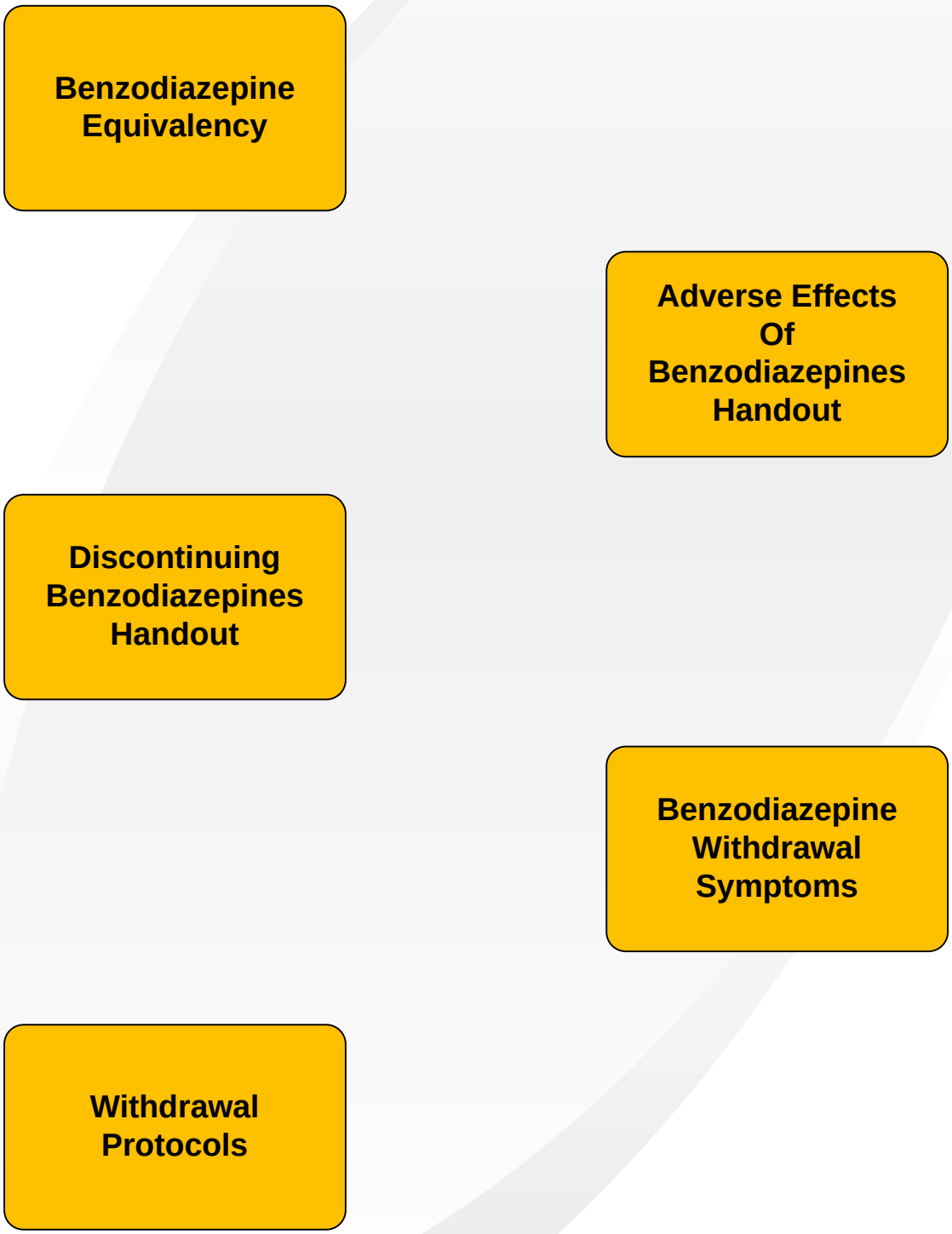
Benzodiazepine Withdrawal



BENZODIAZEPINES AND SIMILAR DRUGS

Benzodiazepines	Half-life (hrs) [active metabolite]	Market Aim anxiolytic (a), hypnotic (h) or antiepileptic (e)	Approximate Equivalent Oral dosages (mg)
Alprazolam (Xanax)	6-12	a	0.5
Chlordiazepoxide (Librium)	5-30 [36-200]	a	25
Clobazam (Frisium)	12-60	a,e	20
Clonazepam (Klonopin, Rivotril)	18-50	a,e	0.5
Diazepam (Valium)	20-100 [36-200]	a	10
Flunitrazepam (Rohypnol)	18-26 [36-200]	h	1
Flurazepam (Dalmane)	[40-250]	h	15-30
Lorazepam (Ativan)	10-20	a	1
Medazepam (Nobrium)	36-200	a	10
Nitrazepam (Mogadon)	15-38	h	10
Oxazepam (Serax, Serenid, Serepax)	4-15	a	20
Temazepam (Restoril, Normison, Euhypnos)	8-22	h	20
Triazolam (Halcion)	2	h	0.5
Non-benzodiazepines with similar effects	These drugs are chemically different from benzodiazepines but have the same effects on the body and act by the same mechanisms		
Zaleplon (Sonata)	2	h	20
Zolpidem (Ambien, Stilnoct)	2	h	20
Zopiclone (Zimovane, Imovane)	5-6	h	15
Eszopiclone (Lunesta)	6 (9 in elderly)	h	3

Adverse Effects of Benzodiazepines

Discontinuing Benzodiazepines

Withdrawal Effects of Benzodiazepines

ADVERSE EFFECTS OF BENZODIAZEPINES

Oversedation. Oversedation is a dose-related extension of the sedative/hypnotic effects of benzodiazepines. Symptoms include drowsiness, poor concentration, incoordination, muscle weakness, dizziness and mental confusion. When benzodiazepines are taken at night as sleeping pills, sedation may persist the next day as "hangover" effects, particularly with slowly eliminated preparations (Table 1). However, tolerance to the sedative effects usually develops over a week or two and anxious patients taking benzodiazepines during the day rarely complain of sleepiness although fine judgement and some memory functions may still be impaired.

Oversedation persists longer and is more marked in the elderly and may contribute to falls and fractures. Acute confusional states have occurred in the elderly even after small doses of benzodiazepines. Oversedation from benzodiazepines contributes to accidents at home and at work and studies from many countries have shown a significant association between the use of benzodiazepines and the risk of serious traffic accidents. People taking benzodiazepines should be warned of the risks of driving and of operating machinery.

Drug interactions. Benzodiazepines have additive effects with other drugs with sedative actions including other hypnotics, some antidepressants (e.g. amitriptyline [Elavil], doxepin [Adapin, Sinequan]), major tranquillisers or neuroleptics (e.g. prochlorperazine [Compazine], trifluoperazine [Stelazine]), anticonvulsants (e.g. phenobarbital, phenytoin [Dilantin], carbamazepine [Atretol, Tegretol]), sedative antihistamines (e.g. diphenhydramine [Benadryl], promethazine [Phenergan]), opiates (heroin, morphine, meperidine), and, importantly, alcohol. Patients taking benzodiazepines should be warned of these interactions. If sedative drugs are taken in overdose, benzodiazepines may add to the risk of fatality.

Memory impairment. Benzodiazepines have long been known to cause amnesia, an effect which is utilised when the drugs are used as premedication before major surgery or for minor surgical procedures. Loss of memory for unpleasant events is a welcome effect in these circumstances. For this purpose, fairly large single doses are employed and a short-acting benzodiazepine (e.g. midazolam) may be given intravenously.

Oral doses of benzodiazepines in the dosage range used for insomnia or anxiety can also cause memory impairment. Acquisition of new information is deficient, partly because of lack of concentration and attention. In addition, the drugs cause a specific deficit in "episodic" memory, the remembering of recent events, the circumstances in which they occurred, and their sequence in time. By contrast, other memory functions (memory for words, ability to remember a telephone number for a few seconds, and recall of long-term memories) are not impaired. Impairment of episodic memory may occasionally lead to memory lapses or "blackouts". It is claimed that in some instances such memory lapses may be responsible for uncharacteristic behaviours such as shop-lifting.

Benzodiazepines are often prescribed for acute stress-related reactions. At the time they may afford relief from the distress of catastrophic disasters, but if used for more than a few days they may prevent the normal psychological adjustment to such trauma. In the case of loss or bereavement they may inhibit the grieving process which may remain unresolved for many years. In other anxiety states, including panic disorder and agoraphobia, benzodiazepines may inhibit the learning of alternative stress-coping strategies, including cognitive behavioural treatment.

Paradoxical stimulant effects. Benzodiazepines occasionally cause paradoxical excitement with increased anxiety, insomnia, nightmares, hallucinations at the onset of sleep, irritability, hyperactive or aggressive behaviour, and exacerbation of seizures in epileptics. Attacks of rage and violent behaviour, including assault (and even homicide), have been reported, particularly after intravenous administration but also after oral administration. Less dramatic increases in irritability and argumentativeness are much more common and are frequently remarked upon by patients or by their families. Such reactions are similar to those sometimes provoked by alcohol. They are most frequent in anxious and aggressive

individuals, children, and the elderly. They may be due to release or inhibition of behavioural tendencies normally suppressed by social restraints. Cases of "baby-battering", wife-beating and "grandma-bashing" have been attributed to benzodiazepines.

Depression, emotional blunting. Long-term benzodiazepine users, like alcoholics and barbiturate-dependent patients, are often depressed, and the depression may first appear during prolonged benzodiazepine use. Benzodiazepines may both cause and aggravate depression, possibly by reducing the brain's output of neurotransmitters such as serotonin and norepinephrine (noradrenaline). However, anxiety and depression often co-exist and benzodiazepines are frequently prescribed for mixed anxiety and depression. Sometimes the drugs seem to precipitate suicidal tendencies in such patients.

"Emotional anaesthesia", the inability to feel pleasure or pain, is a common complaint of long-term benzodiazepine users. Such emotional blunting is probably related to the inhibitory effect of benzodiazepines on activity in emotional centres in the brain. Former long-term benzodiazepine users often bitterly regret their lack of emotional responses to family members - children and spouses or partners - during the period when they were taking the drugs. Chronic benzodiazepine use can be a cause of domestic disharmony and even marriage break-up.

Adverse effects in the elderly. Older people are more sensitive than younger people to the central nervous system depressant effects of benzodiazepines. Benzodiazepines can cause confusion, night wandering, amnesia, ataxia (loss of balance), hangover effects and "pseudodementia" (sometimes wrongly attributed to Alzheimer’s disease) in the elderly and should be avoided wherever possible. Increased sensitivity to benzodiazepines in older people is partly because they metabolise drugs less efficiently than younger people, so that drug effects last longer and drug accumulation readily occurs with regular use. However, even at the same blood concentration, the depressant effects of benzodiazepines are greater in the elderly, possibly because they have fewer brain cells and less reserve brain capacity than younger people.

For these reasons, it is generally advised that, if benzodiazepines are used in the elderly, dosage should be half that recommended for adults, and use (as for adults) should be short-term (2 weeks) only. In addition, benzodiazepines without active metabolites (e.g. oxazepam [Serax], temazepam [Restoril]) are tolerated better than those with slowly eliminated metabolites (e.g. chlordiazepoxide [Librium], nitrazepam [Mogadon]). Equivalent potencies of different benzodiazepines are approximately the same in older as in younger people.

Adverse effects in pregnancy. Benzodiazepines cross the placenta, and if taken regularly by the mother in late pregnancy, even in therapeutic doses, can cause neonatal complications. The foetus and neonate metabolise benzodiazepines very slowly, and appreciable concentrations may persist in the infant up to two weeks after birth, resulting in the "floppy infant syndrome" of lax muscles, oversedation, and failure to suckle. Withdrawal symptoms may develop after about two weeks with hyperexcitability, high-pitched crying and feeding difficulties.

Benzodiazepines in therapeutic doses appear to carry little risk of causing major congenital malformations. However, chronic maternal use may impair foetal intrauterine growth and retard brain development. There is increasing concern that such children in later life may be prone to attention deficit disorder, hyperactivity, learning difficulties, and a spectrum of autistic disorders.

Tolerance. Tolerance to many of the effects of benzodiazepines develops with regular use: the original dose of the drug has progressively less effect and a higher dose is required to obtain the original effect. This has often led doctors to increase the dosage in their prescriptions or to add another benzodiazepine so that some patients have ended up taking two benzodiazepines at once.

However, tolerance to the various actions of benzodiazepines develops at variable rates and to different degrees. Tolerance to the hypnotic effects develops rapidly and sleep recordings have shown that sleep

patterns, including deep sleep (slow wave sleep) and dreaming (which are initially suppressed by benzodiazepines), return to pre-treatment levels after a few weeks of regular benzodiazepine use. Similarly, daytime users of the drugs for anxiety no longer feel sleepy after a few days.

Tolerance to the anxiolytic effects develops more slowly but there is little evidence that benzodiazepines retain their effectiveness after a few months. In fact long-term benzodiazepine use may even aggravate anxiety disorders. Many patients find that anxiety symptoms gradually increase over the years despite continuous benzodiazepine use, and panic attacks and agoraphobia may appear for the first time after years of chronic use. Such worsening of symptoms during long-term benzodiazepine use is probably due to the development of tolerance to the anxiolytic effects, so that "withdrawal" symptoms emerge even in the continued presence of the drugs. However, tolerance may not be complete and chronic users sometimes report continued efficacy, which may be partly due to suppression of withdrawal effects. Nevertheless, in most cases such symptoms gradually disappear after successful tapering and withdrawal of benzodiazepines.

