Mr Brian Almand

Pharmacist

Hutt Hospital Pharmacy

Case Studies in Managing Anxiety - Concurrent Workshop

Saturday, 17 August 2013 Start 4:30pm Duration: 60mins Da Vinci



Managing Anxiety With Medication

Presented by Brian Almand
Mental Health Pharmacist
HVDHB Hutt Hospital Pharmacy
brian.almand@huttvalleydhb.org.nz

“But know also, man has an inborn craving for medicine …the desire to take medicine is one feature which distinguishes man the animal, from his fellow creatures. It is really one of the most serious difficulties with which we have to contend.”

William Osler 1894

Sir William Osler (1st Baronet 1849 – 1919)
The Father of Modern Medicine, he was one of the Big Four founding professors at the Johns Hopkins Hospital as the first Professor of Medicine and founder of the Medical Service there. Osler was a multifaceted physician and individual, functioning as a pathologist, internist, educator, bibliophile, historian, author, and renowned practical joker.

Non-Pharmacological Basics

- Psychotherapy
- Engaging in activity, something stimulating or interesting, employment is good
- Physical exercise, start with physical activity and increase range
- Sunlight exposure
- Social connection, meaningful social engagement
- Simple balanced diet, including hydration
- Enhanced sleep
- Combinations of the above work well, e.g.; volunteer groups, clubs of any sort, etc.
- Granted, it is not easy.

When Someone Presents With Symptoms

- Are they self medicating?
  - Alcohol
  - Cannabis
  - Other drugs

  } Anxiety management compromised
  Alcohol & Other Drug referral soonest

  - Caffeine — **Discontinue slowly**

- Suicidal ideation or self harm?

- Anxiety can be associated with medical conditions and other primary psychiatric disorders – treat the primary illness

Anxiolytics: A to Z

- Alcohol — 8000 yrs
- Opium — 4000+ yrs
- Bromides — 1870
  - Chloral hydrate, paraldehyde
- Barbiturates — 1903-12
  - Carbromal, glutethimide, methaqualone, meprobamate
- Benzodiazepines — 1960
- Z drugs, eg;zopiclone — 1998

Anxiolytics in Current Usage

- Antidepressants
  - Tricyclic antidepressants, not as well tolerated, others are be preferred
  - **Serotonin Selective Reuptake Inhibitors**
  - Serotonin & Noradrenaline Reuptake Inhibitors
- Benzodiazepines, **short term**
- Buspirone
- Beta blockers - propranolol

Serotonergic Antidepressants

- SSRI, SNRI including venlafaxine.
- Established efficacy
- Long-term use possible without tolerance or dependence
- Effects include:
  - Improving mood
  - Reducing avoidance
  - Reducing hyperarousal

- Serotoninergic neurons originating in the raphe nuclei innervate key limbic regions associated with emotional behaviour including anxiety and fear; the cortex, hippocampus, amygdala and peri-aqueductal grey

SSRI Efficacy in Anxiety

- “Perhaps the strongest argument for an etiologic role for serotonin dysregulation in the pathogenesis of anxiety comes from the treatment efficacy of the SSRI”

- Kent JM, Coplan JD, Gorman JM. Clinical Utility of the Selective Serotonin Reuptake Inhibitors in the Spectrum of Anxiety. Biological Psychiatry 1998:44:812-824

SSRI

- Highly effective but takes two to four weeks to realise clinical effect

- SSRI frequently cause increased anxiety in the first week or so of treatment.
  - This can be problematic
  - May cause non-compliance
  - Warn the patient to expect this and that it will pass

- Need a plan for the interim period
- Possibly allow low dose benzodiazepine as required for a few days - in selected cases, not routinely

SSRI in General

- Fluoxetine has a long half-life and interactions which can be problematic, especially in older adults
- Paroxetine has a short half-life and interactions which can be problematic in anyone
- Citalopram, escitalopram and sertraline are very useful
- Non-response to an antidepressant in an elderly patient should trigger consideration of cognitive impairment

Sertraline

- Best documented cardiac safety of any antidepressant
- Proven safe for depression post MI or with angina

Buspirone

- The single approved 5-HT1A agonist
- Lacks interaction with alcohol, benzodiazepines or sedative/hypnotics
- Absence of dependence, withdrawal symptoms or abuse potential
- Well tolerated
- No significant pharmacokinetic drug interactions

Buspirone

- May be used to augment treatment with SSRI in depression, OCD, GAD, although be mindful of serotonin toxicity
- Tends to be used in patients with:
  - Chronic and persistent anxiety
  - Comorbid substance abuse
  - Elderly
- As with antidepressants, does take some time to work

Propranolol

- Best for anxious patients whose main symptom is palpitation or tremor, particularly in social situations
- Appropriate dosing is 10mg either as required or twice daily initially
- Usual dosing in anxiety is quite low but may climb up to 20-40mg three times daily

Prazosin

- Prazosin is considered a first-line treatment for sleep disturbances and nightmares in PTSD because of its superior long-term efficacy and decreased adverse effects compared with antipsychotics
- Start low with 0.5mg nocte and titrate **slowly**
- Adverse effects more common at start of treatment or when increased too quickly or interactions:
  - Sildenafil etc
  - Antihypertensives
- Wide variation of dose in studies; 1-40mg daily
  - Note: starting dose 0.5mg, NZ maximum 20mg
  - Probably require low dose only at night

Graham RL. Current Psychiatry 11;6:59-62E
http://cpnp.org/sites/default/files/2012.06_Savvy_Psych_Colum-PTSD_Nightmares.pdf

Antipsychotics

- Low dose to settle has been in use for many years
  - Thioridazine formerly
  - Quetiapine presently
- Effective for night-time sedation
  - Quetiapine, risperidone or maybe olanzapine
- Effective against ruminating or intrusive thoughts
- Might be effective against nightmares of PTSD, **but**
  - Evidence is not as robust as that for prazosin
- Effective when there is a psychotic driver to the anxiety
- Use is limited by metabolic side effects secondary to weight gain

