CHAPTER 12.

SUBSTANCE-RELATED and ADDICTIVE DISORDERS

“Even though psychological and social factors predominate in the presentation and diagnosis of addiction, the disease is at its core biological: changes that a physical substance causes in vulnerable body tissue.”

Eric Nestler, 2005

“…addiction…is a moral or spiritual condition that will never yield to medical treatment, so called.”

Theodore Dalrymple, 2006

Introduction

The DSM-5 (2013) changed a few things. One of the big ones was to place Gambling Disorder in the chapter dealing with substance use disorders. Some information on this topic is presented at the end of this chapter.

Substance use disorders and Gambling disorder depend on social, cultural, psychological, psychiatric, genetic and legal factors. From the above quotes it is clear that at any point in time experts may have opposing views on the mechanism and most appropriate treatment/management of these disorders.

Theodore Dalrymple is an experienced specialist clinician. The title of his book, “Romancing opiates: pharmacological lies and the addiction bureaucracy”, gives fair warning of his thinking. He states that addiction is “moral weakness” rather than a medical disorder, and that current medical treatment is making matters worse rather than better. He recommends greater stigmatization of illegal drug users and the closure of all clinics claiming to provide treatment for addiction. He argues his views persuasively. As this is a basic text, I will present the orthodox (medical) view.

However, students should be aware that a credible alternative view exist.
**Historic and useful terms**

As terms move from the technical into the general lexicon, they lose meaning and become pejorative labels. ‘Addict’ is an example (‘cretin’ and ‘moron’ are others).

**Addiction** still has value if restricted to severe conditions in which there is evidence of social and personal decline, and tolerance and withdrawal symptoms. Addiction is characterized by preoccupation with maintaining a supply of the desired substance, leading to the neglect of usual responsibilities (family and employment) and often law breaking (to acquire necessary funds).

**Tolerance** refers to the need for larger and larger doses of a substance to produce a desired effect.

**Craving** is the state of motivation to seek out a particular substance. Sub-components include 1) urge and desire to use, 2) intention and planning to use, 3) anticipation of positive outcome, 4) anticipation of relief from withdrawal, and 5) loss of control over use.

[The cognitions of substance using individuals (what they expect to happen) greatly influence the experience of tolerance, withdrawal and craving. This is a good example of the inappropriateness of Cartesian dualism as model for substance use disorders.]

**Alcoholism** is a “chronic disease characterised by a fundamental disturbance of the nervous system which is manifested on a behavioural level by a state of physical dependence. The major forms of this dependence are either inability to stop drinking before drunkenness is achieved, or inability to abstain from drinking because of the appearance of withdrawal” (WHO, 1952).

Many of these older terms/concepts have been subsumed in the DSM-5 classification – but retain some usefulness.

**DSM-5: Substance-Related Addictive Disorders**

For many substances there are three possible ‘diagnoses’

1. **Substance use disorder**
   A cluster of cognitive, behavioural, and physiological symptoms indication that the individual continues using the substance despite significant substance-related problems.

2. **Intoxication**
   The development of a reversible substance-specific syndrome due to recent ingestion of (or exposure to) a substance.
   Clinically significant maladaptive behavioural or psychological changes that are due to the effect of the substance of the central nervous system.

3. **Withdrawal**
   The development of a substance-specific syndrome due to the cessation of (or reduction in) substance use that has been heavy and prolonged.
   The syndrome causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Substances and the brain (COCAINE as the example)

Different substances have different effects on the brain. There are also similarities. For a general introduction we might look first at the consequences of cocaine use (Nestler, 2001).

To people who have never been addicted, the behaviour of people who are addicted, is puzzling. Addicted people may make the decision to stop using drugs for excellent reasons (they may be facing loss of partner, children, job, freedom, and risk to the unborn). They may have good professional and family support and abstain. However, even under ideal circumstances they often relapse (start using drugs again) after weeks, months or even years. Clearly, there are powerful mechanisms at work.