Tolerance to the anticonvulsant effects of benzodiazepines makes them generally unsuitable for long-term control of epilepsy. Tolerance to the motor effects of benzodiazepines can develop to a remarkable degree so that people on very large doses may be able to ride a bicycle and play ball games. However, complete tolerance to the effects on memory and cognition does not seem to occur. Many studies show that these functions remain impaired in chronic users, recovering slowly, though sometimes incompletely, after withdrawal.

Tolerance is a phenomenon that develops with many chronically used drugs (including alcohol, heroin and morphine and cannabis). The body responds to the continued presence of the drug with a series of adjustments that tend to overcome the drug effects. In the case of benzodiazepines, compensatory changes occur in the GABA and benzodiazepine receptors which become less responsive, so that the inhibitory actions of GABA and benzodiazepines are decreased. At the same time there are changes in the secondary systems controlled by GABA so that the activity of excitatory neurotransmitters tends to be restored. Tolerance to different effects of benzodiazepines may vary between individuals - probably as a result of differences in intrinsic neurological and chemical make-up which are reflected in personality characteristics and susceptibility to stress. The development of tolerance is one of the reasons people become dependent on benzodiazepines, and also sets the scene for the withdrawal syndrome.

Dependence. Benzodiazepines are potentially addictive drugs: psychological and physical dependence can develop within a few weeks or months of regular or repeated use. There are several overlapping types of benzodiazepine dependence.

Therapeutic dose dependence. People who have become dependent on therapeutic doses of benzodiazepines usually have several of the following characteristics.

1. They have taken benzodiazepines in prescribed "therapeutic" (usually low) doses for months or years.
2. They have gradually become to "need" benzodiazepines to carry out normal, day-to-day activities.
3. They have continued to take benzodiazepines although the original indication for prescription has disappeared.
4. They have difficulty in stopping the drug, or reducing dosage, because of withdrawal symptoms.
5. If on short-acting benzodiazepines they develop anxiety symptoms between doses, or get craving for the next dose.
6. They contact their doctor regularly to obtain repeat prescriptions.
7. They become anxious if the next prescription is not readily available; they may carry their tablets around with them and may take an extra dose before an anticipated stressful event or a night in a strange bed.
8. They may have increased the dosage since the original prescription.

To Page One

9. They may have anxiety symptoms, panics, agoraphobia, insomnia, depression and increasing physical symptoms despite continuing to take benzodiazepines.

The number of people world-wide who are taking prescribed benzodiazepines is enormous. For example, in the US nearly 11 per cent of a large population surveyed in 1990 reported some benzodiazepine use the previous year. About 2 per cent of the adult population of the US (around 4 million people) appear to have used prescribed benzodiazepine hypnotics or tranquillisers regularly for 5 to 10 years or more. A high proportion of these long-term users must be, at least to some degree, dependent. Exactly how many are dependent is not clear; it depends to some extent on how dependence is defined. However, many studies have shown that 50-100 per cent of long-term users have difficulty in stopping benzodiazepines because of withdrawal symptoms.

Prescribed high dose dependence. A minority of patients who start on prescribed benzodiazepines begin to "require" larger and larger doses. At first they may persuade their doctors to escalate the size of prescriptions, but on reaching the prescriber's limits, may contact several doctors or hospital departments to obtain further supplies which they self-prescribe. Sometimes this group combines benzodiazepine misuse with excessive alcohol consumption. Patients in this group tend to be highly anxious, depressed and may have personality difficulties. They may have a history of other sedative or alcohol misuse. They do not typically use illicit drugs but may obtain "street" benzodiazepines if other sources fail.

SOME SOCIOECONOMIC COSTS OF LONG-TERM BENZODIAZEPINE USE

1. Increased risk of accidents - traffic, home, work.
2. Increased risk of fatality from overdose if combined with other drugs.
3. Increased risk of attempted suicide, especially in depression.
4. Increased risk of aggressive behaviour and assault.
5. Increased risk of shoplifting and other antisocial acts.
6. Contributions to marital/domestic disharmony and breakdown due to emotional and cognitive impairment.
7. Contributions to job loss, unemployment, loss of work through illness.
8. Cost of hospital investigations/consultations/admissions.
9. Adverse effects in pregnancy and in the new-born.
10. Dependence and abuse potential (therapeutic and recreational).
11. Costs of drug prescriptions.
12. Costs of litigation.

DISCONTINUING BENZODIAZEPINES

Long-term use of benzodiazepines can give rise to many unwanted effects, including poor memory and cognition, emotional blunting, depression, increasing anxiety, physical symptoms and dependence. All benzodiazepines can produce these effects whether taken as sleeping pills or anti-anxiety drugs.

Furthermore, the evidence suggests that benzodiazepines are no longer effective after a few weeks or months of regular use. They lose much of their efficacy because of the development of tolerance. When tolerance develops, "withdrawal" symptoms can appear even though the user continues to take the drug. Thus the symptoms suffered by many long-term users are a mixture of adverse effects of the drugs and "withdrawal" effects due to tolerance.

In addition, clinical experience shows that most long-term benzodiazepine users actually feel better after coming off the drugs. Many users have remarked that it was not until they came off their drugs that they realised they had been operating below par for all the years they had been taking them. It was as though a net curtain or veil had been lifted from their eyes: slowly, sometimes suddenly, colours became brighter, grass greener, mind clearer, fears vanished, mood lifted, and physical vigour returned.

Thus there are good reasons for long-term users to stop their benzodiazepines if they feel unhappy about the medication. Many people are frightened of withdrawal, but reports of having to "go through hell" can be greatly exaggerated. With a sufficiently gradual and individualised tapering schedule, as outlined below, withdrawal can be quite tolerable, even easy, especially when the user understands the cause and nature of any symptoms that do arise and is therefore not afraid. Many "withdrawal symptoms" are simply due to fear of withdrawal (or even fear of that fear). People who have had bad experiences have usually been withdrawn too quickly (often by doctors!) and without any explanation of the symptoms. At the other extreme, some people can stop their benzodiazepines with no symptoms at all: according to some authorities, this figure may be as high as 50% even after a year of chronic usage. Even if this figure is correct (which is arguable) it is unwise to stop benzodiazepines suddenly.

The advantages of discontinuing benzodiazepines do not necessarily mean that every long-term user should withdraw. Nobody should be forced or persuaded to withdraw against his or her will. In fact, people who are unwillingly pushed into withdrawal often do badly. On the other hand, the chances of success are very high for those sufficiently motivated. As mentioned before, almost anyone who really wants to come off can come off benzodiazepines. The option is up to you.

BEFORE STARTING BENZODIAZEPINE WITHDRAWAL

Once you have made up your mind to withdraw, there are some steps to take before you start.

(1) Consult your doctor and pharmacist. Your doctor may have views on whether it is appropriate for you to stop your benzodiazepines. In a small number of cases withdrawal may be inadvisable. However, medical opinions differ and, even if complete withdrawal is not advised, it may be beneficial to reduce the dosage or to take intermittent courses with benzodiazepine-free intervals.

It is a good idea to make out a dosage reduction schedule for the initial stages. Remember the importance of flexibility, so that the rate of dosage tapering can be amended at any time. There may even be circumstances when you need to stop for a while at a certain stage. A continuation schedule can follow later depending upon how you get on, and the doctor can continue prescribing in accordance with the new schedule.

(2) Make sure you have adequate psychological support. Support could come from your spouse, partner, family or close friend. An understanding doctor may also be the one to offer support as well as advice. Ideally, your mentor should be someone who understands about benzodiazepine withdrawal or is prepared to read about it and learn. It need not be someone who has gone through withdrawal -

sometimes ex-users who have had a bad experience can frighten others by dwelling on their own symptoms. Often the help of a clinical psychologist, trained counsellor, or other therapist is valuable, especially for teaching relaxation techniques, deep breathing, how to deal with a panic attack etc. Some people find alternative techniques such as aromatherapy, acupuncture or yoga helpful, but these probably act only as an aid to relaxation.

Rather than (or in addition to) expensive therapists, you need someone reliable, who will support you frequently and regularly, long-term, both during withdrawal and for some months afterwards. Voluntary tranquilliser support groups (self-help groups) can be extremely helpful. They are usually run by people who have been through withdrawal and therefore understand the time and patience required, and can provide information about benzodiazepines. It can be encouraging to find that you are not alone, that there are plenty of others with similar problems to yours. However, do not be misled into fearing that you will get all the symptoms described by the others. Everyone is different and some people, with the right schedule and the right support, get no untoward symptoms at all. Many people in fact have managed to come off on their own without any outside help.

(3) Get into the right frame of mind.

- **Be confident** - you **can** do it. If in doubt, try a very small reduction in dosage for a few days (for example, try reducing your daily dosage by about one tenth or one eighth; you may be able to achieve this by halving or quartering one of your tablets). You will probably find that you notice no difference. If still in doubt, aim at first for dosage reduction rather than complete withdrawal. You will probably wish to continue once you have started.
- **Be patient.** There is no need to hurry withdrawal. Your body (and brain) may need time to readjust after years of being on benzodiazepines. Many people have taken a year or more to complete the withdrawal. So don't rush, and, above all, do not try to stop suddenly.
- **Choose your own way** - don't expect a "quick fix". It may be possible to enter a hospital or special centre for "detoxification". Such an approach usually involves a fairly rapid withdrawal, is medically "safe" and may provide psychological support. Such centres may be suitable for a small minority of people with difficult psychological problems. However, they often remove the control of withdrawal from the patient and setbacks on returning home are common, largely because there has been no time to build up alternative living skills. Slow withdrawal in your own environment allows time for physical and psychological adjustments, permits you to continue with your normal life, to tailor your withdrawal to your own lifestyle, and to build up alternative strategies for living without benzodiazepines.

THE WITHDRAWAL

(1) Dosage tapering. There is absolutely no doubt that anyone withdrawing from long-term benzodiazepines must reduce the dosage slowly. Abrupt or over-rapid withdrawal, especially from high dosage, can give rise to severe symptoms (convulsions, psychotic reactions, acute anxiety states) and may increase the risk of protracted withdrawal symptoms. Slow withdrawal means tapering dosage gradually, usually over a period of some months. The aim is to obtain a smooth, steady and slow decline in blood and tissue concentrations of benzodiazepines so that the natural systems in the brain can recover their normal state. Long-term benzodiazepines take over many of the functions of the body's natural tranquilliser system, mediated by the neurotransmitter GABA. As a result, GABA receptors in the brain reduce in numbers and GABA function decreases. Sudden withdrawal from benzodiazepines leaves the brain in a state of GABA-underactivity, resulting in hyperexcitability of the nervous system. This hyperexcitability is the root cause of most of withdrawal symptoms. However, a sufficiently slow, and smooth, departure of benzodiazepines from the body permits the natural systems to regain control of the functions which have been damped down by their presence. There is scientific evidence that reinstatement of brain function takes a long time. Recovery after long-term benzodiazepine use is not unlike the gradual recuperation of the body after a major surgical operation. Healing, of body or mind, is a slow process.

The precise rate of withdrawal is an individual matter. It depends on many factors including the dose and type of benzodiazepine used, duration of use, personality, lifestyle, previous experience, specific vulnerabilities, and the (perhaps genetically determined) speed of your recovery systems. Usually the best judge is you, yourself; you must be in control and must proceed at the pace that is comfortable for you. You may need to resist attempts from outsiders (clinics, doctors) to persuade you into a rapid withdrawal. The classic six weeks withdrawal period adopted by many clinics and doctors is much too fast for many long-term users. Actually, the rate of withdrawal, as long as it is slow enough, is not critical. Whether it takes 6 months, 12 months or 18 months is of little significance if you have taken benzodiazepines for a matter of years.

It is sometimes claimed that very slow withdrawal from benzodiazepines "merely prolongs the agony" and it is better to get it over with as quickly as possible. However, the experience of most patients is that slow withdrawal is greatly preferable, especially when the subject dictates the pace. Indeed, many patients find that there is little or no "agony" involved. Nevertheless there is no magic rate of withdrawal and each person must find the pace that suits him best. People who have been on low doses of benzodiazepine for a relatively short time (less than a year) can usually withdraw fairly rapidly. Those who have been on high doses of potent benzodiazepines such as Xanax are likely to need more time.

As a very rough guide, a person taking 40mg diazepam a day (or its equivalent) might be able to reduce the daily dosage by 2mg every 1-2 weeks until a dose of 20mg diazepam a day is reached. This would take 10-20 weeks. From 20mg diazepam a day, reductions of 1 mg in daily dosage every week or two might be preferable. This would take a further 20-40 weeks, so the total withdrawal might last 30-60 weeks. Yet some people might prefer to reduce faster and some might go even slower.

However, it is important in withdrawal always to go forwards. If you reach a difficult point, you can stop there for a few weeks if necessary, but you should try to avoid going backwards and increasing your dosage again. Some doctors advocate the use of "escape pills" (an extra dose of benzodiazepines) in particularly stressful situations. This is probably not a good idea as it interrupts the smooth decline in benzodiazepine concentrations and also disrupts the process of learning to cope without drugs which is an essential part of the adaptation to withdrawal. If the withdrawal is slow enough, "escape pills" should not be necessary.

(2) Switching to a long-acting benzodiazepine. With relatively short-acting benzodiazepines such as alprazolam (Xanax) and lorazepam (Ativan), it is not possible to achieve a smooth decline in blood and tissue concentrations. These drugs are eliminated fairly rapidly with the result that concentrations fluctuate with peaks and troughs between each dose. It is necessary to take the tablets several times a day and many people experience a "mini-withdrawal", sometimes a craving, between each dose.