Generalised Anxiety Disorder

- Psychotherapy
- There are several options depending on severity and risk
  - Buspirone
  - Antidepressants: SSRI, venlafaxine
- These require two to six weeks to realise clinical effects
- If patients fail to respond to these or symptoms are severe and there is no history of alcohol or other substance abuse, then benzodiazepines
- Got alcohol or other substance abuse – treat that first

Stress-Related Anxiety

- Psychotherapy
- Antidepressants effective long term
- Benzodiazepines effective short term;
  - Lorazepam 0.5mg up to twice daily increasing slowly
  - Monitor for signs of increasing dosage without advice

Stress Insomnia

- Middle insomnia and early wakening are more indicative of depression, so treat that:
  - Antidepressants
  - NOT benzodiazepines, they exacerbate depression
- Recent environmental stress;
  - Zopiclone
  - Antihistamine e.g.; promethazine
- Management strategy in place for the stressors?
- End point to the stressors in sight?
- May not require medication
- Chronic insomnia hard to treat & another subject entirely

Panic Attacks

- It is not a panic attack if it lasts for days, that is persistent anxiety – see above
  - Most panic attacks come out of the blue
  - And last minutes not hours or days
- Psychotherapy very effective as the person learns to recognise the anxiety and manage it for life
- Antidepressants are very effective but take some time to work and adverse effects can be troublesome, generally worthwhile
- If symptoms are severe or risk is high a benzodiazepine as required will be effective but complicates psychotherapy as the person comes to believe they cannot cope without the drug

OCD

- Psychotherapy
- Maybe occupational therapy
- Can be very sensitive to the effects of medication:
  - The emotional blunting of SSRI may cause non-compliance
  - Start low at 10-25mg clomipramine or half a tablet of SSRI, titrate slowly
- Clomipramine is the drug of choice
- No other tricyclics as effective as SSRI
- May need high doses e.g.;
  - 40-80mg of fluoxetine
  - Up to 150mg clomipramine

Social Anxiety

- Psychotherapy is the treatment of choice in most cases
- Some extremely fearful of rejection, this is when SSRI or venlafaxine may be of help
- When there are specific phobias or performance anxiety, like stage-fright, beta-blockers may assist, e.g.; low dose propranolol

WHO on Acute Traumatic Stress

- Re-experiencing, avoidance, hyperarousal associated with significant functional impairment in first month:
- Similar symptoms to PTSD occurring before PTSD is assessed
- Recommend Cognitive Behavioural Therapy with Trauma focus (CBT-T)
- For the insomnia;
  - Recommend relaxation techniques and sleep hygiene
  - Recommend against benzodiazepines

WHO Recommend

Benzodiazepines should not be offered to adults to reduce acute traumatic stress symptoms associated with significant impairment in daily functioning in the first month after a potentially traumatic event

- No evidence to support benzodiazepines on symptoms of traumatic stress after a recent traumatic event
- Benzodiazepines may slow down the time to recover
- Many people develop tolerance to their effects
- Many gain little therapeutic benefit from chronic use
- Many become dependent and suffer a withdrawal syndrome when they stop taking benzodiazepines
- WHO also notes that benzodiazepines can have their use for other mental disorders.

WHO on PTSD

- Psychotherapy
  - Individual or group CBT-T
- Eye Movement Desensitisation Reprogramming (EMDR)
- Antidepressants not recommended due to small effect size for the treatment of PTSD
- Recommend against benzodiazepines

Gamma-Amino Butyric Acid, GABA

- GABA is an inhibitory neurotransmitter,
- GABA activity is widespread in the brain,
- GABA hyperpolarises neurons making them less responsive.

- GABA is a safety mechanism for the very excitable human brain and counters the stimulatory glutamatergic system

- Excessive stimulation produced by exogenous chemicals, like benzodiazepines, makes the GABA system more of a dimmer switch.

What Benzodiazepines do with GABA

- All benzodiazepines interact with a booster site on GABA to enhance the inhibitory effect of GABA, the ongoing nerve impulse may be completely blocked.

Excitatory Neurotransmission Reduced

- Consequently, brain output of excitatory neurotransmitters is reduced, including; acetylcholine, dopamine, noradrenaline, and serotonin.

- These are responsible for
  - normal alertness and memory
  - muscle tone and coordination
  - emotional responses and endocrine gland secretions
  - heart rate
  - blood pressure
  - and a host of other functions, all of which may be impaired by benzodiazepines, and this could be more pronounced with long-term therapy.

Clinical Uses of Benzodiazepines

Action	Clinical Uses
Hypnotic	Short-term treatment of insomnia.
Anxiolytic	Short-term or intermittent treatment of some anxiety disorders. Short-term aid to alcohol/other CNS depressant drug withdrawal.
Anticonvulsant	Status epilepticus. Drug-induced convulsions. Short-term or adjuvant treatment of some types of epilepsy.
Amnesic	Premedication before surgery. Minor surgical procedures.
Myorelaxant	Painful muscle spasms. Some dystonias and involuntary movements.

Benzodiazepines Gain Favour

- Late 1970's; Most commonly prescribed drugs in the world.
- 1 in 5 women and 1 in 10 men in Europe took them at some time each year.
- Prescribed long-term, often for many years,
- Prescribed for anxiety, depression, insomnia and ordinary life stresses.

