionally amitriptyline can cause insomnia; if this happens it is better to take it in the morning.

Worth trying

If side effects are a problem, there are other similar drugs (for example, nortriptyline and imipramine) that are worth trying. Many of the patients I have seen have stayed on amitriptyline for years and say that it has transformed their lives. When dealing with pain, it is worth giving drug therapy a chance and working with your doctor to try different approaches so that you find the particular approach that is right for you, which brings you the benefits of pain relief, allows you to do more, and gives you the quality of life that you and your doctor both want.