For people withdrawing from these potent, short-acting drugs it is advisable to switch to a long-acting, slowly metabolised benzodiazepine such as diazepam. Diazepam (Valium) is one of the most slowly eliminated benzodiazepines. It has a half-life of up to 200 hours, which means that the blood level for each dose falls by only half in about 8.3 days. The only other benzodiazepines with similar half-lives are chlordiazepoxide (Librium), flunitrazepam (Rohypnol) and flurazepam (Dalmane), all of which are converted to a diazepam metabolite in the body. The slow elimination of diazepam allows a smooth, gradual fall in blood level, allowing the body to adjust slowly to a decreasing concentration of the benzodiazepines. The switch-over process needs to be carried out gradually, usually in stepwise fashion, substituting one dose at a time. There are several factors to consider. One is the difference in potency between different benzodiazepines. Many people have suffered because they have been switched suddenly to a different, less potent drug in inadequate dosage because the doctor has not adequately considered this factor.

A second factor to bear in mind is that the various benzodiazepines, though broadly similar, have slightly different profiles of action. For example, lorazepam (Ativan) seems to have less hypnotic activity than diazepam (probably because it is shorter acting). Thus if someone on, say, 2mg Ativan three times a day is directly switched to 60mg diazepam (the equivalent dose for anxiety) he is liable to become extremely

sleepy, but if he is switched suddenly onto a much smaller dose of diazepam, he will probably get withdrawal symptoms. Making the changeover one dose (or part of dose) at a time avoids this difficulty and also helps to find the equivalent dosage for that individual. It is also helpful to make the first substitution in the night-time dose, and the substitution may not always need to be complete. For example, if the evening dose was 2mg Ativan, this could in some cases be changed to 1 mg Ativan plus 8mg diazepam. A full substitution for the dropped 1 mg of Ativan would have been 10mg diazepam. However, the patient may actually sleep well on this combination and he will have already made a dosage reduction - a first step in withdrawal.

A third important practical factor is the available dosage formulations of the various benzodiazepines. In withdrawal you need a long-acting drug which can be reduced in very small steps. Diazepam (Valium) is the only benzodiazepine that is ideal for this purpose since it comes in 2mg tablets, which are scored down the middle and easily halved into 1 mg doses. By contrast, the smallest available tablet of lorazepam (Ativan) is 0.5mg (equivalent to 5mg diazepam); the smallest tablet of alprazolam (Xanax) is 0.25mg (also equivalent to 5mg diazepam). Even by halving these tablets the smallest reduction one could easily make is the equivalent of 2.5mg diazepam. Because of limited dose formulations, it may be necessary to switch to diazepam even if you are on a fairly long-acting benzodiazepine of relatively low potency. Liquid preparations of some benzodiazepines are available and if desired slow reduction from these can be accomplished by decreasing the volume of each dose, using a graduated syringe.

(3) Designing and following the withdrawal schedule. Some examples of withdrawal schedules are given on later pages. Most of them are actual schedules which have been used and found to work by real people who withdrew successfully. But each schedule must be tailored to individual needs; no two schedules are necessarily the same. Below is a summary of points to consider when drawing up your own schedule.

1. Design the schedule around your own symptoms. For example, if insomnia is a major problem, take most of your dosage at bedtime; if getting out of the house in the morning is a difficulty, take some of the dose first thing (but not a large enough dose to make you sleepy or incompetent at driving!).
2. When switching over to diazepam, substitute one dose at a time, usually starting with the evening or night-time dose, then replace the other doses, one by one, at intervals of a few days or a week. Unless you are starting from very large doses, there is no need to aim for a reduction at this stage; simply aim for an approximately equivalent dosage. When you have done this, you can start reducing the diazepam slowly.

   If, however, you are on a high dose, such as 6mg alprazolam (equivalent to 120mg diazepam), you may need to undertake some reduction while switching over, and may need to switch only part of the dosage at a time. The aim is to find a dose of diazepam which largely prevents withdrawal symptoms but is not so excessive as to make you sleepy.

3. Diazepam is very slowly eliminated and needs only, at most, twice daily administration to achieve smooth blood concentrations. If you are taking benzodiazepines three or four times a day it is advisable to space out your dosage to twice daily once you are on diazepam. The less often you take tablets the less your day will revolve around your medication.
4. The larger the dose you are taking initially, the greater the size of each dose reduction can be. You could aim at reducing dosage by up to one tenth at each decrement. For example, if you are taking 40mg diazepam equivalent you could reduce at first by 2-4mg every week or two. When you are down to 20mg, reductions could be 1-2mg weekly or fortnightly. When you are down to 10mg, 1mg reductions are probably indicated. From 5mg diazepam some people prefer to reduce by 0.5mg every week or two.
5. There is no need to draw up your withdrawal schedule right up to the end. It is usually sensible to plan the first few weeks and then review and if necessary amend your schedule according to your progress. Prepare your doctor to be flexible and to be ready for your schedule to be adjusted to a slower (or faster) pace at any time.

To Page One

6. As far as possible, never go backwards. You can stand still at a certain stage in your schedule and have a vacation from further withdrawal for a few weeks if circumstances change (if for instance there is a family crisis), but try to avoid ever increasing the dosage again. You don't want to back over ground you have already covered.
7. Avoid taking extra tablets in times of stress. Learn to gain control over your symptoms. This will give you extra confidence that you can cope without benzodiazepines.
8. Avoid compensating for benzodiazepines by increasing your intake of alcohol, cannabis or non-prescription drugs. Occasionally your doctor may suggest other drugs for particular symptoms, but do not take the sleeping tablets zolpidem (Ambien), zopiclone (Zimovane, Imovane) or zaleplon (Sonata) as they have the same actions as benzodiazepines.
9. Getting off the last tablet: Stopping the last few milligrams is often viewed as particularly difficult. This is mainly due to fear of how you will cope without any drug at all. In fact, the final parting is surprisingly easy. People are usually delighted by the new sense of freedom gained. In any case the 1mg or 0.5mg diazepam per day which you are taking at the end of your schedule is having little effect apart from keeping the dependence going. Do not be tempted to spin out the withdrawal to a ridiculously slow rate towards the end (such as 0.25mg each month). Take the plunge when you reach 0.5mg daily; full recovery cannot begin until you have got off your tablets completely. Some people after completing withdrawal like to carry around a few tablets with them for security "just in case", but find that they rarely if ever use them.
10. Do not become obsessed with your withdrawal schedule. Let it just become a normal way of life for the next few months. Okay, you are withdrawing from your benzodiazepines; so are many others. It's no big deal.
11. If for any reason you do not (or did not) succeed at your first attempt at benzodiazepine withdrawal, you can always try again. They say that most smokers make 7 or 8 attempts before they finally give up cigarettes. The good news is that most long-term benzodiazepine users are successful after the first attempt. Those who need a second try have usually been withdrawn too quickly the first time. A slow and steady benzodiazepine withdrawal, with you in control, is nearly always successful.

(4) Withdrawal in older people. Older people can withdraw from benzodiazepines as successfully as younger people, even if they have taken the drugs for years. A recent trial with an elderly population of 273 general practice patients on long-term (mean 15 years) benzodiazepines showed that voluntary dosage reduction and total withdrawal of benzodiazepines was accompanied by better sleep, improvement in psychological and physical health and fewer visits to doctors. These findings have been repeated in several other studies of elderly patients taking benzodiazepines long-term.

There are particularly compelling reasons why older people should withdraw from benzodiazepines since, as age advances, they become more prone to falls and fractures, confusion, memory loss and psychiatric problems.

BENZODIAZEPINE WITHDRAWAL SYMPTOMS, ACUTE AND PROTRACTED

To Page One

It cannot be too strongly stressed that withdrawal symptoms can be minimised and largely avoided by slow tapering, tailored to the individual's needs. However, some long-term benzodiazepine users begin to experience "withdrawal" symptoms even though they continue taking the drug. This is due to the development of drug tolerance which sometimes leads doctors to increase the dosage or add another benzodiazepine. Analysis of the first 50 patients who attended my benzodiazepine withdrawal clinic showed that all of them had symptoms on first presentation while still on benzodiazepines (12 of them were taking two prescribed benzodiazepines at once). Their symptoms included the full range of psychological and physical symptoms usually described as benzodiazepine withdrawal symptoms. The process of slow benzodiazepine tapering in these patients caused only slight exacerbation of these symptoms, which then declined after withdrawal.

People who develop severe symptoms on benzodiazepine withdrawal have usually come off the drugs too rapidly. Lack of explanation of the symptoms has often added to their distress and has introduced fears ("Am I going mad?") which themselves magnify the symptoms. A few, because of these frightening experiences, have ended up with a condition akin to post-traumatic stress disorder (PTSD). But a proper understanding of the reasons for and nature of any symptoms that arise can do much to allay the bewilderment and fear associated with benzodiazepine withdrawal and can also help prevent long-term sequelae. Withdrawal reactions are in fact a normal response to the discontinuation of many chronically used drugs including alcohol, opiates, antipsychotics, antidepressants, and even some medications for angina and hypertension.

Mechanisms of withdrawal reactions. Drug withdrawal reactions in general tend to consist of a mirror image of the drugs' initial effects. In the case of benzodiazepines, sudden cessation after chronic use may result in dreamless sleep being replaced by insomnia and nightmares; muscle relaxation by increased tension and muscle spasms; tranquillity by anxiety and panic; anticonvulsant effects by epileptic seizures. These reactions are caused by the abrupt exposure of adaptations that have occurred in the nervous system in response to the chronic presence of the drug. Rapid removal of the drug opens the floodgates, resulting in rebound overactivity of all the systems which have been damped down by the benzodiazepine and are now no longer opposed. Nearly all the excitatory mechanisms in the nervous system go into overdrive and, until new adaptations to the drug-free state develop, the brain and peripheral nervous system are in a hyperexcitable state, and extremely vulnerable to stress.

Acute withdrawal symptoms. The most prominent effect of benzodiazepines is an anti-anxiety effect - that is why they were developed as tranquillisers. As a consequence, nearly all the acute symptoms of withdrawal are those of anxiety. They have been described in anxiety states in people who have never touched a benzodiazepine and were recognised as psychological and physical symptoms of anxiety long before benzodiazepines were discovered. However, certain symptom clusters are particularly characteristic of benzodiazepine withdrawal. These include hypersensitivity to sensory stimuli (sound, light, touch, taste and smell) and perceptual distortions (for example sensation of the floor undulating, feeling of motion, impressions of walls or floors tilting, sensation of walking on cotton wool). There also appears to be a higher incidence than usually seen in anxiety states of depersonalisation, feelings of unreality, and tingling and numbness. Visual hallucinations, distortion of the body image ("my head feels like a football/balloon"), feelings of insects crawling on the skin, muscle twitching and weight loss are not uncommon in benzodiazepine withdrawal but unusual in anxiety states.

Table 1 gives a list of symptoms which were spontaneously described by patients in my withdrawal clinic. It is clearly a long list and is probably not inclusive. Of course, not all patients get all the symptoms, and none of the symptoms are inevitable. Withdrawal often seems to seek out the individual's most vulnerable points: if he is prone to headaches, worse headaches may feature in withdrawal; if he is prone to "irritable bowel", digestive symptoms may be aggravated. Such symptoms are nearly always temporary and can

To Page One

be minimised. They are less frightening and seem less important or bizarre if their cause is understood. Furthermore, patients can learn techniques to alleviate or control many of the symptoms: there is a lot they can do to help themselves.

TABLE 1. BENZODIAZEPINE WITHDRAWAL SYMPTOMS

PSYCHOLOGICAL SYMPTOMS

- Excitability (jumpiness, restlessness)
- Insomnia, nightmares, other sleep disturbances
- Increased anxiety, panic attacks
- Agoraphobia, social phobia
- Perceptual distortions
- Depersonalisation, derealisation
- Hallucinations, misperceptions
- Depression
- Obsessions
- Paranoid thoughts
- Rage, aggression, irritability
- Poor memory and concentration
- Intrusive memories
- Craving (rare)

PHYSICAL SYMPTOMS

- Headache
- Pain/stiffness - (limbs, back, neck, teeth, jaw)
- Tingling, numbness, altered sensation - (limbs, face, trunk)
- Weakness ("jelly-legs")
- Fatigue, influenza-like symptoms
- Muscle twitches, jerks, tics, "electric shocks"
- Tremor
- Dizziness, light-headedness, poor balance
- Blurred/double vision, sore or dry eyes
- Tinnitus
- Hypersensitivity - (light, sound, touch, taste, smell)
- Gastrointestinal symptoms - (nausea, vomiting, diarrhoea, constipation, pain, distension, difficulty swallowing)
- Appetite/weight change
- Dry mouth, metallic taste, unusual smell
- Flushing/sweating/palpitations
- Overbreathing
- Urinary difficulties/menstrual difficulties
- Skin rashes, itching
- Fits (rare)

These symptoms have all been described by patients withdrawing from benzodiazepines; they are not arranged in any particular order, and few if any are specific to benzodiazepine withdrawal. The list is probably not inclusive. Different individuals experience different combinations of symptoms. Do not expect to get **all** these symptoms!

INDIVIDUAL SYMPTOMS, THEIR CAUSES AND HOW TO DEAL WITH THEM

Insomnia, nightmares, sleep disturbance. The sleep engendered by benzodiazepines, though it may seem refreshing at first, is not a normal sleep. Benzodiazepines inhibit both dreaming sleep (rapid eye movement sleep, REMS) and deep sleep (slow wave sleep, SWS). The extra sleep time that benzodiazepines provide is spent mainly in light sleep, termed Stage 2 sleep. REM and SWS are the two most important stages of sleep and are essential to health. Sleep deprivation studies show that any deficit is quickly made up by a rebound to above normal levels as soon as circumstances permit.