Benzodiazepines Lose Favour

- Early 1980's; in England long-term prescribed users realised
- The drugs tended to lose their efficacy over time, and
- Became associated with adverse effects
- Patients found it difficult to stop because of withdrawal effects
- Many complained that they had become addicted,
- Throughout the 1980s there was a public outcry against benzodiazepines in the U.K. resulting in widespread media coverage in the press, radio and television and a burgeoning of self-help groups and withdrawal clinics

Long-Term Patients Found

1. They have taken benzodiazepines in prescribed therapeutic doses for months or years, usually low doses
2. Gradually become to need benzodiazepines to carry out normal, day-to-day activities - disempowered
3. Continue to take benzodiazepines although the original indication for prescription has disappeared
4. Difficulty in stopping the drug, or even reducing dose, because of withdrawal symptoms
5. Develop anxiety symptoms between doses of short-acting benzodiazepines, or get craving for the next dose

Long-Term Patients Found

6. Contact their doctor regularly to obtain repeat prescriptions.
7. Become anxious if the next prescription is not readily available
8. May carry their tablets around with them
9. May take an extra dose before an anticipated stressful event or a night in a strange bed.
10. May have increased the dosage since the original prescription.
11. May have anxiety symptoms, panics, agoraphobia, insomnia, depression and increasing physical symptoms despite continuing to take benzodiazepines.

Use should not exceed two to four weeks

- Canada 1982 – Health Canada, continuous use of benzodiazepines should not exceed 2 weeks.

- United Kingdom 1988 – Committee on Safety of Medicines, bulletin to all doctors; Benzodiazepines are indicated for the short-term relief, 2-4 weeks only, of anxiety or insomnia that is severe, disabling or subjecting the individual to unacceptable distress. Benzodiazepines can cause or exacerbate depression and increase the risk of suicide.

- New Zealand 1989 – Department of Health, short-term treatment with benzodiazepines may be beneficial but use for more than 4 weeks could well be harmful.

And still should not exceed four weeks

- United Kingdom 1999 – Department of Health – repeated same message.
- Ireland 2002 – Report of the Benzodiazepine Committee, benzodiazepines should not be prescribed for more than 1 month for anxiety or more than 2-4 weeks for insomnia.
- Denmark 2003 – National Board of Health, prescription of benzodiazepines should be restricted to a maximum of 2 weeks as sleeping pills or 4 weeks as anxiolytics.
- United Kingdom 2004 – Chief Medical Officer, Department of Health – same message.

Committee on Safe Use of Medicines Advice

1. Benzodiazepines are indicated for the short-term relief (two to four weeks only) of anxiety that is severe, disabling or subjecting the individual to unacceptable distress, occurring alone or in association with insomnia or short-term psychosomatic, organic or psychotic illness.
2. The use of benzodiazepines to treat short-term ‘mild’ anxiety is inappropriate and unsuitable.
3. Benzodiazepines should be used to treat insomnia only when it is severe, disabling, or subjecting the individual to extreme distress.

Prescribing Benzodiazepines Caution

When to be cautious:

- Personal or family history of substance abuse
- Course starting to get beyond 2-4 weeks
- Long-term use may still be clinically effective in a few patients but must be monitored
- Patient requests increasing doses or more frequent prescribing
- Immediate discontinuation or rapid taper from long-term treatment can result in significant withdrawal

Prescribing Benzodiazepines to Elderly

- Can cause cognitive impairment
- Contribute to unsteady gait and falls
- Diazepam has a very long half-life and will accumulate to the detriment of the patient as above, a benzodiazepine with a shorter half-life should be considered: clonazepam or lorazepam
- Clonazepam drops are an advantageous dose form in some cases

Prescribing Benzodiazepines: Misdiagnosis

Failure to recognise depression:

- Benzodiazepines can cause worsening depression

Failure to recognise emerging psychotic symptoms:

- Benzodiazepines will fail to treat psychosis

A Useful Analogy

Analgesics are very effective at relieving tooth pain

But at some stage,
you are going to have to pull out the tooth!

To continue the analogy:
Psychotherapy is the forceps

Guidelines for Prescribing Sedative/Hypnotics

- Avoid in: patients with respiratory disease
  patients with severe hepatic impairment
  addiction-prone individuals
- Assess falls risk including concurrent medication and disease
- Advise patient of the interaction with alcohol and other sedating agents
- Advise patient of risk to driving and operating machinery
- Use lowest effective dose
- Use intermittent dosing where possible: alternate nights or less
- Short course one week perhaps two generally sufficient in the majority of cases, up to four weeks if necessary
- Discontinue slowly after medium to long-term use
- Be alert for rebound insomnia or withdrawal symptoms

Items in red added by this author

Drugs that may cause anxiety

Stimulants

- Amphetamine, aminophylline, caffeine, cocaine, methylphenidate, theophylline, party pills

Sympathomimetics

- Adrenaline, ephedrine, phenylpropanolamine, pseudoephedrine

Anticholinergics

- Benztropine, diphenhydramine, oxybutinin, TCA

Dopaminergics

- Amantadine, bromocriptine, levodopa, metoclopramide, neuroleptics

Miscellaneous

- Baclofen, hallucinogens, indomethacin, pethidine, cannabis, nicotine

Drug withdrawal

- Alcohol, barbiturates, benzodiazepines, narcotics, sedatives

Adverse Effects of Benzodiazepines

- Oversedation → If sedative drugs are taken in overdose, e.g. alcohol, benzodiazepines may add to the risk of fatality
- Hypotension
- Respiratory depression
- Memory impairment
- Depression, emotional blunting
- Gastrointestinal, genitourinary
- Tremor, dysarthria, visual disturbances
- Paradoxical stimulant effects → Possible increased risk of poor impulse control and hostility. Under-dosed?
- Tolerance
- Dependance

Risk Factors for Increased Adverse Effects

Conditions Associated	Risks
Older age (65 years and over)	Mental confusion, amnesia, ataxia, falls, and fractures.
Pregnancy	Neonatal CNS depression, withdrawal reactions in infant, floppy infant syndrome
Chronic respiratory disease	Respiratory depression.
Liver disease	Oversedation.
Depression	Aggravation of depression, precipitation of suicide.
History of alcohol or sedative abuse	Dependence & abuse
Alcohol or drug intoxication	Acute: CNS depression, excessive sedation
Personality disorder	Dependence, abuse, aggression.