One mechanism is that drugs of addiction increase the availability of transcription factors (proteins that bind to regulatory regions of genes and thereby increase of decrease the transcription of particular genes). Prominent examples include CREB (cAMP response element binding protein), and delta Fos B. Delta Fos B survives for 6-8 weeks before being metabolised. The long-term effects of delta Fos B are on a nerve growth factor, and ultimately, structural change. Nucleus accumbens (NAc) cells of cocaine exposed animals show increased offshoots on their dendrites. This means, the volume (and effect) of memory signals coming from the hippocampus and amygdala are increased.

Another is epigenetic changes – which are discussed in more detail below.

The pleasure centres of the brain are old in evolutionary terms (2 billion years) and serve to encourage organisms to engage in activities which ensure survival of the individual (food intake) and the species (sexual activities).

The pleasure centres are adorned with dopamine receptors, which are activated when dopamine is released.

A leading pleasure structure is the mesolimbic dopamine system (Nestler, 2013), which involves dopamine neurons in the ventral tegmental area (VTA) of the midbrain innervating medium spiny neurons of the NAc - a grey matter structure deep to the medial frontal cortex. It can be classified as belonging to the limbic system (as part of the limbic striatum), and the basal ganglia (as part of the ventral striatum). Thus, it forms a link between feelings and behaviour. The VTA neurons also innervated many other forebrain regions including the hippocampus, amygdala and the prefrontal cortex (PFC).

Synaptic dopamine levels are regulated in large part by the action of the dopamine transporter protein. This is a cell membrane structure which transports dopamine back into cells. (There are no dopamine receptors inside the cells, thus once transported in, the dopamine does not cause stimulation.) Cocaine inactivates the dopamine transporter. This raises synaptic dopamine levels, dopamine receptor stimulation, and the pleasure experience.

Cocaine causes dopamine release far in excess of that released in natural circumstances. This results in extreme pleasure, often termed euphoria. Humans and
other animals will find cocaine more attractive than food and sex. Animals with access to cocaine and food will choose cocaine, ignore food, and starve to death (Nutt & Law, 2000).

The hippocampus and amygdala (limbic structures) are memory centres which record how pleasure is achieved. As the pleasure from cocaine is extremely high, the people, places and other things associated with the drug, and the drug taking behaviour all become connected with message - PLEASURE.

The frontal cortex is a source of inhibitory functions. It acts as a brake when we decide to forgo pleasure, in order to avoid negative consequences. Another action of cocaine is to impair the braking ability of the frontal cortex, making it less able to inhibit urges.

In summary, for cocaine at least, the addictive drug has many actions which predispose to addiction and relapse (even after long term abstinence). The drug stimulates the pleasure centres beyond the range of the natural world. The memories of this experience and the circumstances leading to this unnatural pleasure are retained. There are structural changes in pleasure centres such that the memories from the memory centres are magnified and enduring. In addition, there is damage to the structures which usually inhibit destructive activities. Under these circumstances, it is surprising that any addicted person is able to remain abstinent.

**Neuroimaging**

Ma et al (2010) proposed that chronic addictive drugs alter the functional organization of the brain leading to habitual hypersensitivity to the drug and drug-related cues. They investigated this proposal using heroin consumers and “resting-state functional connectivity”, a recent neuroimaging technique [fMRI and BOLD] which provides a measure of functional organization.

They were interested in the functional connectivity between many of the regions mentioned above:

1. NAc (associated with pleasure)
2. Amygdala and hippocampus (associated with memory)
3. Prefrontal cortex and Dorsal anterior cingulate (associated with cognition)
4. Orbitofrontal cortex (associated with drive).
5. Ventral anterior cingulate (emotional regulation)

They found **increased** functional connectivity between:

1. NAc (pleasure) and the ventral anterior cingulate (emotional regulation)
2. NAc (pleasure) and the orbitofrontal cortex (drive)
3. Amygdala (memory) and orbitofrontal cortex (drive)

Thus, there was increased functional connectivity between the centres associated with pleasure, drive and memory.
They found **decreased** functional connectivity between:

1. Prefrontal cortex (cognition) and dorsal anterior cingulate (cognition)
2. Prefrontal cortex (cognition) and orbitofrontal cortex (drive)
3. Dorsal anterior cingulate (cognition) and ventral anterior cingulate (emotional regulation).