In regular benzodiazepine users REMS and SWS tend to return to pre-drug levels (because of tolerance) but the initial deficit remains. On withdrawal, even after years of benzodiazepine use, there is a marked rebound increase in REMS which also becomes more intense. As a result, dreams become more vivid, nightmares may occur and cause frequent awakenings during the night. This is a normal reaction to benzodiazepine withdrawal and, though unpleasant, it is a sign that recovery is beginning to take place.

When the deficit of REMS is made up, usually after about 4-6 weeks, the nightmares become less frequent and gradually fade away.

Return of SWS seems to take longer after withdrawal, probably because anxiety levels are high, the brain is overactive and it is hard to relax completely. Subjects may have difficulty in getting off to sleep and may experience "restless legs syndrome", sudden muscle jerks (myoclonus) just as they are dropping off or be jolted suddenly by a hallucination of a loud bang (hypnagogic hallucination) which wakes them up again. These disturbances may also last for several weeks, sometimes months.

However, all these symptoms do settle in time. The need for sleep is so powerful that normal sleep will eventually reassert itself. Meanwhile, attention to sleep hygiene measures including avoiding tea, coffee, other stimulants or alcohol near bedtime, relaxation tapes, anxiety management techniques and physical exercise may be helpful. Taking all or most of the dose of benzodiazepine at night during the reduction period may also help. Occasionally another drug might be indicated.

Intrusive memories. A fascinating symptom in patients undergoing benzodiazepine withdrawal is that they often mention the occurrence of what seem to be intrusive memories. Their minds will suddenly conjure up a vivid memory of someone they have not thought about or seen for years. Sometimes the other person's face will appear when looking in the mirror. The memory seems uncalled for and may recur, intruding on other thoughts. The interesting thing about these memories is that they often start to occur at the same time that vivid dreams appear; these may be delayed until one or more weeks after the dosage tapering has started. Since recent sleep research indicates that certain stages of sleep (REMS and SWS) are important for memory functions, it is likely that the dreams and the memories are connected. In both cases the phenomena may herald the beginning of a return in normal memory functions and, although sometimes disturbing, can be welcomed as a sign of a step towards recovery.

Poor memory and concentration are also features of benzodiazepine withdrawal, and are probably due to continued effects of the drug. Mentors should be prepared to repeat encouragements again and again, week after week, as their words are soon forgotten.

Panic attacks. Panic attacks may appear for the first time during withdrawal, although some patients have long experience with this distressing symptom. The actress Glenda Jackson, who was not on benzodiazepines, described them as follows: "God, those panic attacks. You think you're dying; your heart pounds so strongly it feels like it's going to jump out of your chest; you choke and begin to feel you can't breathe - and all this is accompanied by terrible shaking and tremor, and feeling freezing cold". These attacks are characteristic of some anxiety states and are the result of storms of central and peripheral nervous system hyperactivity, especially the centres normally concerned with fear and flight reactions in response to emergencies. The brain centres that control these fear reactions have been damped down by benzodiazepines and may rebound with renewed vigour as the benzodiazepines leave the body.

Distressing as they are, panic attacks are never fatal and usually last little more than 30 minutes. What is more, it is possible to learn to exercise control over them. Various approaches are described below. Learning to control a panic attack is a skill that improves with practice and needs to be worked on at home. However, panic attacks (and other withdrawal symptoms) have a knack of coming on at inappropriate moments away from home. In such circumstances it is important to stand your ground, resisting the impulse to run away. The following manoeuvre can be done when a severe withdrawal symptom such as a panic attack comes on:

"Take much slower and deeper breaths, making sure that you get air deep down into the lungs instead of just at the top of the chest."

"As you do this you will find that your arms and hands relax so that the whites of your knuckles no longer show as you grip the supermarket trolley."

To Page One

"Do not move on until you feel the tension flowing out of your hands. With each deep breath you should feel your tension flowing away and, as it does, your symptoms will lessen or disappear."

The discovery that a panic attack can be controlled without resorting to a tablet is a great boost to self-confidence, and the development of new stress-coping strategies is often the key to successful benzodiazepine withdrawal. Panic attacks usually disappear within six weeks of withdrawal.

Generalised anxiety, panics and phobias. There are many non-pharmacological techniques for helping people with anxiety. Some of these are listed below, but it is beyond the scope of this handout to give details of each technique or to mention all of them. None of them are essential for everybody coming off tranquillisers, but can be helpful for those having difficulty.

(1) Psychological techniques

Behaviour therapy

- aims to replace anxiety-related behaviours with better adapted behaviours
- Progressive muscular relaxation (reduces muscle tension and anxiety)
- Diaphragmatic breathing (many anxious people hyperventilate)
- Guided imaging (focus on pleasant, relaxing situations; relaxation tapes with music and calm words can also be used at home)
- Controlled exposure to frightening situations, gradually increasing till anxiety diminishes

Cognitive-behavioural therapy

- Teaches patients to understand their thinking patterns so that they can react differently to anxiety-provoking situations
- Coping skills therapy/anxiety management (learning techniques) to avoid anxiety-provoking situations and to deal with anxiety (if it occurs)
- Cognitive retraining skills

(2) Complementary medicine techniques

- Acupuncture
- Aromatherapy
- Massage, reflexology
- Homeopathy

(3) Exercise and other techniques

- Sports - aerobics, jogging, swimming, "pilates", walking and anything active that you find enjoyable
- Yoga - Many different types and techniques
- Meditation - Many different types and techniques

The choice of, and response to, each of these measures depends very much on the individual. The various psychological techniques have been formally tested and give the best long-term results. However, the outcome depends largely on the skill of the therapist, including his/her knowledge of benzodiazepines, and the rapport between therapist and client.

Of the complementary medicine techniques, all can help with relaxation during the procedure but the effects tend to be short-lived.

Certain individuals respond very well to yoga and meditation techniques. One particular patient who was confined to a wheelchair with a spastic paralysis and who was also blind, was able to come off all his benzodiazepines with the help of a meditation technique. His spasticity actually improved. However, not everyone is able to devote the mental and physical concentration required for these techniques. Physical exercise, within your own limitations, is good for everyone.

On the whole, different approaches suit different individuals and need to be personalised. If you believe in a certain approach, it will probably do you good.

Sensory hypersensitivity. A characteristic feature of benzodiazepine withdrawal is a heightened sensitivity to all sensations - hearing, sight, touch, taste and smell. When extreme, these sensations can be disturbing. One lady had to stop all the clocks in the house because their ticking sounded unbearably loud; many have had to don dark glasses because ordinary light seemed dazzlingly bright. Some find that the skin and scalp becomes so sensitive that it feels as if insects are crawling over them. Heartbeats become audible and there may be a hissing or ringing sound in the ears (tinnitus). Many people complain of a metallic taste in the mouth and several notice strange, unpleasant, smells which seem to emanate from the body. These sensations, including an unpleasant smell (which usually no-one else can detect) have been described in anxiety states in the absence of benzodiazepines. Like insomnia and panics, they are probably reflections of heightened activity in the central nervous system. Such hypervigilance is part of the normal fear and flight response which is damped down by benzodiazepines but undergoes a rebound during withdrawal.

These sensations return towards normal as withdrawal progresses, and some people are pleased with the new, seemingly extraordinary, clarity of their perceptions. Only in withdrawal do they realise how much their senses have been obscured by benzodiazepines. One lady described how thrilled she was when she could suddenly see individual blades of grass in her newly bright green lawn; it was like the lifting of a veil. Thus, these sensations need not give rise to fear; they can be viewed as signs of recovery.

Depersonalisation, derealisation. Feelings of depersonalisation and of unreality are associated with benzodiazepine withdrawal, although they also occur in anxiety states. They occur most often during over-rapid withdrawal from potent benzodiazepines and are, anecdotally, particularly marked on withdrawal from clonazepam (Klonopin). In these states, the person seems detached from his body and seems almost to be observing it from the outside. Similar experiences are described in near-death states when the individual feels that he is hovering above his body, detached from the events occurring below. They are also described by people involved in extreme emergencies and in individuals subjected to torture. They are clearly not specific to benzodiazepines.

Such experiences probably represent a normal defensive reaction evolved as a protection against intolerable suffering. They may involve a primitive brain mechanism similar to the "freezing" of some animals when presented with an inescapable danger. Like other benzodiazepine withdrawal symptoms, these feelings resolve in time and should not be interpreted as abnormal or crazy.

Hallucinations, illusions, perceptual distortions. The benzodiazepine withdrawal symptom that raises most fear of going mad is hallucination. Terrifying hallucinations have occurred in people undergoing rapid or abrupt withdrawal from high doses, but the reader can be reassured that they are exceedingly rare with slow dosage tapering. If hallucinations occur, they are usually visual - patients have described hallucinations of a large bat sitting on the shoulder, or the appearance of horns sprouting from a human head - but auditory, olfactory and tactile hallucinations can also occur. Somewhat less frightening are hallucinations of small creatures, usually insects, which may be associated with the sensations of insects crawling on the skin (similar hallucinations occur in cocaine and amphetamine withdrawal). Sometimes hallucinations merge with illusions and misperceptions. For example, a coat hanging on the door may give the illusion of being a person. Floors apparently tilting and walls that seem to slope inwards are perceptual distortions.

The mechanisms of these bizarre symptoms are probably similar to those which cause delirium tremens (hallucinations, classically of pink elephants or rats, in the "DTs" of alcohol withdrawal). Benzodiazepines cause profound perturbations throughout the brain, and abrupt withdrawal may be accompanied by uncontrolled release of dopamine, serotonin and other neurotransmitters which cause hallucinations in psychotic disorders as well as in alcohol withdrawal and cocaine, amphetamine and LSD abuse.

Once the hallucinations, which seem real at the time, are recognised as "merely" hallucinations, they quickly become less alarming. They do not herald the onset of madness; they are simply instances of benzodiazepines playing tricks on the brain which will right itself in time. A good mentor can usually reassure and "talk down" a person suffering from benzodiazepine withdrawal-induced hallucinations. In any case they should not worry anyone undergoing slow withdrawal.

Depression, aggression, obsessions. Depressive symptoms are common both during long-term benzodiazepine use and in withdrawal. It is not surprising that some patients feel depressed considering the amalgam of other psychological and physical symptoms that may assail them. Sometimes the depression becomes severe enough to qualify as a "major depressive disorder", to use the psychiatric term. This disorder includes the risk of suicide and may require treatment with psychotherapy and/or antidepressant drugs.

Severe depression may result from biochemical changes in the brain induced by benzodiazepines. Benzodiazepines are known to decrease the activity of serotonin and norepinephrine (noradrenalin), neurotransmitters believed to be closely involved in depression. Antidepressant drugs including the selective serotonin reuptake inhibitors (SSRIs such as Prozac) are thought to act by increasing the activity of such neurotransmitters.

Depression in withdrawal may become protracted and if it does not lift within a few weeks and is unresponsive to simple reassurance and encouragement, it is worth seeking a medical opinion and possibly taking an antidepressant drug. Depression in withdrawal responds to antidepressant drugs in the same way as depressive disorders where benzodiazepines are not involved. If, as in many cases, an antidepressant drug is already being taken along with the benzodiazepine, it is important to continue the antidepressant until after benzodiazepine withdrawal is complete. Withdrawal from the antidepressant can be considered separately at a later stage.

Aggressive disorders are also associated with low serotonin activity (among other factors) and the appearance of anger and irritability during benzodiazepine withdrawal may involve similar mechanisms as depression. However, these symptoms usually disappear spontaneously and do not last very long. Obsessive disorders (Obsessive Compulsive Disorder, OCD) also respond to SSRIs, suggesting a similar mechanism. Obsessive traits may be temporarily increased during withdrawal and seem to reflect a mixture of anxiety and depression. These tend to settle spontaneously as anxiety levels decline.

Muscle symptoms. Benzodiazepines are efficient muscle relaxants and are used clinically for spastic conditions ranging from spinal cord disease or injury to the excruciating muscle spasms of tetanus or rabies. It is therefore not surprising that their discontinuation after long-term use is associated with a rebound increase in muscle tension. This rebound accounts for many of the symptoms observed in benzodiazepine withdrawal. Muscle stiffness affecting the limbs, back, neck and jaw are commonly reported, and the constant muscle tension probably accounts for the muscle pains which have a similar distribution. Headaches are usually of the "tension headache" type, due to contraction of muscles at the back of the neck, scalp and forehead - often described as a "tight band around the head". Pain in the jaw and teeth is probably due to involuntary jaw clenching, which often occurs unconsciously during sleep.

At the same time, the nerves to the muscles are hyperexcitable, leading to tremor, tics, jerks, spasm and twitching, and jumping at the smallest stimulus. All this constant activity contributes to a feeling of fatigue and weakness ("jelly-legs"). In addition, the muscles, especially the small muscles of the eye, are not well co-ordinated, which may lead to blurred or double vision or even eyelid spasms (blepharospasm).

None of these symptoms is harmful, and they need not be a cause of worry once they are understood. The muscle pain and stiffness is actually little different from what is regarded as normal after an unaccustomed bout of exercise, and would be positively expected, even by a well-trained athlete, after running a marathon.

There are many measures that will alleviate these symptoms, such as muscle stretching exercises as taught in most gyms, moderate exercise, hot baths, massage and general relaxation exercises. Such measures may give only temporary relief at first, but if practised regularly can speed the recovery of normal muscle tone - which will eventually occur spontaneously.

Bodily sensations. All sorts of strange tinglings, pins and needles, patches of numbness, feelings of electric shocks, sensations of hot and cold, itching, and deep burning pain are not uncommon during benzodiazepine withdrawal. It is difficult to give an exact explanation for these sensations but, like motor nerves, the sensory nerves, along with their connections in the spinal cord and brain, become hyperexcitable during withdrawal. It is possible that sensory receptors in skin and muscle, and in the tissue sheaths around bones, may fire off impulses chaotically in response to stimuli that do not normally affect them.