Prof. C H Ashton, Psychiatric Annals Volume 25: pp158-165 March 1995

Common Acute Symptoms of Benzodiazepine Withdrawal

Common to Anxiety States	Relatively specific to Benzodiazepine Withdrawal Less common with Anxiety States
Anxiety, panic attacks, agoraphobia	Perceptual disturbances, sense of movement
Insomnia, nightmares	Depersonalisation, derealisation
Depression dysphoria	Hallucinations (visual, auditory) misperceptions
Excitability, jumpiness, restlessness	Distortion of body image
Poor memory and concentration	Tingling, numbness, altered sensation
Dizziness, light-headedness	Formication
Weakness (jelly-legs)	Sensory hypersensitivity (light, sound, smell, taste)
Tremor, Muscle pain	Muscle twitches, jerks, fasciculation
Stiffness (limbs, back, neck, jaw, head)	Tinnitus
Sweating, night sweats	Confusion, ***delirium, psychotic symptoms***
Palpitations	***Seizures***

Bold italics: Usually confined to rapid withdrawal from high doses

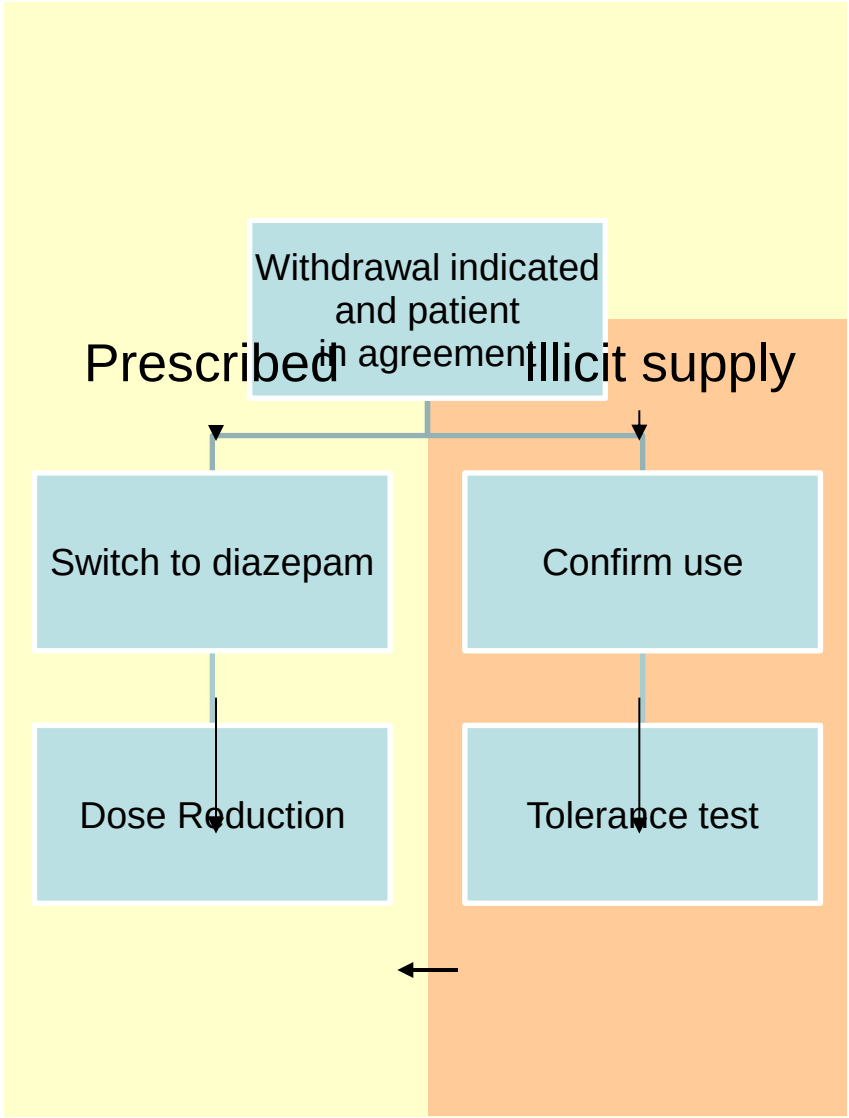
Symptoms of Protracted Withdrawal

Symptom	Usual Course
Anxiety	Gradually diminishing over a year
Insomnia	Gradually diminishing six to twelve months
Depression	Months, responds to antidepressants
Perceptual symptoms; tinnitus, paraesthesiae – tingling, numbness, pain in limbs or extremities	Gradually receding but may last at least a year and occasionally permanent
Motor symptoms; muscle pain, weakness, tension, painful cramps, tremor, shaking attacks, jerks, blepharospasm	Gradually receding but may last at least a year and occasionally permanent
Gastro-intestinal symptoms	Gradually receding but may last at least a year and occasionally permanent

Mechanisms for protracted symptoms are not known, but may include both psychological and pharmacological factors, possibly structural brain injury.

Prof. C H Ashton, Psychiatric Annals Volume 25: pp158-165 March 1995

Managing Benzodiazepine Withdrawal



- When clinically indicated AND with the patient in agreement
- When using illicit supply confirm use by urine testing
- Then Tolerance Test to find dose
- People taking short or intermediate acting agents should be offered equivalent dose of diazepam which has a longer half-life so causes less severe withdrawal.
- Systematic reduction is more likely to lead to abstinence

Pharmacokinetic Comparison

Anxiolytic or Hypnotic Agent		Elimination Half-life in Hours:Range (Active Metabolite)	Dose Approximately Equivalent to Diazepam 10mg	Note
Alprazolam	A	**11**:6-26	0.5-1mg	
Clonazepam	A*	**30**:19-50	1mg	T1/2 similar in Elderly
Clobazam	*	**18**:9-77	20mg	
Diazepam	A*	**32**:20-50 (50-100)	10mg	T1/2 has been reported as 20-100 (50-200)
Lorazepam	A	**13**:10-20	2mg	T1/2 similar in Elderly
Nitrazepam	AH *	**30**:18-40	10mg	
Oxazepam	A	**8**:5-15	20-30mg	T1/2 similar in Elderly
Temazepam	H	**9**:8-22	20mg	
Triazolam (w/d UK1991)	H	**2**	0.5-1mg	T1/2 similar but peak much higher in Elderly
Zopiclone	H	**5:**3.5-8	15mg	