Thus, there was decreased connectivity which could be expected a reduced capacity for cognition to hold emotion and drive in check.

Illustration. Resting-state functional connectivity of heroine users compared to healthy controls. [Adapted from Ma et al, 2010.] Heroin users display increased (solid line) functional connectivity between areas involved with memory, reward, drive and emotional regulation, and decreased (broken line) functional connectivity between cognitive areas which provide constraint.

Many different substances are used, each is different from the others, and there are many different imaging techniques.

The following reports give a taste of recent progress. **Do not attempt to learn the following preliminary material.**
Verdejo-García et al (2007) review the full range of substance use and reached the general conclusion that significant alterations could be identified in the cortex, subcortical structures and the basal ganglia. They found that cocaine was associated with the most pronounced and widespread changes (see also, Burger et al. 2018).

Wrege et al (2014) report that structural imaging of cannabis users found differences in reduced prefrontal volumes and white matter integrity – this may be associated with impulsivity, which has been observed in cannabis users. It is not clear if impulsivity predisposes to cannabis consumption, or is a consequence.

Chang et al (2007) found that methamphetamine use is associated with enlarged striatal volumes and abnormalities of the chemistry, dopamine and serotonin transporter densities, and dopamine 2 receptors of the basal ganglia.

Schmidt et al (2014) found that acute administration of heroin in dependent individuals impairs cognitive control by reducing activity in the anterior cingulate cortex and the functional connectivity from the anterior cingulate cortex and the right inferior gyrus.

Bora et al (2014) investigated white matter microstructure in opiate addiction using detrusor tensor imaging (DTI). They examined fractional anisotropy (FA) in multiple pathways including the corpus callosum, thalamic radiation and inferior longitudinal fasciculus. They demonstrated widespread myelin pathology and effects on neuronal connectivity and function.

Kish et al (2010) using positron emission tomography (PET) combined with MRI, studied cortical serotonin transporter density in ecstasy (MDMA) users. They found serotonin transporter density in ecstasy users was significantly reduced in all cerebral cortices, particularly in the insular and occipital cortices. Surprisingly, there was sparing of the serotonin transporter-rich striatum. Transporter loss was related to extent of use.

**Personality and substance use**

There is a high comorbidity of personality disorder and substance use, which increases the difficulties of management (Di Lorenzo et al, 2014).

Evidence suggests that particular personality types are attracted to different substances and different patterns of substance use. Nevertheless, a broad spectrum of personality types become involved, and each individual must be considered separately.

Chester and De Wall (2018) found that people with aggressive dispositions were at greater risk of using alcohol, and that alcohol led to aggressive behaviour.

People are more likely to experiment with substances when they display high levels of sensation-seeking or impulsive behaviour. However, once substance dependence has developed, obsessional, dependent and anxious characteristics make stopping more difficult (Tyrer, 1989).
**Mental disorder** – De Matos et al (2018) report that GAD and PTSD are associated with illicit substance abuse, and agoraphobia is associated with tobacco use (legal).

**Genetics and substance use**

Brief mention is made here; some further details are listed, when available, under separate substances.

There is 50% heritability of drug use, but the genes for vulnerability are yet to be determined. Perhaps hundreds of genetic variations summate in a single individual to confer addiction (Nestler, 2013).

Considering all substances, using a large twin data base, Kendler et al (2007) identified 2 genetic factors and an environmental factor. One genetic factor loaded strongly on cocaine and cannabis dependence, the other, on alcohol and nicotine dependence.

Another twin study (Huggett et al, 2018) indicates genetic influence on the age of initiation of alcohol and tobacco use, and progression to dependency.

Four different sub-types of alcoholism have been described – 1) pure alcoholism, 2) anxiety/depression alcoholism, 3) antisocial alcoholism, and 4) mixed alcoholism – which may have separate genetic underpinning (Lee et al, 14).

A meta-analysis found that gene variants of the serotonin 1B receptor is associated with alcohol, cocaine, and heroin abuse (Cao et al, 2013).

**Epigenetics**

Epigenetics is a new area of enormous interest to students of human behaviour – and frequently mentioned in the Download of Psychiatry – It describes a process which changes gene expression without altering the DNA sequence.