These sensory symptoms, though disconcerting, are usually nothing to worry about. Very occasionally, they may persist. Meanwhile, the same measures suggested under muscle symptoms can do much to alleviate them, and they usually disappear after withdrawal.

Heart and lungs. Palpitations, pounding heart, rapid pulse, flushing, sweating, and breathlessness are usual accompaniments of panic attacks, but may occur without panics. They do not signify heart or lung disease but are simply the expression of an overactive autonomic nervous system. Slow deep breathing and relaxation can do much to control these symptoms. Do not worry about them: they would be accepted as normal if you were running for a bus, and will do no more harm than if you really were!

Problems with balance. Some people during benzodiazepine withdrawal report feeling unsteady on their feet; sometimes they feel they are being pushed to one side or feel giddy, as if things were going round and round. An important organ in controlling motor stability and maintaining equilibrium is a part of the brain called the cerebellum. This organ is densely packed with GABA and benzodiazepine receptors and is a prime site of action of benzodiazepines. Excessive doses of benzodiazepines, like alcohol, cause unsteadiness of gait, slurred speech and general incoordination, including inability to walk in a straight line. It may take some time for the cerebellar systems to restabilise after benzodiazepine withdrawal and the symptoms can last until this process is complete. Exercises, such as standing on one leg, first with eyes open, then with eyes closed, can speed recovery.

Digestive problems. Some people have no problems at all with their digestive systems during or after withdrawal, and may even notice that they are enjoying their food more. Others, perhaps more prone constitutionally, may complain of a range of symptoms associated with "irritable bowel syndrome" (IBS). These can include nausea, vomiting, diarrhoea, constipation, abdominal pain, flatulence, gaseous distension and heartburn. Quite a few have found these symptoms so uncomfortable that they have undergone hospital gastrointestinal investigations, but usually no abnormality is found. The symptoms may be partly due to overactivity in the autonomic nervous system, which controls the motility and secretions of the gut and is very reactive to stress, including the stress of benzodiazepine withdrawal. In addition, there are benzodiazepine receptors in the gut. It is not clear what the functions of these receptors are or how they are affected by benzodiazepines or benzodiazepine withdrawal, but alterations in these receptors may play some part in increasing gut irritability.

Considerable loss of weight (8-10lb or more) sometimes occurs in withdrawal. This may be due to a rebound effect on appetite, since benzodiazepines have been shown to increase appetite in animals. On the other hand, some people gain weight in withdrawal. In any case, weight changes are not severe enough to worry about and normal weight is soon regained after withdrawal. A few people have difficulty

in swallowing food - the throat seems to tighten up especially if eating in company. This is usually a sign of anxiety and is well-known in anxiety states. Practising relaxation, eating alone, taking small well chewed mouthfuls with sips of liquid and not hurrying make things easier and the symptom settles as anxiety levels decline.

Immune system. "Why do I get so many infections?" This question is commonly asked by patients withdrawing from benzodiazepines. They seem to be prone to colds, sinusitis, ear infections, cystitis, oral and vaginal thrush (candida), other fungal infections of the skin and nails, cracked lips, mouth ulcers and influenza. Also common are complaints of adverse reactions to antibiotics used to treat some of the bacterial infections.

It is not clear whether there really is an increased incidence of infections in people undergoing benzodiazepine withdrawal, because there have been no comparisons with otherwise similar populations who have not been exposed to benzodiazepines. However, many factors affect the immune system. One of these is stress, with increased output of the stress hormone, cortisol, which inhibits immune responses. Another factor is depression, also related to stress and associated with increased cortisol secretion. Increased cortisol levels can reduce resistance to infection and also cause flare-ups of incipient infection. Benzodiazepine withdrawal can clearly be stressful but, strangely, in patients that I have tested, blood cortisol concentrations have been low. So this subject remains a mystery and probably merits further research. The message for people undergoing benzodiazepine withdrawal is to try to lead a healthy lifestyle, which includes a balanced diet, plenty of exercise and rest, and avoidance of extra stress where possible. Slow dosage tapering is the best way to reduce the stress of withdrawal.

Endocrine problems. Benzodiazepines undoubtedly have effects on the endocrine system, but these have not been closely studied in humans, either during long-term benzodiazepine use or in withdrawal. Many women complain of menstrual problems but these are common in the general population and there is no clear evidence that they are directly attributable to benzodiazepines. A proportion of female long-term benzodiazepine users have had hysterectomies, but again there is no evidence of a direct link with benzodiazepine use. Occasionally both men and women on benzodiazepines complain of breast swelling or engorgement and it is possible that benzodiazepines affect secretion of the hormone prolactin. Endocrine symptoms that are due to benzodiazepines improve after withdrawal.

Fits, convulsions. Benzodiazepines are potent anticonvulsants. They can be life-saving in status epilepticus (repeated fits, one after another) and in fits caused by overdose of certain drugs (for example, tricyclic antidepressants). However, rapid withdrawal, especially from high potency benzodiazepines, can precipitate epileptic fits as a rebound reaction. Such an occurrence is extremely rare with slowly eliminated benzodiazepines (e.g. diazepam) or with slow dosage tapering. If a fit does occur in these circumstances, it is usually only a single fit and causes no lasting damage. Other phenomena seen in rapid withdrawal are psychotic symptoms, severe confusion and delirium, but again these hardly ever occur with slow dosage tapering. By following the withdrawal schedules, you can be confident of avoiding these complications.

EXTRA MEDICATION DURING BENZODIAZEPINE WITHDRAWAL

"Is there any medication I can take to help me through withdrawal?" This question is sometimes asked by people embarking on a benzodiazepine tapering program. In contrast, others are so against drugs when they decide on withdrawal that they are loth to take anything, even the simplest pain killer. The answer to the first question is that there is no medication which will substitute for a benzodiazepine, unless it is another benzodiazepine, or a drug with benzodiazepine-like properties (such as barbiturates or zolpidem [Ambien]). All such drugs should be avoided as they only substitute one type of dependence for another. (There is a method, advocated by some US doctors, in which phenobarbitone, a long-acting barbiturate, is substituted for a benzodiazepine and then slowly withdrawn, but this method has no particular advantages over tapering directly from a long-acting benzodiazepine).

However, there are some drugs which may help to control particular symptoms in withdrawal and which deserve consideration in certain situations though not recommended for routine use. Usually they will only be required temporarily, but they can sometimes ease a difficult situation and enable the user to proceed with the withdrawal program.

Antidepressants. Antidepressants are the most important adjuvant drugs to consider in withdrawal. As mentioned before, depression can be a real problem in withdrawal and can sometimes be severe enough to pose a risk of suicide, though this is unusual with slow tapering. Like any other depression, the depression in withdrawal responds to antidepressant drugs and is probably caused by the same chemical changes in the brain. Both the "old fashioned" tricyclic antidepressants (doxepin [Sinequan], amitriptyline [Elavil]) and the selective serotonin reuptake inhibitors (SSRIs; fluoxetine [Prozac], paroxetine [Paxil]) can be effective and an antidepressant drug may be indicated if depression is severe. There is a school of thought, mainly amongst ex-tranquilliser users, that is opposed to the taking of any other drugs during withdrawal. But suicides have occurred in several reported clinical trials of benzodiazepine withdrawal. If depression is severe during benzodiazepine withdrawal as in any other situation, it seems foolhardy to leave it untreated.

There are, however, some disadvantages with antidepressants. One is that they take 2-3 weeks or more to become really effective. This means that the patient, and his/her mentor, must be on the look-out for depression so that treatment, if advised by the doctor, can start early. The second drawback is that anxiety may be temporarily worsened at the start of treatment either with tricyclics or SSRIs. This is a particular risk during benzodiazepine withdrawal when anxiety levels are usually high. To avoid aggravation of anxiety, it is important to start with the lowest possible dose of an antidepressant and then work up slowly, over two or three weeks. Do not be persuaded by your doctor to start immediately on the "therapeutic" dose for depression. There are also fears that antidepressants such as Prozac may in some patients induce an agitated, violent or suicidal state at the start of treatment; low initial dosage and careful monitoring may avoid this risk.

It is usually possible to continue with slow benzodiazepine tapering while starting on an antidepressant, although some may prefer to halt their programme for 2-3 weeks until the antidepressant has "taken hold" (but increasing the benzodiazepine dose should be strenuously avoided). Antidepressants not only alleviate depression but also, after 2-3 weeks, have anti-anxiety effects. They are in fact a better long-term treatment than benzodiazepines for anxiety, panic and phobic disorders, and may in some cases actively help the benzodiazepine withdrawal process.

Once started on an antidepressant for depression, the treatment should be continued for some months (usually about 6 months) to avoid recurrence of the depression. Benzodiazepine tapering can continue during this time, and the antidepressant will sometimes act as a welcome umbrella during the last stages of withdrawal. It is important to finish the benzodiazepine withdrawal before starting to withdraw the antidepressant. Quite often, people taking long-term benzodiazepines are already taking an antidepressant as well. In this case they should stay on the antidepressant until the benzodiazepine withdrawal is complete.

Another drawback of antidepressants is that they, too, cause withdrawal reactions if they are stopped suddenly, a fact which has not always been appreciated by doctors. Antidepressant withdrawal symptoms include increased anxiety, sleep difficulties, influenza-like symptoms, gastrointestinal symptoms, irritability and tearfulness - not much different, in fact, from benzodiazepine withdrawal symptoms. These reactions can be prevented by slow tapering of the antidepressant dosage over about 1-3 months. Most people who have withdrawn from benzodiazepines will be experts at tapering dosages when the time comes to stop the antidepressant and will be able to work out a rate of withdrawal that suits them.

Apart from their therapeutic effects in depression and anxiety, some antidepressants have a sedative effect which patients who are particularly plagued with insomnia have found helpful. Low doses (10-50mg) of amitriptyline (Elavil) or doxepin (Sinequan) are remarkably effective in promoting sleep if taken at bed-time. These can be taken for short periods of a few weeks and stopped by reducing the dosage

stepwise or taking the drug every other night. Withdrawal is not a problem when small doses are taken for short periods or intermittently.

TABLE 2. ANTIDEPRESSANT WITHDRAWAL SYMPTOMS

PHYSICAL SYMPTOMS

Gastrointestinal: abdominal pain, diarrhoea, nausea, vomiting
Influenza-like: fatigue, headache, muscle pain, weakness, sweating, chills, palpitations
Sleep disturbance: insomnia, vivid dreams, nightmares
Sensory disturbances: dizziness, light-headedness, vertigo,
pins and needles, electric shock sensations
Motor disorders: tremor, loss of balance, muscle stiffness, abnormal movements

PSYCHOLOGICAL SYMPTOMS

Anxiety, agitation
Crying spells
Irritability
Overactivity
Aggression
Depersonalisation
Memory Problems
Confusion
Lowered mood

Beta-blockers. In a few cases, severe palpitations, muscle tremors or motor jerks develop during benzodiazepine withdrawal and hinder progress. These symptoms can be controlled or ameliorated by beta-blocking drugs such as propranolol (Inderal). Drugs of this type inhibit the effects of excess epinephrine and norepinephrine (adrenaline and noradrenaline) released by an overactive sympathetic nervous system. They slow the heart and prevent excess muscle activity. Although they have little effect on psychological symptoms, they can cut the vicious circle in which palpitations or tremor create anxiety which leads to yet more palpitations. Some people in benzodiazepine withdrawal take small doses of these drugs (10-20mg Inderal three times daily) regularly, while others reserve them to take only if the physical symptoms of a panic attack seem uncontrollable. They are not a cure, but can sometimes help people through a difficult situation. In larger doses, beta-blockers are used for raised blood pressure and angina, but such doses are not advised in benzodiazepine withdrawal. They should not be taken by anyone who has asthma as they can cause constriction of the bronchial tubes. If beta-blockers have been used regularly for any length of time, they should be withdrawn slowly by tapering the dosage, as they too can cause a withdrawal reaction of increased heart rate and palpitations.

Hypnotics and sedatives. Most other hypnotics and sedatives act in a similar way to benzodiazepines, including barbiturates, chloral derivatives (Noctec), ethchlorvynol (Placidyl), zopiclone (Zimovane, Imovane), zolpidem (Ambien), zaleplon (Sonata) and, incidentally, alcohol. None of these drugs should be used as alternative sleeping pills or sleeping draughts during benzodiazepine withdrawal. All can cause a similar type of dependence and some are more toxic than benzodiazepines.

If sleep is really a problem, a small dose of a tricyclic antidepressant with sedative effects is a possible option. Alternatively, an antihistamine with sedative effects (e.g. diphenylhydramine [Benadryl], promethazine [Phenergan]) may be used temporarily. Neither antidepressants nor antihistamines act by the same mechanisms as benzodiazepines.

Some drugs related to major tranquillisers have sedative effects and are also used for nausea, vertigo and motion sickness. These are sometimes prescribed during withdrawal, especially prochlorperazine (Compazine). However, such drugs can have serious side effects (motor disorders like Parkinson's disease) and are not recommended for long-term use or as a substitute for benzodiazepines.

Other drugs. Several other drugs have been tested in clinical trials of benzodiazepine withdrawal to see if they could speed the process, prevent or alleviate withdrawal symptoms, or improve the long-term success rate. Many of these trials have involved what is considered here as over-rapid withdrawal.