Reducing the Dose of Diazepam

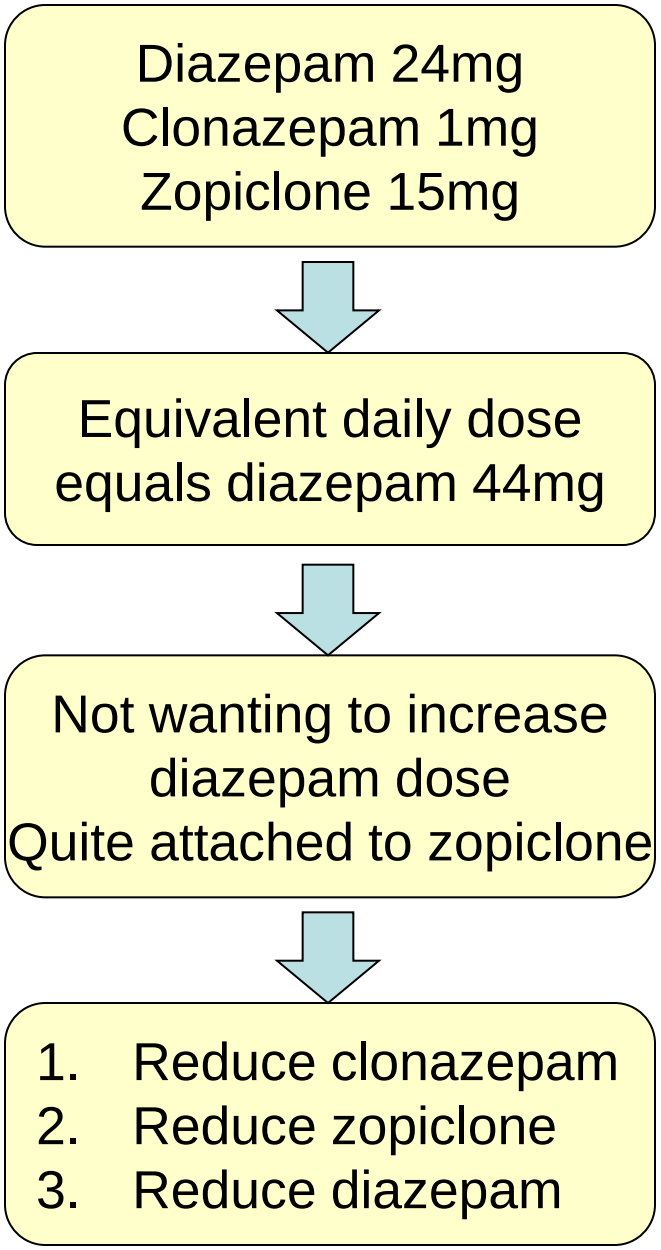
- Reduce by 10mg per day to a daily dose of 50mg
- Reduce by 5mg per day to a daily dose of 30mg
- Reduce by 2mg per day to a daily dose of 20mg
- Reduce by 1mg per day until stopped

- This could be varied depending on the starting dose of diazepam but should be no longer than the above.

Rate of Withdrawal

- Not well defined and can be contentious
- Recommended:
  - Weekly intervals during changeover to diazepam
  - One to two weekly intervals thereafter
- A schedule that is longer than six months could become so much a focus of the patient's existence as to be inadvisable, at least requiring a good deal more support
- The patient should be involved in deciding time frame
- Always go forward, the schedule may be halted temporarily but try not to go backwards
- Learning to cope without benzodiazepines is essential to the adaptation in withdrawal so no doses outside of the schedule: no PRN

Case One


Diazepam 24mg
Clonazepam 1mg
Zopiclone 15mg
Equivalent daily dose
equals diazepam 44mg
Not wanting to increase
diazepam dose
Quite attached to zopiclone
1. Reduce clonazepam
2. Reduce zopiclone
3. Reduce diazepam

Interval Number	Diazepam Dose				Zopiclone Dose 7.5mg tablets		Clonazepam Dose 0.5mg tablets	
		10mg tablets	5mg tablets	2mg tablets				
	Dose in mg	number of tablets	number of tablets	number of tablets	Dose in mg	number of tablets	Dose in microgram	number of tablets
1	24	two	-	two	15	two	**875**	one & 3/4
2	24	two	-	two	15	two	**750**	one & a half
3	24	two	-	two	15	two	**625**	one & 1/4
4	24	two	-	two	15	two	**500**	one
5	24	two	-	two	15	two	**375**	three quarters
6	24	two	-	two	15	two	**250**	half
7	24	two	-	two	15	two	**125**	one quarter
8	24	two	-	two	15	two	**stop**	-
9	24	two	-	two	**11.25**	one & a half	-	-
10	24	two	-	two	**7.5**	one	-	-
11	24	two	-	two	**3.75**	half	-	-
12	24	two	-	two	**stop**	-	-	-
13	**23**	two	-	one & a half	-	-	-	-
14	**22**	two	-	one	-	-	-	-
15	**21**	two	-	half	-	-	-	-
16	**20**	two	-	-	-	-	-	-
17	**19**	-	three	two	-	-	-	-
18	**18**	-	three	one & a half	-	-	-	-
19	**17**	-	three	one	-	-	-	-
20	**16**	-	three	half	-	-	-	-
21	**15**	-	three	-	-	-	-	-
22	**14**	-	two	two	-	-	-	-
23	**13**	-	two	one & a half	-	-	-	-
24	**12**	-	two	one	-	-	-	-
25	**11**	-	two	half	-	-	-	-
26	**10**	-	two	-	-	-	-	-
27	**9**	-	one	two	-	-	-	-
28	**8**	-	one	one & a half	-	-	-	-
29	**7**	-	one	one	-	-	-	-
30	**6**	-	one	half	-	-	-	-
31	**5**	-	one	-	-	-	-	-
32	**4**	-	-	two	-	-	-	-
33	**3**	-	-	one & a half	-	-	-	-
34	**2**	-	-	one	-	-	-	-
35	**1**	-	-	half	-	-	-	-
36	**stop**	-	-		-	-	-	-