Information which is stated elsewhere will not be repeated here. However, much of what we know of epigenetics has come from studies in substance use. This is not surprising – continued drug use in the face of detrimental effects is difficult to understand, but makes sense when we grasp that drugs ‘do something’ to the brain which facilitates continued use.

Nestler (2001) showed that drug abuse can alter gene expression in the reward areas, NAc, ventral tegmental area and prefrontal cortex.

Bidwell et al (2018) have shown methylation of the promoter region of the dopamine D2 receptor gene is probably involved in alcohol problems. The literature provides a host of other examples associated with the use of other substances.
Motivations to take substances

The following may be involved in the motivation to take substances.

- to get “a buzz”, or “high” – a unique, pleasure experience
- to “self-medicate” to reduce anxiety, depression or irritability
- to achieve mystical experiences
- to comply with the behaviour of peers

[A comprehensive assessment for the individual will include a consideration of his/her genetics, life experience, personality and current life circumstances.]

Screening test (Two-Item)
A full assessment is mandatory when drug or alcohol use is suspected.

However, a two item screening test has been shown to detect 80% of young and middle-aged individuals with problems (Brown et al, 2001):

1. “In the last year, have you ever drunk or used drugs more than you meant to?”
2. “In the last year, have you felt you wanted or needed to cut down on your drinking or drug use?”

Respondents who score 0, 1, 2, have a 7.3%, 36.5% and 72.5% chance of a current substance use disorder. These items should be included in any assessment of substance use.

ALCOHOL

12% of men and 3% of women in many western countries take more than 14 standard drinks per week, which places them in the ‘at-risk’ category.

The threshold of the at-risk category varies from one country to another, being 21 standard drinks per week in the United Kingdom, and 14 in Canada and the United States. The Australian Government Department of Veteran’s Affairs describes “Low-risk drinking” for males as no more than 4 standard drinks per day, no more than 6 standard drinks on any one day, and 1 or 2 alcohol days per week. For women lower intakes are recommended.

The size of the “standard drink” is frequently misunderstood. Examples include, a middy/pot (285 ml) of full strength beer, a standard serve (100 ml) of wine, a standard serve (60 ml) of port/sherry, and a nip (30 ml) of spirits. People frequently pour themselves larger amounts, particularly when drinking wine and spirits.

There are two models of alcoholism. The social learning model contends that excessive drinking is an acquired behaviour and regards the alcoholic individual as no different from any other drinker in his/her capacity to exert control over their drinking. The medical model, in contrast, views alcoholism as the result of heavy exposure and constitutional vulnerability. This model takes account of brain changes caused by chronic use and holds that, once established, loss of control over drinking is irreversible. The medical model is recommended.

The prevalence of alcohol problems varies across cultural and social settings. Heavy use of alcohol and treatment for alcoholism is more common in men. The risk of
hospital admission for alcoholic psychosis, acute intoxication, and liver cirrhosis is elevated in unskilled workers (Hemmingsson et al, 1997). Alcoholism is more common in occupations with flexible work schedules and those which facilitate access to alcohol.

In general, chronic consumption results in structural and functional brain changes. There is tissue loss, predominantly a reduction in cerebral white matter, but also cerebral cortex. A 22% neuronal cell loss has been reported in the superior frontal cortex (Harper et al, 1987), and shrinkage of surviving neurons in other frontal areas, and the motor and cingulate cortex.

The most powerful predictor of excessive alcohol use is the occurrence of alcoholism in a first-degree relative. The concurrence of alcoholism in monozygotic twins is 30-60%. Adoption studies consistently report increased risk of alcoholism in the children of people with alcoholism, irrespective on the drinking status of the homes in which they were raised. Evidence indicates that alcoholism-antisocial personality is more ‘heritable’ than alcoholism alone, suggesting a “common gene hypothesis” (Haber et al, 2005).