There have been some reports that gabapentin (Neurontin), tiagabine (Gabitril) and possibly pregabalin (yet to be licensed) help with sleep and anxiety in withdrawal. However, there have been no controlled trials and it is not clear whether these drugs themselves cause withdrawal effects. In practice additional drugs are seldom needed with very slow benzodiazepine tapering. Only in special situations there might be a place for an antidepressant, beta blocker, sedative antihistamine or anticonvulsant. There is no need to avoid ordinary pain killers such as Tylenol, Feldene etc. for everyday aches and pains.

BENZODIAZEPINE USE DURING AND AFTER WITHDRAWAL

What happens if someone who is in the course of benzodiazepine withdrawal or has successfully withdrawn needs a surgical operation? Benzodiazepines are of value as premedication before major operations and for sedation and amnesia during minor surgical procedures. Yet many ex-users are terrified that if they are given a benzodiazepine for these purposes they will become dependent all over again. They can be reassured: a single dose of a benzodiazepine given for an operation does not bring back the addiction, although the stress of an operation may re-awaken the anxiety symptoms experienced during benzodiazepine withdrawal. Symptoms reported under these circumstances have usually been the result of fear. Many personally observed patients have had repeated doses of midazolam (Versed, Hypnovel), a short-acting benzodiazepine, for dental procedures (dental phobia is common in withdrawal), and other benzodiazepines including diazepam for major and minor surgery and have recovered without complications.

Also, people who have gone back on benzodiazepines, having failed at the first attempt at withdrawal, can be just as successful at tapering as first-timers.

DIET, FLUIDS AND EXERCISE

There has been increasing interest in the question of diet in benzodiazepine withdrawal, particularly in North America. What food/drinks should be excluded? What supplements should be added? These are frequent questions. In my opinion there is no need to be over-obsessive about diet. Some people advise that caffeine and alcohol should be completely ruled out. However, the point about gradual dosage tapering at home is that people should get used to living a normal lifestyle without drugs. In my experience, coffee or tea in moderation (about two cups a day), or reasonable amounts of cocoa, chocolate or coca cola, are perfectly compatible with benzodiazepine withdrawal - except in the few individuals who are exquisitely sensitive to caffeine or those with very high anxiety levels. Clearly one should not take caffeine late in the evening or drink cups of tea/coffee (unless decaffeinated) in the middle of the night if insomniac, but to prohibit a cup of tea/coffee at breakfast is in general unduly restrictive. One is, after all, striving to be normal and sociable, not fussy.

Similarly with alcohol: a glass or two of wine is perfectly permissible (and even said by some to be advisable for health). Although it is important not to substitute increasing doses of alcohol for decreasing doses of benzodiazepines, there is no need to deny oneself small pleasures. Moderation is the key: there is no call to be puritanical.

The same principles apply to food. Humans are singularly well adapted through evolution to obtain the nutrients they need from a wide variety of diets and to eliminate unwanted products. A normal healthy diet which includes generous amounts of fruit and vegetables and a source of protein and fats (from meat or vegetables), and not too much pure sugar or "junk foods", provides all the nutrients a person needs. There is no general need for dietary supplements or extra vitamins or minerals or for "detoxifying" measures. All these can be harmful in excess. Advice to cut out white flour, white sugar etc. may help certain individuals but I have also observed that overly restrictive diets can have adverse effects. Some people say they have felt much better after going on a particular diet - this makes one wonder what sort of diet they were eating before!

Individuals may find they are intolerant of certain foods although this is not usually a true allergy. In this case, let common sense prevail and avoid such foods for a while. If in doubt, get the advice of a reliable and unbiased nutritionist, but in general stick to a normal healthy diet without food fads. Before diets became "fashionable" thousands of people successfully came off their benzodiazepines in many different countries with widely varying dietary habits without restriction - and this continues today.

A normal diet includes a normal amount of fluid consumption. Requirements for water and salt vary with body size, environmental temperature, amount of exercise, etc. so cannot be stated categorically. However, there is no need to drink extra amounts of fluid during withdrawal with the idea of "flushing out impurities/toxins". The body is very good at doing this, even at minimal fluid consumption, and surplus water is simply excreted.

Regular moderate exercise is recommended during withdrawal as it maintains general fitness, builds up stamina, increases the circulation to brain, muscle and skin and improves mood, but there is no point in slavishly doing exercises that you hate. The aim is to lead a healthy lifestyle which by definition includes some exercise in a form that is enjoyable for you.

Smoking. I hardly dare to mention smoking in view of present day attitudes to this unfortunate addiction, but for those who are smokers it is probably asking too much to attempt to stop smoking and withdraw benzodiazepines at the same time. Many people have found that giving up smoking is easier when they are off benzodiazepines, when the desire for nicotine may even wane somewhat. In general, excessive worrying over your undesirable habits (or your diet) can add to the stress of withdrawal. It is better to relax a bit and be gentle with yourself.

COURSE OF WITHDRAWAL

During benzodiazepine withdrawal, symptoms characteristically wax and wane, varying in severity and type from day to day, week to week, and even during the course of a day. Some symptoms come and go; others may take their place. There is no need to be discouraged by these wave-like recurrences; the waves become less severe and less frequent as time passes. Typically "Windows" of normality, when you feel positively well for a few hours or days, appear after some weeks; gradually the "Windows" become more frequent and last longer, while any intervening discomfort ebbs away.

It is impossible to give an exact time for the duration of withdrawal symptoms. It depends on where you start from, how much support you need and receive, how you manage your taper and many other factors. With slow tapering, some long-term users have virtually lost all their symptoms by the time they take their last tablet, and in the majority symptoms disappear within a few months. Vulnerability to extra stress may last somewhat longer and a severe stress may - temporarily - bring back some symptoms. Whatever your symptoms, it is best not to dwell on them. Symptoms are just symptoms after all and most of them in withdrawal are not signs of illness but signals of recovery. Furthermore, as your mind clears, you can work out more and more effective ways to deal with them so that they become less significant.

One reassuring finding from many clinical studies is that eventual success in withdrawal is not affected by duration of use, dosage or type of benzodiazepine, rate of withdrawal, severity of symptoms, psychiatric diagnosis, or previous attempts at withdrawal. Thus from almost any starting point, the motivated long-term user can proceed in good heart.

PROTRACTED WITHDRAWAL SYMPTOMS

A minority of people who have withdrawn from benzodiazepines seem to suffer long-term effects - protracted symptoms that just don't go away after months or even years. It has been estimated that perhaps 10-15 per cent of long-term benzodiazepine users develop a "post-withdrawal syndrome". Many of these people have taken benzodiazepines for 20 years or more and/or have had bad experiences in

withdrawal. The incidence of protracted symptoms in those who have undergone a slow taper under their own control is almost certainly very much lower.

Table 3 shows the symptoms most likely to be long-lasting. These include anxiety, insomnia, depression, various sensory and motor symptoms, gastrointestinal disturbances, and poor memory and cognition. The reasons why these symptoms persist in some people are not clear. Probably many factors are involved, some directly due to the drug and some to indirect or secondary effects.

TABLE 3. SOME PROTRACTED BENZODIAZEPINE WITHDRAWAL SYMPTOMS

Symptoms	Usual Course
Anxiety	- Gradually diminishing over a year
Depression	- May last a few months; responds to antidepressant drugs
Insomnia	- Gradually diminishing over 6-12 months
Sensory symptoms: tinnitus, tingling, numbness, deep or burning pain in limbs, feeling of inner trembling or vibration, strange skin sensations	- Gradually receding but may last at least a year and occasionally several years
Motor symptoms: muscle pain, weakness, painful cramps, tremor, jerks, spasms, shaking attacks	- Gradually receding but may last at least a year and occasionally several years
Poor memory and cognition	- Gradually receding but may last at least a year and occasionally several years
Gastrointestinal symptoms	- Gradually improving but may last a year and occasionally several years

TABLE 4. SOME POSSIBLE CAUSES OF PROTRACTED BENZODIAZEPINE WITHDRAWAL SYMPTOMS

Possible mechanisms	Effects
1. Learning of stress-coping strategies blocked by benzodiazepine use exposed on withdrawal	Anxiety, vulnerability to stress
2. Impairment of memory caused by benzodiazepines prevents normal resolution of distressing life events which are exposed on withdrawal	Anxiety, depression
3. Traumatic experiences during previous withdrawal	Post-traumatic stress symptoms
4. (?) Biochemical alterations caused by benzodiazepines (serotonin, norepinephrine [noradrenalin], stress hormones)	Depression
5. Nervous system hyperexcitability due to persisting changes in GABA/benzodiazepine receptors	Sensory and motor symptoms, anxiety, insomnia
6. (?) Structural or functional damage to brain tissue	Poor memory and cognition
7. (?) Changes in gut and immune systems	Gastrointestinal symptoms
8. (?) Long-term retention of benzodiazepines in tissues of the body	Prolongs nervous system hyperexcitability

(?) indicates possible mechanisms for which at present there is no scientific evidence

Anxiety. Anxiety persisting after the acute phase of withdrawal may be partly due to the uncovering of a learning defect caused by the benzodiazepines. These drugs specifically impair the learning of new skills,

including stress-coping strategies. Such skills are normally acquired continuously from childhood to middle age or later as experience of life accumulates. Their development may be blocked for a period of years during which benzodiazepines are taken. After withdrawal the ex-user is left in a vulnerable state with a decreased ability to deal with stressful situations. Full recovery may require many months of learning new stress-coping strategies to replace the years when this facility was blanketed by pills.

Secondly, benzodiazepine withdrawal may uncover life problems that have never been fully addressed. For example, the impairment of memory caused by benzodiazepines may prevent the normal resolution of personal stresses such as bereavement or a car crash. Such buried or half-forgotten experiences may have to be faced after withdrawal and may prolong both anxiety and depression. It is not uncommon for a widow or widower, first prescribed benzodiazepines on the death of the spouse, to go through the grieving process for the first time after withdrawal, even though the bereavement had occurred many years previously.

A third factor may operate in people who have had frightening experiences during withdrawal. This is not uncommon in those who have undergone rapid withdrawal without adequate explanation, often in hospital or detoxification centres but sometimes at home when their doctor has withdrawn prescriptions. Such people may develop symptoms of post-traumatic stress disorder (PTSD) in which their experiences are constantly repeated as flashbacks or nightmares and so prolong the anxiety.

In addition, many (though by no means all) long-term benzodiazepine users are constitutionally highly strung, sensitive people with relatively low self-esteem, whose anxiety problems have led to the prescription of benzodiazepines in the first place and whose continuing anxiety (possibly heightened by the benzodiazepines) has prompted the doctor to go on prescribing the drugs. It may take a long time for these people to regain, or attain, full confidence in themselves.

Despite these factors, protracted anxiety symptoms, including agoraphobia and panics, do tend to subside gradually and rarely last more than a year. The process may be hastened by good psychological support and by the measures described under acute anxiety symptoms. Believe it or not, people often feel more self-confident after withdrawal than they did before starting to take benzodiazepines.

Depression. Depression may be caused or aggravated by chronic benzodiazepine use, but is also a feature of the withdrawal syndrome. Depressive symptoms may appear for the first time after withdrawal, sometimes after a delay of a few weeks, and it can be severe and protracted for some months. It is not clear whether people who have had depression before, or have a family history of depression, are more prone to this complication, and its causes are not understood. Benzodiazepines disrupt the function of many neurotransmitters and hormones and depression could be the result, for example, of low serotonin activity combined with the stress of withdrawal. If severe enough to require definitive treatment, the depression in withdrawal responds to antidepressant drugs and/or cognitive therapy and usually diminishes gradually over 6-12 months.

Insomnia. Poor sleep is a common accompaniment of both anxiety and depression. In anxiety there is typically a difficulty in falling asleep, while depression is associated with early morning waking as well as frequent waking during the night. Insomnia is also common as an acute withdrawal symptom along with nightmares and other sleep disturbances. Occasionally, however, insomnia (sometimes with "restless legs" and muscle jerks) persists as an isolated symptom after other symptoms have disappeared, and may last for many months. However, poor sleepers can be reassured that an adequate sleep pattern does return at last. There are powerful natural mechanisms in the body which ensure that the brain does not become severely sleep-deprived.

Sensory and motor disturbances. There is no doubt that benzodiazepine withdrawal leaves in its wake a nervous system that is exquisitely sensitive to all sensory and motor stimuli. Usually this state settles in a few weeks but occasionally disturbing sensations persist.

To Page One

One of the most distressing sensory symptoms is **tinnitus**, a constant ringing or hissing in the ears which has been noted in several studies of benzodiazepine withdrawal. One lady described her tinnitus as a "needle of sound" piercing deep inside her head. Tinnitus is often associated with a degree of hearing loss and is not uncommon in people with partial nerve deafness who have never taken benzodiazepines. Nevertheless, it often makes its first appearance during benzodiazepine withdrawal in people who have had hearing loss for years. Also, it may be unilateral or precisely localised, even in those with symmetrical bilateral hearing loss. Whether people who have taken long-term benzodiazepines are particularly prone to tinnitus and if so why, is not known. It can persist for years and does not always respond to the usual treatments for tinnitus (maskers, etc); nor is it always relieved by restarting benzodiazepines. However, people with persisting tinnitus after withdrawal should seek the advice of a hearing specialist and may be lucky enough to find a clinic which specialises in this symptom.

A number of unpleasant bodily sensations may persist after withdrawal including tingling, "pins and needles" or patches of numbness in the trunk, face, limbs and fingers. These may be accompanied by burning pain or aches that sometimes seem to originate deep in the muscles or bones. Some people complain of an "inner trembling" or a sense of vibration, and some have described bizarre sensations as of water or slime running over the body or a serpent-like writhing on the scalp. Motor symptoms that may persist include muscle tension, weakness, cramps, jerks, spasms and shaking attacks.