Advice from Psychiatry

- “Primary anxiety is in the DSM IV but I have never seen it, there is always something causing the anxiety.”
- When you see anxiety look for whatever is behind it:
  - Substance abuse, especially alcohol and include caffeine
  - Abuse; physical, emotional, mental
  - PTSD
  - Depression
  - Medical illness: MVP, IBS, asthma, CVD, cancer
  - Chronic pain
  - Medication

From Psychologists

- Counsellors would prefer patients benzodiazepine free

  - Become an avoidance behaviour
  - Preventing engagement with challenging therapies
  - Delay progression and in the worst cases prevent it

Drugs that may cause anxiety

- **Stimulants:** amphetamine, aminophylline, caffeine, cocaine, methylphenidate, theophylline, party pills
- **Sympathomimetics:** adrenaline, ephedrine, phenylpropanolamine, pseudoephedrine
- **Anticholinergics:** benztropine, diphenhydramine, oxybutinin
- **Dopaminergics:** amantadine, bromocriptine, levodopa, metoclopramide, neuroleptics
- **Miscellaneous: alcohol,** baclofen, barbiturates, benzodiazepines, cannabis, hallucinogens, indomethacin, narcotics, nicotine, pethidine,
- **Drug withdrawal:** alcohol, barbiturates, benzodiazepines, narcotics, sedatives

Case Two: Panic Attacks

- Businessman, 32 years old, no psychiatric history
- Reports anxiety attacks for the past three months
- Occur out of the blue, include tachycardia and shortness of breath
- Most recently in his car on the way to work, pulled over and called 111 although resolved during the call
- Increase stress at work over the last six months
- Has not been sleeping as long as he used to but not over tired
- Has increased his coffee intake to cope, bought an espresso machine for home, and uses energy drinks to refuel for the afternoons
- Estimate he could be consuming ≥1200mg caffeine daily

On Caffeine

- Patients with anxiety disorders should consume no caffeine

- Partial responses or break-through symptoms often due to unreported caffeine use

Case Three: Claustrophobia

- 54 year old woman works in catering
- Unremarkable medical history and generally well
- Describes fear of enclosed spaces especially elevators and large walk-in refrigerators like those at work.
- Gets panicked, hyperventilates and heart races.
- Fears she will die when elevator gets stuck or refrigerator is locked and no-one finds her
- Quite unreasonable fear with no evidence
- Has felt silly about this for years and only seeking help now because she wants to go on a cruise

Case Three: Panic Management

Has now completed three of six sessions of CBT

Last session successfully travelled in seven elevators and completed homework of being locked in work refrigerator

In such cases benzodiazepines are very unhelpful:

- Take away the person's ability to see themselves cope with the fear
- The person feels they cannot face the fear without benzodiazepines
- This greatly complicates Cognitive Behavioural Therapy

Case Four: Meltdowns

- Slight 55 year old woman, Hx cerebral palsy, low IQ, traumatic childhood with early separation from mother and invalidating environments through developmental life
- A great many episodes of self harm or risky behaviour and frequent use of inpatient services
- Diagnoses include Borderline Personality Disorder, depression and anxiety, managed by CMHT for years
- Commenced on benzodiazepines 15 years ago, most recent years using clonazepam 1-2mg daily
- For the last 14 years or so has experienced daily meltdowns – fits of hopeless crying that persist for hours, are a source of considerable distress for her

Case Four: Meltdowns melted

- A change in community psychiatric nurse was beneficial:
  - Collaborative approach as not psychologically minded
  - Reduction in use of inpatient unit
  - Diarising meltdown occurence and severity, down to one sometimes two most days.
- Change of RC two years ago (she has had twenty one psychiatrists involved in her care over time)
- Finally agreed to trial reduction of benzodiazepines
- Swapped to diazepam 5mg twice daily
- Small change in frequency of meltdowns after four weeks
- Titrated down to 5mg daily
- Patient discontinued this and told us two weeks later

Case Four: Result

- Use of inpatient unit has dropped off to maybe twice in the last four months
- No incidents of self harm in that time
- No presentations to A&E, they’re delighted
- No meltdowns in the last month at all
- Euthymic and cheerful

Case Five: Dementia?

- 85 year old woman presents secondary to falls
- Bewildered, poorly oriented to time and place, history of reducing function, inattentive family
- Looks strained and anxious
- States she is worried about loss of function and forgetfulness, feels she is dementing, fears loss of independence
- Current medication trimipramine 25mg mane and 50mg nocte, diazepam 2mg QDS, has been increasing over recent months

Case Five:

- Plan to switch trimipramine to nortriptyline 50mg, step down to 25mg, 10mg off.
- Discontinue diazepam in two-weekly steps:

Morning	Midday	Evening	Night
2	2	2	2
2	1	2	2
2	1	1	2
1	1	1	2
1	1	1	1
1	0	1	1
1	0	0	1
0	0	0	1

- Now half-way through this schedule
- Seems to be improving in function

Brain is Normally Switched On

Alertness (Sedative) ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Anxiety (Anxiolytic) ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Excitability (Anticonvulsant) ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Attention ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Visuo-spatial perception ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Co-ordination ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Memory ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Cognition ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Verbal learning ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Concentration ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Reaction time ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Motivation ☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑☑

Benzodiazepines Switch Brain Off

Personal Safety Rating? Judgement? Driving ability?