**Alcohol intoxication** needs no description. It may be associated with blackouts.

**Blackouts** refers to amnesia for a period during an episode of intoxication.

**Alcohol withdrawal** generally occurs 6-12 hours after the last drink, and may last for up to 5 days. Alcohol is a CNS depressant; when it is withdrawn there is marked excitatory action, mainly mediated by the glutamaterigic system. There may be delirium (*delirium tremens*; DTs). Cardinal features include disorientation in time and place, visual, tactile and auditory hallucinations or illusions, sweating, tachycardia, hypertension, dilated pupils, ataxia and marked tremor. Less common features include seizure (“rum fits”). Mortality is 5%. Complications include post-withdrawal Wernicke’s encephalopathy and Korsakoff’s syndrome/psychosis (an amnestic syndrome). Treatment is sedation (usually benzodiazepine), fluid replacement and high doses of vitamins (particularly thiamine).

**Wernicke’s encephalopathy** is caused by thiamine deficiency, resulting from poor dietary intake, reduced gastrointestinal absorption and decreased liver storage. Only a proportion of thiamine deficient heavy drinkers develop Wernicke’s encephalopathy, suggesting an inherited abnormality of the thiamine-dependent enzyme transketolase. Degenerative changes (gliosis and haemorrhages) occur in structures around the 3rd ventricle and aqueduct (mamillary bodies, hypothalamus, mediiodorsal thalamic nucleus, colliculi, and midbrain tegmentum). Clinical features include memory deficits, ocular signs (nystagmus, weakness of external rectus, paralysis of conjugate gaze) and global confusional states.

**Korsakoff’s syndrome** occurs in about 80% of those who recover from Wernicke’s encephalopathy. However, it may appear without an antecedent Wernicke’s episode. There are histopathological lesions in the dorsomedial thalamus. Clinical features are anterograde and retrograde memory loss and apathy, occurring in a clear sensorium and with the preservation of other intellectual abilities.
**Alcoholic dementia** is associated with white and grey matter loss, and is believed to be due to numerous interacting mechanisms.

**Cerebellar degeneration** with loss of Purkinje cells in the cerebellar cortex manifests as dysarthria and limb ataxia.

**Alcoholic hallucinosis** is a rare disorder in which auditory hallucinations are experienced in a clear sensorium. These are usually unpleasant and the patient is usually distressed by them. These symptoms usually respond to antipsychotic medication, but if they have persisted for some months, they may be permanent.

**Alcohol-induced depressive symptoms** occur in 80% of those with the alcohol dependence. 1/3 of male and 1/2 of female alcohol dependent people experience depressive disorder. 15% of alcoholic people die by suicide. In most cases depressive symptoms disappear with abstinence; few require antidepressant treatment.

**Alcohol-induced anxiety disorders** have been reported in up to 70% of heavy drinkers. One female twin study found evidence of a common genetic factor underlying both alcoholism and panic disorder (Kendler et al, 1995).

**Other effects** include peripheral neuropathy, myopathy, cirrhosis, pancreatitis, skin lesions, cardiomyopathy, hypertension and cancer of the bronchodigestive tract.

**Treatment of alcohol dependence**

Alcohol dependence is best considered as a chronic relapsing disorder, such as asthma. Social and cultural factors are stronger in alcohol dependence than in other relapsing medical conditions. There is need for long-term monitoring and the management of exacerbations/relapses. The predominant medical view is that in alcohol dependence, the ability of the individual to change his/her drinking habit is less than that of other drinkers. Nevertheless, current legislation leaves ultimate responsibility for action with the individual. While “controlled drinking” is advocated by some, the predominant medical view is that abstinence is the necessary course. Some independent individuals will be able to achieve sobriety without assistance, others will require professional assistance. Alcoholics Anonymous (AA) is of great assistance to many individuals.

Denial at conscious and unconscious levels is a feature of the condition. Individuals may rationalise their behaviour by claiming to be “just a social drinker” and excuse episodes of intoxication on the basis of some event such as abandonment by a spouse (many of which are a consequence, rather than a cause, of drinking).

Withdrawal can be managed in out-patient or in-patient settings, depending on local circumstances.

Withdrawal is easy. Prevention and management of relapse are more difficult. Prolonged psychotherapy aimed at finding the psychological “causes” for excessive drinking are usually unprofitable and may make matters worse. Useful activities include systematically helping people anticipate and cope with high risk situations
(“relapse prevention”), motivational enhancement, social skills training, cognitive therapy, behavioural contracting, and marital therapy.