Possible mechanisms of persisting sensory and motor symptoms. Although the above symptoms are often made worse by stress, they are clearly not simply due to anxiety. They suggest a dysfunction in motor and sensory pathways in the spinal cord and/or brain. A possible clue to their mechanism is provided by a trial with flumazenil (Anexate, Romazicon) a benzodiazepine receptor antagonist. This drug, when infused intravenously brought rapid relief of protracted symptoms (muscle tension, "pins and needles", weakness, muscle cramps or jerks, burning, tremor or shaking) that had been present for 5-42 months post-withdrawal in 11 patients. The symptoms were improved by 27-82 percent and the greatest response occurred in patients with the lowest anxiety ratings. There was no response to infusions of saline solution.

Flumazenil is thought to act by "resetting" GABA/benzodiazepine receptors so that they are more receptive to the inhibitory actions of GABA. The results suggest that some protracted symptoms are due to the failure of the receptors to revert to their normal state after they have become unresponsive to GABA, due to the development of tolerance. The response to flumazenil also shows that benzodiazepines can cause longer-lasting pharmacological effects than previously believed.

Unfortunately, flumazenil does not at present offer a practical cure for protracted symptoms. The drug has to be infused intravenously and is very short acting so that symptom relief is only temporary. The drug cannot be given to a person who is still taking benzodiazepines as it precipitates an acute withdrawal reaction. However, although protracted sensory and motor symptoms may sometimes seem to be almost permanent, they do in fact decline in severity over the years, even without flumazenil, and they do not signify a major neurological illness. Such symptoms may be partially alleviated by relaxation techniques; some motor and sensory systems may respond to carbamazepine (Tegretol) and motor symptoms may respond to propranolol (Inderal).

Poor memory and cognition. Although it is well known that benzodiazepines impair memory and some cognitive functions, particularly the ability to sustain attention, some long-term users complain of continued loss of intellectual abilities persisting after withdrawal. There have been several studies on this question which indicate that improvement may be very slow. The longest studies in therapeutic dose long-term users extend for only 10 months after withdrawal. Cognitive impairment, though slowly improving, persisted for at least this time and was not related to anxiety levels. Some Swedish studies have found that intellectual impairment, although improved, was still present 4-6 years after cessation of benzodiazepine use, but it was not clear whether high dosage and/or alcohol use were added factors.

Do benzodiazepines cause structural brain damage? These results have raised the question of whether benzodiazepines can cause structural brain damage. Like alcohol, benzodiazepines are fat

soluble and are taken up by the fat-containing (lipid) membranes of brain cells. It has been suggested that their use over many years could cause physical changes such as shrinkage of the cerebral cortex, as has been shown in chronic alcoholics, and that such changes may be only partially reversible after withdrawal. However, despite several computed tomography (CT) scan studies, no signs of brain atrophy have been conclusively demonstrated in therapeutic dose users, and even the results in high dose abusers are inconclusive. It is possible that benzodiazepines can cause subtle changes which are not detected by present methods, but on the available evidence there is no reason to think that any such changes would be permanent.

Gastrointestinal symptoms. Gastrointestinal symptoms may be prolonged after withdrawal, usually in people who have a previous history of digestive troubles. Such people may develop apparent intolerance to certain foods, although reliable tests for true food allergy (e.g. antibodies against specific food constituents) are nearly always negative. Nevertheless many sufferers feel that they have damage to the immune system or have developed intestinal candidiasis. There is at present no clear scientific evidence on these topics, though as mentioned before, benzodiazepine receptors are present in the gut and benzodiazepine use or withdrawal may affect immune responses. There is some evidence that chronic hyperventilation provokes the release of histamine (a substance released in allergic reactions) and that the incidence of food-intolerance and "pseudo-allergic" reactions is high in chronic hyperventilators. Advice on diet, breathing and candida infections is given in books by Shirley Trickett quoted at the end of this chapter. It is usually inadvisable to stick to a strict exclusion diet; with a normal balanced diet and sensible general health measures, including regular exercise, gastrointestinal symptoms due to withdrawal gradually abate.

Coping with protracted symptoms. A number of people are expressing fears that some benzodiazepine withdrawal symptoms last for ever, and that they can never completely recover. Particular concerns have been raised about impairment of cognitive functions (such as memory and reasoning) and other lingering problems such as muscle pains and gastrointestinal disturbances.

People with such worries can be reassured. All the evidence shows that a steady decline in symptoms almost invariably continues after withdrawal, though it can take a long time - even several years in some cases. Most people experience a definite improvement over time so that symptoms gradually decrease to levels nowhere near as intense as in the early days of withdrawal, and eventually almost entirely disappear. All the studies show steady, if slow, improvement in cognitive ability and physical symptoms. Although most studies have not extended beyond a year after withdrawal, the results suggest that improvement continues beyond this time. There is absolutely no evidence that benzodiazepines cause permanent damage to the brain, nervous system or body.

People bothered by long-term symptoms can do a lot to help themselves. For example:

1. Exercise your body. Physical exercise improves the circulation and function of both brain and body. Find an exercise that you enjoy: start at low level, work up gradually and keep it up regularly. Exercise also helps depression, decreases fatigue and increases general fitness.
2. Exercise your brain. Use your brain to devise methods to improve its efficiency: make lists, do crossword puzzles, find out what bothers you most - there is always a way round it. Cognitive retraining helps people to find ways around their temporary impairment.
3. Increase your interests. Finding an outside interest which you have to work at employs the brain, increases motivation, diverts attention away from your own symptoms and may even help others.
4. Calm your emotions. Above all, stop worrying. Worry, fear and anxiety increase all withdrawal symptoms. Many of these symptoms are actually due to anxiety and not signs of brain or nervous system damage. People who fear withdrawal have more intense symptoms than those who just take it as it comes and think positively and confidently about recovery.

To Page One

How long do benzodiazepines stay in the body after withdrawal? This question is often asked by people with long-term symptoms. Is it possible that one cause of protracted symptoms is that benzodiazepines remain in the body even after months, lurking perhaps deep in such tissues as brain and bones? Could slow elimination from these sites keep the withdrawal symptoms going?

Like many other issues concerning benzodiazepines, the answers to these questions are still unclear. Benzodiazepine concentrations in the blood have been measured and shown to reach undetectable levels in 3-4 weeks after cessation of use in people withdrawn from clinical doses. Information on benzodiazepine concentrations in the brain and other tissues is difficult to obtain, especially in humans. Benzodiazepines certainly enter the brain and also dissolve in all fatty (lipid-containing) tissues including fat deposits all over the body. It is possible that they linger in such tissues for some time after blood levels have become undetectable. However, most body tissues are in equilibrium with the blood that constantly perfuses them, and there is no known mechanism whereby benzodiazepines could be "locked up" in tissues such as the brain. There is no data on how long benzodiazepines remain in bones, which have a lower fat content but also a slower rate of cell turnover.

Nevertheless, the concentration of benzodiazepines remaining in body tissues after withdrawal must be very low, otherwise the drugs would leak back into the blood in discernible amounts. It is difficult to imagine that such concentrations would be sufficient to produce clinical effects or that any direct effects could last for months or years. However, it is not inconceivable that even low concentrations might be enough to prevent the return of GABA/benzodiazepine receptors in the brain to their pre-benzodiazepine state. If so, the receptors would continue to be resistant to the natural calming actions of GABA.

To Page One

Benzodiazepine Withdrawal Protocols

Diazepam

Temazopam (Restoril) 30mg/day

Lorazepam 6mg/day

Lorazepam 3mg/day

Alprazolam (Xanax) 6mg/day

Alprazolam (Xanax) 4mg/day

Oxazepam (Serax) 60mg/day

Zopiclone 15mg/night

Simple withdrawal from diazepam (Valium) 40mg daily

	Morning	Night	Total Daily Dosage
Starting dosage	diazepam 20mg	diazepam 20mg	40mg
Stage 1 (1-2 weeks)	diazepam 18mg	diazepam 20mg	38mg
Stage 2 (1-2 weeks)	diazepam 18mg	diazepam 18mg	36mg
Stage 3 (1-2 weeks)	diazepam 16mg	diazepam 18mg	34mg
Stage 4 (1-2 weeks)	diazepam 16mg	diazepam 16mg	32mg
Stage 5 (1-2 weeks)	diazepam 14mg	diazepam 16mg	30mg
Stage 6 (1-2 weeks)	diazepam 14mg	diazepam 14mg	28mg
Stage 7 (1-2 weeks)	diazepam 12mg	diazepam 14mg	26mg
Stage 8 (1-2 weeks)	diazepam 12mg	diazepam 12mg	24mg
Stage 9 (1-2 weeks)	diazepam 10mg	diazepam 12mg	22mg
Stage 10 (1-2 weeks)	diazepam 10mg	diazepam 10mg	20mg
Stage 11 (1-2 weeks)	diazepam 8mg	diazepam 10mg	18mg
Stage 12 (1-2 weeks)	diazepam 8mg	diazepam 8mg	16mg
Stage 13 (1-2 weeks)	diazepam 6mg	diazepam 8mg	14mg
Stage 14 (1-2 weeks)	diazepam 5mg	diazepam 8mg	13mg
Stage 15 (1-2 weeks)	diazepam 4mg	diazepam 8mg	12mg
Stage 16 (1-2 weeks)	diazepam 3mg	diazepam 8mg	11mg
Stage 17 (1-2 weeks)	diazepam 2mg	diazepam 8mg	10mg
Stage 18 (1-2 weeks)	diazepam 1mg	diazepam 8mg	9mg
Stage 19 (1-2 weeks)	--	diazepam 8mg	8mg
Stage 20 (1-2 weeks)	--	diazepam 7mg	7mg
Stage 21 (1-2 weeks)	--	diazepam 6mg	6mg
Stage 22 (1-2 weeks)	--	diazepam 5mg	5mg
Stage 23 (1-2 weeks)	--	diazepam 4mg	4mg
Stage 24 (1-2 weeks)	--	diazepam 3mg	3mg
Stage 25 (1-2 weeks)	--	diazepam 2mg	2mg
Stage 26 (1-2 weeks)	--	diazepam 1mg	1mg

Withdrawal from alprazolam (Xanax) 4mg daily with diazepam (Valium) substitution (4mg alprazolam is approximately equivalent to 80mg diazepam)

	Morning	Midday	Afternoon	Evening	Daily Diazepam Equivalent
Starting dosage	alprazolam 1mg	alprazolam 1mg	alprazolam 1mg	alprazolam 1mg	80mg
Stage 1 (1 week)	alprazolam 1mg	alprazolam 1mg	alprazolam 1mg	alprazolam 0.5mg diazepam 10mg	80mg
Stage 2 (1 week)	alprazolam 1mg	alprazolam 0.5mg diazepam 10mg	alprazolam 1mg	alprazolam 0.5mg diazepam 10mg	80mg
Stage 3 (1 week)	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	alprazolam 1mg	alprazolam 0.5mg diazepam 10mg	80mg
Stage 4 (1 week)	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	80mg
Stage 5 (1 week)	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	80mg
Stage 6 (1-2 weeks)	alprazolam 0.5mg diazepam 10mg	alprazolam 0.25mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	diazepam 20mg	75mg
Stage 7 (1-2 weeks)	alprazolam 0.25mg diazepam 10mg	alprazolam 0.25mg diazepam 10mg	alprazolam 0.5mg diazepam 10mg	diazepam 20mg	70mg
Stage 8 (1-2 weeks)	alprazolam 0.25mg diazepam 10mg	alprazolam 0.25mg diazepam 10mg	alprazolam 0.25mg diazepam 10mg	diazepam 20mg	65mg
Stage 9 (1-2 weeks)	alprazolam 0.25mg diazepam 10mg	Stop alprazolam diazepam 10mg	alprazolam 0.25mg diazepam 10mg	diazepam 20mg	60mg
Stage 10 (1-2 weeks)	Stop alprazolam diazepam 10mg	diazepam 10mg	alprazolam 0.25mg diazepam 10mg	diazepam 20mg	55mg
Stage 11		diazepam 10mg	Stop alprazolam	diazepam	50mg

To Page One

(1-2 weeks)	diazepam 10mg		diazepam 10mg	20mg	
Stage 12 (1-2 weeks)	diazepam 10mg	diazepam 5mg	diazepam 10mg	diazepam 20mg	45mg
Stage 13 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 10mg	diazepam 20mg	40mg
Stage 14 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 5mg	diazepam 20mg	35mg
Stage 15 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 5mg	diazepam 15mg	30mg
Stage 16 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 5mg	diazepam 12.5mg	27.5mg
Stage 17 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 5mg	diazepam 10mg	25mg
Stage 18 (1-2 weeks)	diazepam 5mg	diazepam 2.5mg	diazepam 5mg	diazepam 10mg	22.5mg
Stage 19 (1-2 weeks)	diazepam 5mg	Stop diazepam	diazepam 5mg	diazepam 10mg	20mg
Stage 20 (1-2 weeks)	diazepam 4mg	--	diazepam 5mg	diazepam 10mg	19mg
Stage 21 (1-2 weeks)	diazepam 4mg	--	diazepam 4mg	diazepam 10mg	18mg
Stage 22 (1-2 weeks)	diazepam 4mg	--	diazepam 3mg	diazepam 10mg	17mg
Stage 23 (1-2 weeks)	diazepam 3mg	--	diazepam 3mg	diazepam 10mg	16mg
Stage 24 (1-2 weeks)	diazepam 3mg	--	diazepam 2mg	diazepam 10mg	15mg
Stage 25 (1-2 weeks)	diazepam 2mg	--	diazepam 2mg	diazepam 10mg	14mg
Stage 26 (1-2 weeks)	diazepam 2mg	--	Stop diazepam	diazepam 10mg	12mg
Stage 27 (1-2 weeks)	Stop diazepam	--	--	diazepam 10mg	10mg
Continue reducing diazepam by 1mg every 2 weeks (see Schedule 3, Stage 26)					