Tolerance Develops 0+2-4weeks

Tolerance Develops 0+8-12 weeks

Long-Term Benzodiazepines

Alertness
Anxiety
Excitability
Attention
Visuo-spatial perception
Co-ordination
Memory
Cognition
Verbal learning
Concentration
Reaction time
Motivation

Increased risk of falls

note the contribution of other medication, e.g.; antihypertensives, sedative drugs

Increased risk of road traffic accident, persists.

Cognitive function impaired, may persist.

Benzodiazepines & Dementia

- ‘Forgetfulness, amnesic episodes, or confusion should not be ascribed facilely to old age or dementia' in older patients taking benzodiazepines.’

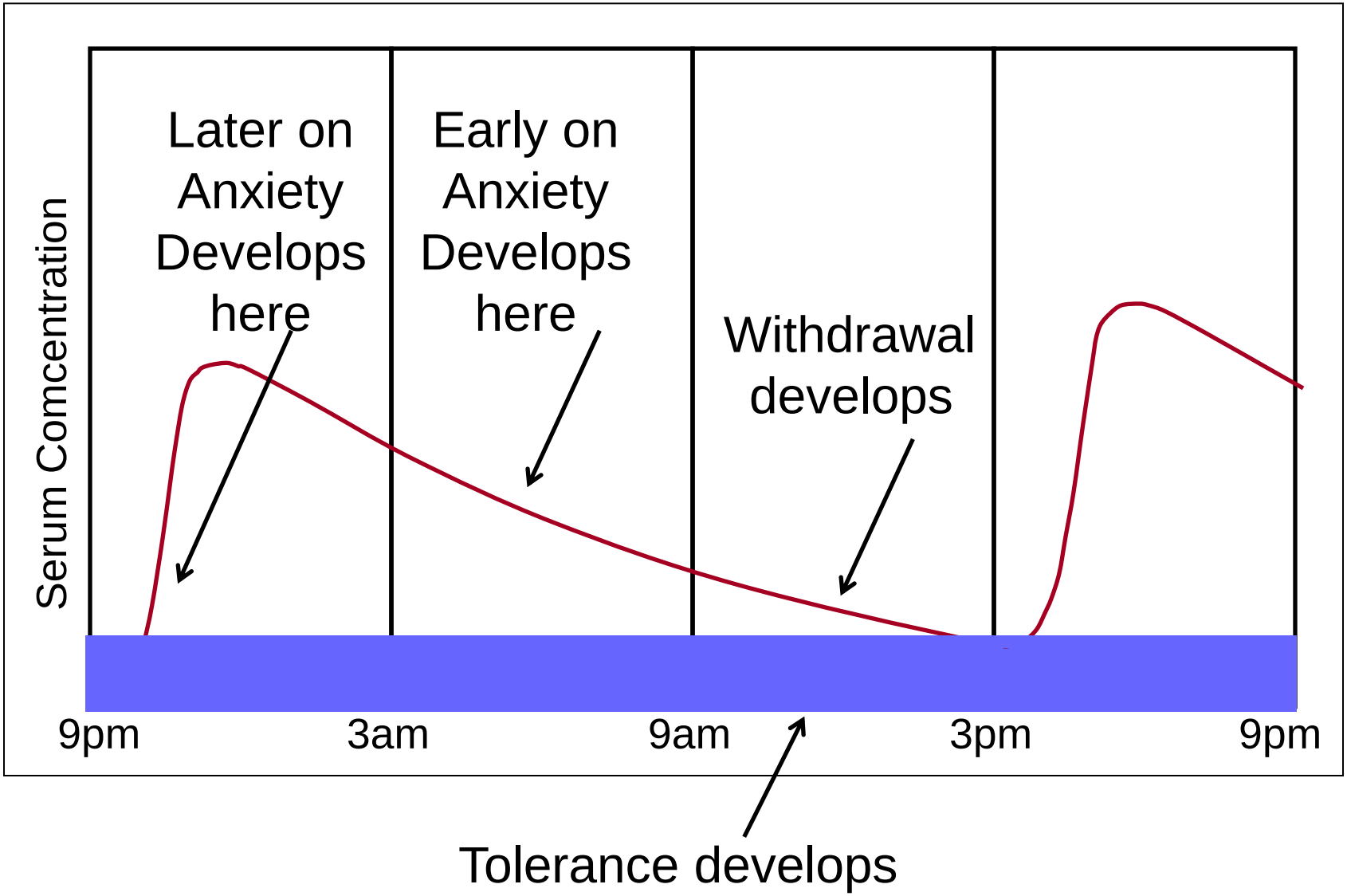
- Lader M. Benzos and Memory Loss: More Than Just 'Old Age.' Prescriber, 1992: 3;13

Long-Term Cognitive Risk?

- After withdrawal of benzodiazepines patients recover in many cognitive domains, but these patients are often still impaired when compared with control groups begging the question of long-term neuropathology associated with benzodiazepine use.