**Medication** alone is not the answer, and must be part of a specialized treatment programme.

**Acamprosate** enhances GABA transmission, antagonizes glutamate transmission, and reduces craving. In trials, compared to placebo, acamprosate has increased the percentage remaining abstinent for 12 months (from 10 to 25%, and from 20 to 50% in two different studies), doubles the time to first relapse, and halves the total alcohol consumed. However, 50% of alcohol dependent individuals do not benefit. Those who do benefit should remain on acamprosate for at least 6 months.

**Naltrexone** antagonizes endorphins which are released as one of ethanol’s many acute actions on the limbic system. Elevated endorphin levels may contribute to loss of control. Some patients who drink while taking naltrexone report they feel less “high” than usual. In placebo controlled trials, patients taking naltrexone report greater total abstinence and reduction in total alcohol consumed.

**Disulfiram** blocks the metabolism of ethanol causing the accumulation of acetaldehyde, an intermediate metabolite. If taken in sufficient doses for 3 to 4 days, there is an unpleasant reaction (flushing, palpitations and possible vomiting), 15 to 20 minutes after the ingestion of alcohol. Disulfiram is not a first line approach, but can be useful for co-operative patients who seek something to “help” them when faced with the temptation to drink.

**Depressive symptoms associated with alcohol dependence.** As mentioned, depressive symptoms are common in alcohol dependence. Individuals and their relatives frequently seek out these symptoms. They often claim the “depression” is the “cause” of the excessive alcohol use, and that if the doctor would only “cure” the depression, the excessive alcohol use would cease. While this appears to be so in a minority of cases, in the majority, the depressive symptoms are secondary to the alcohol use and improve with abstinence. Antidepressant treatments have no significant effect (even in the case of primary depressive disorder) if the individual continues taking alcohol.
OPIATES  
(heroin, morphine, methadone, buprenorphine)

The family and social effects of opiate use are great. There is frequently divorce and unemployment. Criminal conviction is high. Approximately 60% of the deaths of people using opiates are associated with drug use. Suicide and accidental overdose account for 1/3 of the deaths of opiate users. A 22 year follow-up of 128 heroin users revealed that 43 (>1/3) were dead (Oppenheimer, et al, 1994).

Opiate receptors belong to the G family of protein-coupled receptors, and all inhibit adenylate cyclase and calcium channels. There are two important subtypes: mu and kappa.

Acutely, opiates lead to the inhibition of adenylate cyclase. This decreases the conversion of ATP to cAMP, which in turn results in a reduction in the firing of noradrenergic neurons in the locus coeruleus. Chronic administration leads to a compensatory upregulation of cAMP. On cessation, withdrawal is characterized by a massive upsurge in noradrenergic activity. This is sometimes managed using the alpha 2 agonist, clonidine. Opiate administration leads to increased dopamine activity which mediates the positive reinforcement (euphoria, sedation, emotional numbing, and dream-like state) and drive to use.

Different types of opiates and modes of administration have different speeds of onset and effects. The modes of administration include swallowing, snorting, smoking, and subcutaneous and intravenous injection.
Withdrawal is more marked for heroin (diamorphine). The classic heroin withdrawal syndrome appears in 4-12 hours, peaks at 48-72 hours, and subsides by 7-10 days. Objective measures include tachycardia, hypertension, lacrimation, rhinorrhoea, dilated pupils, and “goose flesh” (piloerection; “going cold turkey”). There is evidence that the expectations of the withdrawing individual greatly experience his/her withdrawal experience. Those who are most fearful and expect to suffer are those who most suffer.

Dalrymple (2006) states the “pain” of withdrawal has been greatly exaggerated by poets and other “romantic writers”, and that this distortion has entered lay and professional belief systems.

Physical harm depends on the route of administration and adulterants. The risk of viral transmission (HIV, hepatitis B and C) led to the “harm minimization” focus of services (“needle exchange” being a feature).