Withdrawal from high dose (6mg) alprazolam (Xanax daily with diazepam (Valium) substitution. (6mg alprazolam is approximately equivalent to 120mg diazepam)

	Morning	Midday/Afternoon	Evening/Night	Daily Diazepam Equivalent
Starting dosage	alprazolam 2mg	alprazolam 2mg	alprazolam 2mg	120mg
Stage 1 (one week)	alprazolam 2mg	alprazolam 2mg	alprazolam 1.5mg diazepam 10mg	120mg
Stage 2 (one week)	alprazolam 2mg	alprazolam 2mg	alprazolam 1mg diazepam 20mg	120mg
Stage 3 (one week)	alprazolam 1.5mg diazepam 10mg	alprazolam 2mg	alprazolam 1mg diazepam 20mg	120mg
Stage 4 (one week)	alprazolam 1mg diazepam 20mg	alprazolam 2mg	alprazolam 1mg diazepam 20mg	120mg
Stage 5 (1-2 weeks)	alprazolam 1mg diazepam 20mg	alprazolam 1mg diazepam 10mg	alprazolam 1mg diazepam 20mg	110mg
Stage 6 (1-2 weeks)	alprazolam 1mg diazepam 20mg	alprazolam 1mg diazepam 10mg	alprazolam 0.5mg diazepam 20mg	100mg
Stage 7 (1-2 weeks)	alprazolam 1mg diazepam 20mg	alprazolam 1mg diazepam 10mg	Stop alprazolam diazepam 20mg	90mg
Stage 8 (1-2 weeks)	alprazolam 0.5mg diazepam 20mg	alprazolam 1mg diazepam 10mg	diazepam 20mg	80mg
Stage 9 (1-2 weeks)	alprazolam 0.5mg diazepam 20mg	alprazolam 0.5mg diazepam 10mg	diazepam 20mg	80mg
Stage 10 (1-2 weeks)	alprazolam 0.5mg diazepam 20mg	Stop alprazolam diazepam 10mg	diazepam 20mg	60mg
Stage 11 (1-2 weeks)	Stop alprazolam diazepam 20mg	diazepam 10mg	diazepam 20mg	50mg
Stage 12 (1-2 weeks)	diazepam 25mg	Stop midday dose; divert 5mg each to morning and night doses	diazepam 25mg	50mg
Stage 13 (1-2 weeks)	diazepam 20mg	--	diazepam 25mg	45mg
Stage 14 (1-2 weeks)	diazepam 20mg	--	diazepam 20mg	40mg

Withdrawal from lorazepam (Ativan) 3mg daily with diazepam (Valium) substitution. (3mg lorazepam is approximately equivalent to 30mg diazepam)

	Morning	Midday/Afternoon	Evening/Night	Daily Diazepam Equivalent
Starting dosage	lorazepam 1 mg	lorazepam 1 mg	lorazepam 1 mg	30mg
Stage 1 (1 week)	lorazepam 1 mg	lorazepam 1 mg	lorazepam 0.5mg diazepam 5mg	30mg
Stage 2 (1 week)	lorazepam 0.5mg diazepam 5mg	lorazepam 1 mg	lorazepam 0.5mg diazepam 5mg	30mg
Stage 3 (1 week)	lorazepam 0.5mg diazepam 5mg	lorazepam 0.5mg diazepam 5mg	lorazepam 0.5mg diazepam 5mg	30mg
Stage 4 (1 week)	lorazepam 0.5mg diazepam 5mg	lorazepam 0.5mg diazepam 5mg	Stop lorazepam diazepam 10mg	30mg
Stage 5 (1 week)	Stop lorazepam diazepam 10mg	lorazepam 0.5mg diazepam 5mg	diazepam 10mg	30mg
Stage 6 (1 week)	diazepam 10mg	Stop lorazepam diazepam 10mg	diazepam 10mg	30mg
Stage 7 (1-2 weeks)	diazepam 10mg	diazepam 8mg	diazepam 10mg	28mg
Stage 8 (1-2 weeks)	diazepam 8mg	diazepam 8mg	diazepam 10mg	26mg
Stage 9 (1-2 weeks)	diazepam 8mg	diazepam 6mg	diazepam 10mg	24mg
Stage 10 (1-2 weeks)	diazepam 6mg	diazepam 6mg	diazepam 10mg	22mg
Stage 11 (1-2 weeks)	diazepam 6mg	diazepam 4mg	diazepam 10mg	20mg
Stage 12 (1-2 weeks)	diazepam 6mg	diazepam 2mg	diazepam 10mg	18mg
Stage 13 (1-2 weeks)	diazepam 6mg	Stop diazepam	diazepam 10mg	16mg
Stage 14 (1-2 weeks)	diazepam 5mg	--	diazepam 10mg	15mg
Stage 15 (1-2 weeks)	diazepam 4mg	--	diazepam 10mg	14mg
Stage 16 (1-2 weeks)	diazepam 3mg	--	diazepam 10mg	13mg
Stage 17 (1-2 weeks)	diazepam 2mg	--	diazepam 10mg	12mg
Stage 18 (1-2 weeks)	diazepam 1mg	--	diazepam 10mg	11mg
Stage 19 (1-2 weeks)	Stop diazepam	--	diazepam 10mg	10mg
Continue reducing night time diazepam by 1 mg every 1-2 weeks (See Schedule 3, Stage 26)				

Withdrawal from lorazepam (Ativan) 6mg daily with diazepam (Valium) substitution. (6mg lorazepam is approximately equivalent to 60mg diazepam)

	Morning	Midday/Afternoon	Evening/Night	Daily Diazepam Equivalent
Starting dosage	lorazepam 2mg	lorazepam 2mg	lorazepam 2mg	60mg
Stage 1 (one week)	lorazepam 2mg	lorazepam 2mg	lorazepam 1mg diazepam 10mg	60mg
Stage 2 (one week)	lorazepam 1.5mg diazepam 5mg	lorazepam 2mg	lorazepam 1mg diazepam 10mg	60mg
Stage 3 (one week)	lorazepam 1.5mg diazepam 5mg	lorazepam 2mg	lorazepam 0.5mg diazepam 15mg	60mg
Stage 4 (one week)	lorazepam 1.5mg diazepam 5mg	lorazepam 1.5mg diazepam 5mg	lorazepam 0.5mg diazepam 15mg	60mg
Stage 5 (1-2 weeks)	lorazepam 1.5mg diazepam 5mg	lorazepam 1.5mg diazepam 5mg	Stop lorazepam diazepam 20mg	60mg
Stage 6 (1-2 weeks)	lorazepam 1mg diazepam 5mg	lorazepam 1.5mg diazepam 5mg	diazepam 20mg	55mg
Stage 7 (1-2 weeks)	lorazepam 1mg diazepam 5mg	lorazepam 1mg diazepam 5mg	diazepam 20mg	50mg
Stage 8 (1-2 weeks)	lorazepam 0.5mg diazepam 5mg	lorazepam 1mg diazepam 5mg	diazepam 20mg	45mg
Stage 9 (1-2 weeks)	lorazepam 0.5mg diazepam 5mg	lorazepam 0.5mg diazepam 5mg	diazepam 20mg	40mg
Stage 10 (1-2 weeks)	Stop lorazepam diazepam 5mg	lorazepam 0.5mg diazepam 5mg	diazepam 20mg	35mg
Stage 11 (1-2 weeks)	diazepam 5mg	Stop lorazepam diazepam 5mg	diazepam 20mg	30mg
Stage 12 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 18mg	28mg
Stage 13 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 16mg	26mg
Stage 14 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 14mg	24mg
Stage 15 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 12mg	22mg
Stage 16 (1-2 weeks)	diazepam 5mg	diazepam 5mg	diazepam 10mg	20mg
Stage 17	diazepam 5mg	diazepam 4mg	diazepam 10mg	19mg

To Page One

(1-2 weeks)				
Stage 18 (1-2 weeks)	diazepam 4mg	diazepam 4mg	diazepam 10mg	18mg
Stage 19 (1-2 weeks)	diazepam 4mg	diazepam 3mg	diazepam 10mg	17mg
Stage 20 (1-2 weeks)	diazepam 3mg	diazepam 3mg	diazepam 10mg	16mg
Stage 21 (1-2 weeks)	diazepam 3mg	diazepam 2mg	diazepam 10mg	15mg
Stage 22 (1-2 weeks)	diazepam 2mg	diazepam 2mg	diazepam 10mg	14mg
Stage 23 (1-2 weeks)	diazepam 2mg	diazepam 1mg	diazepam 10mg	13mg
Stage 24 (1-2 weeks)	diazepam 1mg	diazepam 1mg	diazepam 10mg	12mg
Stage 25 (1-2 weeks)	diazepam 1mg	Stop diazepam	diazepam 10mg	11mg
Stage 26 (1-2 weeks)	Stop diazepam	--	diazepam 10mg	10mg
Stage 27 (1-2 weeks)	--	--	diazepam 9mg	9mg
Stage 28 (1-2 weeks)	--	--	diazepam 8mg	8mg
Stage 29 (1-2 weeks)	--	--	diazepam 7mg	7mg
Stage 30 (1-2 weeks)	--	--	diazepam 6mg	6mg
Stage 31 (1-2 weeks)	--	--	diazepam 5mg	5mg
Stage 32 (1-2 weeks)	--	--	diazepam 4mg	4mg
Stage 33 (1-2 weeks)	--	--	diazepam 3mg	3mg
Stage 34 (1-2 weeks)	--	--	diazepam 2mg	2mg
Stage 35 (1-2 weeks)	--	--	diazepam 1mg	1mg
Stage 36	--	--	Stop diazepam	--

Withdrawal from temazepam (Restoril) 30mg nightly with diazepam substitution. (30mg temazepam is approximately equivalent to 15mg diazepam)

	Night time	Equivalent diazepam dosage
Starting dosage	temazepam 30mg	15mg
Stage 1 (1-2 weeks)	temazepam 15mg diazepam 7.5mg	15mg
Stage 2 (1-2 weeks)	temazepam 7.5mg diazepam 12mg	15.75mg
Stage 3 (1-2 weeks)	Stop temazepam diazepam 15mg	15mg
Stage 4 (1-2 weeks)	diazepam 14mg	14mg
Stage 5 (1-2 weeks)	diazepam 13mg	13mg
Stage 6 (1-2 weeks)	diazepam 12mg	12mg
Stage 7 (1-2 weeks)	diazepam 11mg	11mg
Stage 8 (1-2 weeks)	diazepam 10mg	10mg
Stage 9 (1-2 weeks)	diazepam 9mg	9mg
Stage 10 (1-2 weeks)	diazepam 8mg	8mg
Stage 11 (1-2 weeks)	diazepam 7mg	7mg
Stage 12 (1-2 weeks)	diazepam 6mg	6mg
Stage 13 (1-2 weeks)	diazepam 5mg	5mg
Stage 14 (1-2 weeks)	diazepam 4mg	4mg
Stage 15 (1-2 weeks)	diazepam 3mg	3mg
Stage 16 (1-2 weeks)	diazepam 2mg	2mg
Stage 17 (1-2 weeks)	diazepam 1mg	1mg
Stage 18	Stop diazepam	--

Withdrawal from oxazepam (Serax) 20mg three times daily (60mg) with diazepam (Valium) substitution (20mg oxazepam is approximately equivalent to 10mg diazepam)

	Morning	Midday	Evening/Night	Daily Diazepam Equivalent
Starting dosage	oxazepam 20mg	oxazepam 20mg	oxazepam 20mg	30mg
Stage 1 (1 week)	oxazepam 20mg	oxazepam 20mg	oxazepam 10mg diazepam 5mg	30mg
Stage 2 (1 week)	oxazepam 10mg diazepam 5mg	oxazepam 20mg	oxazepam 10mg diazepam 5mg	30mg
Stage 3 (1 week)	oxazepam 10mg diazepam 5mg	oxazepam 10mg diazepam 5mg	oxazepam 10mg diazepam 5mg	30mg
Stage 4 (1-2 weeks)	oxazepam 10mg diazepam 5mg	oxazepam 10mg diazepam 5mg	Stop oxazepam diazepam 8mg	28mg
Stage 5 (1-2 weeks)	Stop oxazepam diazepam 8mg	oxazepam 10mg diazepam 5mg	diazepam 8mg	26mg
Stage 6 (1-2 weeks)	diazepam 8mg	Stop oxazepam diazepam 8mg	diazepam 8mg	24mg
Stage 7 (1-2 weeks)	diazepam 10mg	diazepam 2mg	diazepam 10mg	22mg
Stage 8 (1-2 weeks)	diazepam 10mg	Stop diazepam	diazepam 10mg	20mg
Stage 9 (1-2 weeks)	diazepam 8mg	--	diazepam 10mg	18mg
Continue as on Schedule 2 from Stage 12				

Withdrawal from zopiclone (Zimovane) 15mg with diazepam (Valium) substitution. (15mg zopiclone is approximately equivalent to 10mg diazepam)

	Night time	Daily Diazepam Equivalent
Starting dosage	zopiclone 15mg	10mg
Stage 1 (1 week)	zopiclone 7.5mg diazepam 5mg	10mg
Stage 2 (1 week)	Stop zopiclone diazepam 10mg	10mg
Stage 3 (1-2 weeks)	diazepam 9mg	9mg
Stage 4 (1-2 weeks)	diazepam 8mg	8mg
Then continue reducing diazepam by 1mg every 1-2 weeks as on Schedule 2		