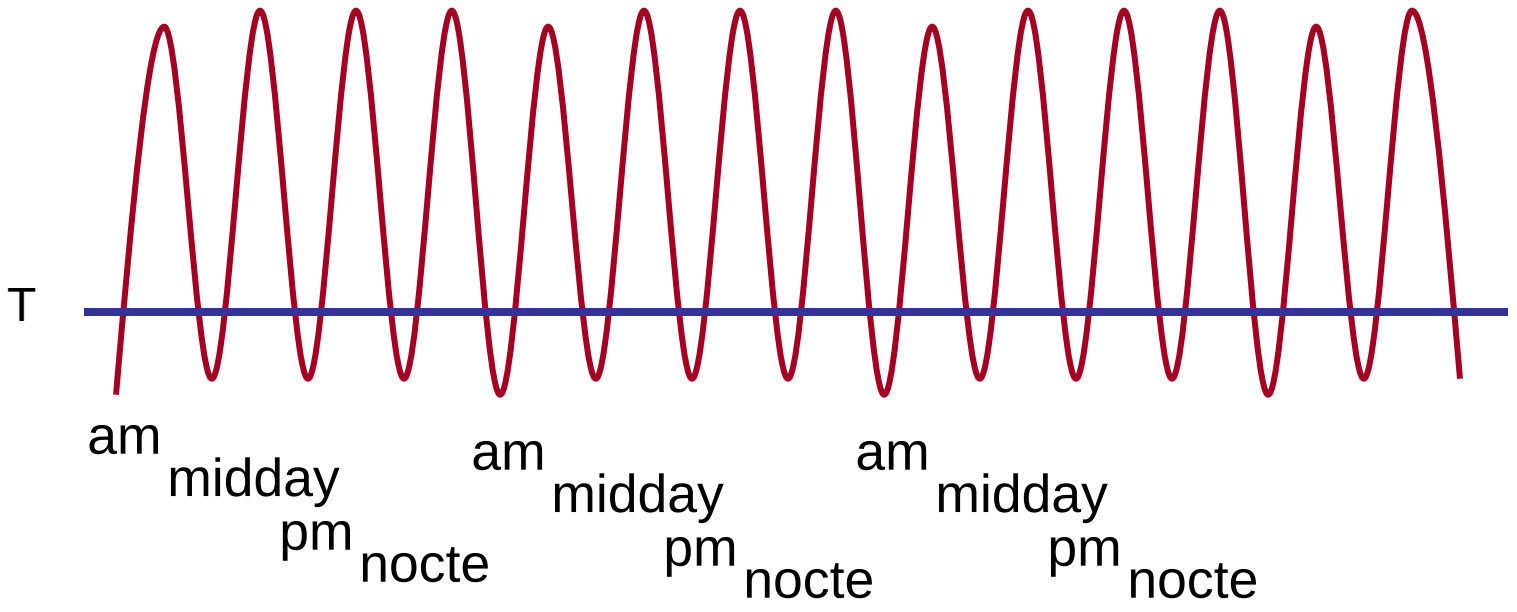
- Stewart SA. The Effects of Benzodiazepines on Cognition. Journal of Clinical Psychiatry, 2005:66(suppl 2):9-13.
- Salzman C, Fisher J, Nobelk, Glassman R, Wolfson A, Kelly M. Cognitive Improvement Following Benzodiazepine Discontinuation in Elderly Nursing Home Residents. Int J of Geriatric Psychiatry, 1992:7:89-93.

Case Six: Long-Term Alprazolam



Case Six: The Alprazolam Trap

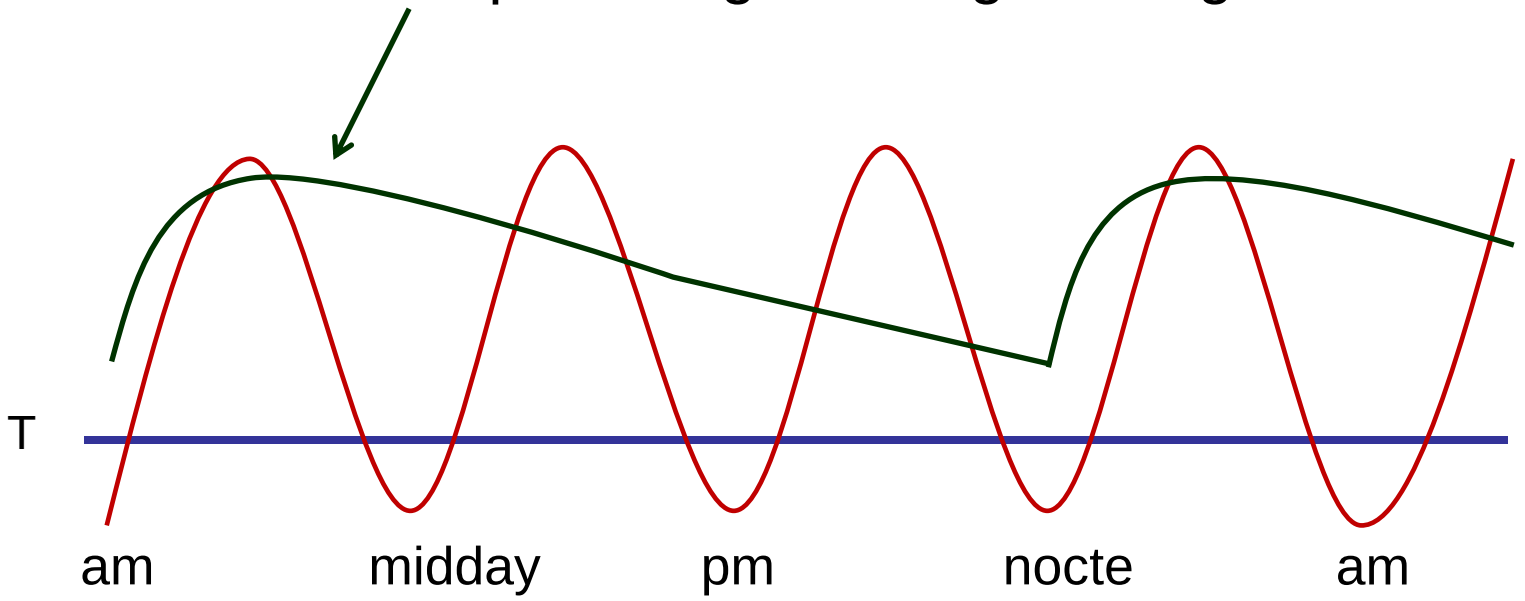
Unwell looking, 68 year old woman, intense, drug seeking
Husband is engaged to keep dosing to 0.5mg four times daily



Constantly stressed, worries about the next dose and checks with husband that he has sufficient medication

Case Six: The Alprazolam Trap

Psychiatrist stopped alprazolam and started clonazepam 1mg morning and night



Plan to reduce by 0.25mg every 1 – 2 weeks

Seems to be going well