Psychiatric comorbidity has been demonstrated in 70% of heroin users, predominantly antisocial personality disorder (Seiveright & Daly, 1997), alcohol dependency, and depressive symptoms. These may be primary or secondary to opiate use.

Heroin (diamorphine) is metabolized to morphine. However, it is more lipophilic than morphine and provides a stronger “rush”.

Methadone is an orally effective opiate with a longer half-life than heroin (24-36 hours), which makes it suitable for daily administration. At above 80 mg per day it provides a reasonable level of opiate receptor blockade, such that euphoria from illicit drugs “used on top” is disinhibited. It has been the mainstay of treatment of opiate dependency in the western world.

Buprenorphine is a partial mu receptor agonist and kappa receptor antagonist, which is being used in the stabilization and detoxification of opiate using people.

Management of opiate dependency begins with a trusting patient-doctor relationship. Methadone may be used as a substitute for the previously used opiates. It is prescribed long-term with the aim of achieving stable (non-injecting) opiate dependence (methadone maintenance). The benefits include reduced risks from injecting, other drug use, criminal behaviour, and suicide/overdose, and increased likelihood of maintenance of treatment contact. Methadone should be part of a multidisciplinary, biopsychosocial treatment package (Gossop et al, 2006).

Relapse prevention elements include identification of cues or triggers for craving (people, places, paraphenalia, moods) and techniques to handle high-risk situations (distraction, relaxation, imagery). Motivational interviewing aims to move people along in the “cycle of change”, from pre-contemplatory (no interest in changing behaviour) to contemplation, and then to determination and action. Motivational interviewing is not authoritarian, and rests on the following principles: expression of empathy, helping the patient see discrepancies in their behaviours, avoiding argument, tolerating resistance and supporting the patient’s sense of self-sufficiency.
STIMULANTS
(amphetamine, cocaine)

Illustration. A genuine illustration from 1885. Interestingly, before he developed the field of psychoanalysis, Sigmund Freud pioneered the use of cocaine as an analgesic in eye surgery.

Illustration. Perhaps the most common source of stimulants is modified ephedrine, a component of many over-the-counter ‘cold’ treatments.

The stimulants increase energy and elevate mood, due to enhanced dopamine and noradrenaline activity. A more potent street preparation of methylamphetamine is “ice”, and a more potent form of cocaine is “crack”. The stimulants can be swallowed, snorted, or injected. Crack can be smoked.

As with other illegal substances, stimulant use is more common among young males of lower socio-economic status, in areas with high rates of other social problems. In Australia about 2% of the population has used cocaine. These are mainly inner-city polysubstance users (Hando et al, 1997).

Methylamphetamine use is associated with increased violence, independent of psychosis (McKetin et al, 2014).
Chronic use may lead to paranoid delusions. The psychosis may be managed by
cessation of the stimulant and commencement of an antipsychotic medication (often
in an inpatient setting).

Withdrawal symptoms include depression, irritability, agitation, craving, hyperphagia
and hypersomnia. There is some debated about whether the stimulants are
“addictive”. The con argument is that the listed “withdrawal” symptoms are not true
withdrawal, but simply “catching up” eating and sleeping. This semantic argument is
a legacy of Cartesian dualism, and psychological dependency is frequently observed.

Chronic exposure of rodents to stimulants causes increased dendritic branching and
increased numbers of dendritic spines.

Illustration. Neurones from rodents exposed to stimulants. The number closest to the
neuron is a measure of dendritic branching, the number to the right is a measure of the
number of dendritic spines. For both amphetamine and cocaine, the dendritic
branching and spines numbers are up by 8-12%. From, Robinson & Kolb, 1999.

Occasional recreational use is possible. Complications are more common with
injecting, and when there is concurrent use of other drugs.

There is little evidence to support any specific treatment of stimulant use (Price et al,
2018). Resperine, modafinil, buspirone and ondansetron may be of some use
(Susukida et al, 2018).

Harm minimization is the recommended approach. There is the promise of a unique
approach: a cocaine vaccine which will slow entry of the substance into the brain
(Sofuoglu & Kosten, 2006).
EXTACY
(3,4-methylenedioxymethamphetamine, MDMA)

Ecstasy, a ring-substituted amphetamine, was one of the first “rave” or “party” drugs. It is taken by mouth. It is popular and has been taken by 13% of 3000 UK university students (Webb, et al, 1996), and 4.6% of 15-64 year olds in Spain (Brugal et al, 2006).

Ecstasy causes the release of serotonin from nerve terminals. It also inhibits tryptophan hydroxylase, the rate-limiting enzyme in serotonin synthesis, resulting in central serotonin depletion. Lowering of mood is frequently reported in the post use period, which is consistent with depletion of central serotonin.

Ecstasy has both stimulant and hallucinogenic effects. It also causes an altered state of consciousness and profound feelings of attachment and connection. (When first developed, it was used in marital therapy.) However, the effects are unpredictable, especially when combined with other drugs and in exciting circumstances.

Physical effects are reminiscent of amphetamines use, with tachycardia, anorexia, increased motor activity, bruxism (teeth grinding), elevated temperature, and sweating.

Animal evidence indicates MDMA is toxic to serotonergic neurons. Human neurotoxicity has not been conclusively demonstrated. However, MDMA use is clearly associated with cognitive problems and the evidence for neurotoxicity is strong (Roberts et al, 2018).

Mental complication include anxiety and panic, major depression, prolonged depersonalization, suicidal ideation, and psychosis. Physical complications are more common when taken in combination with other substances and include hyperthermia, dehydration, idiosyncratic organ failure of heart and liver, and cerebral oedema. The serotonin and neuroleptic malignant syndromes have been described. 70 deaths were recorded in the UK in the 1990s.
CANNABIS
(tetrahydrocannabinol, THC)

Cannabis sativa, leaf (female plant)

Cannabis is derived from the Cannabis sativa (female plant). The principal psychoactive component: delta-9-tetrahydrocannabinol (THC).

Cannabis may be eaten, but the most efficient and common mode is smoking. It increases dopamine release. A specific receptor (for the endogenous ligand anandamide) is located in regions associated with memory, reward, pain perception and motor co-ordination.

Use is widespread. A New Zealand study (Boden et al, 2006) found that by 25 years of age, 76.7% of the population had used cannabis, and 12.5% met DSM-IV criteria for ‘cannabis dependence’. Most cease cannabis use in their mid to late 20s. “Heavy” cannabis use is defined as daily or near-daily use, and such use places the individual at risk of mental disorder.

Acute mental effects include euphoria and relaxation, perceptual alterations (time distortion), intensification of ordinary sensory experiences (for example, while eating and listening to music) and impaired short-term memory and attention. Impairment in cognition and behavioural functions, such as driving are dose-related. The most commonly reported adverse mental effects are anxiety and panic reactions, and these may lead to discontinuation by naive users.

Earlier opinion was that cannabis was not a drug of dependence was incorrect. Tolerance (Adams & Martin, 1996) and withdrawal symptoms (Copersino et al, 2006) have been observed. Cannabis dependence, with inability to abstain is listed in the DSM-IV. It is not clear how cannabis dependence is best managed; some evidence indicates the use of CBT and social support.

“Cannabis psychosis” has been a matter of debate. A major difficulty is that we do not know whether psychotic symptoms lead to cannabis abuse, or whether cannabis use causes psychosis. It is likely that the relationship is bidirectional (Hides et al, 2006).
Another difficulty is to know whether cannabis can produce psychosis in all users, or only those who are genetically vulnerable. Moore et al (2007) finds that all those who use cannabis are at risk of psychosis.

There is good evidence that cannabis can at least precipitate (bring forward) the first episode (which would otherwise have occurred later) of schizophrenia in a vulnerable person.

Cognitive impairment, which is subtle and involves the higher functions of memory, attention and organization, and the integration of complex information, has been demonstrated in individuals with a long history of cannabis use (Solowij, 1998).

Cannabis use by people with schizophrenia is a major problem. Clinical experience indicates that cannabis is a potent cause of relapse and exacerbation of symptoms. Concurrent use of cannabis is associated with a worse prognosis for schizophrenia.

Cannabis provides people who have lost much (career, prospects, income, family) with some comfort. Prevalence of use among people one year after first diagnosis of schizophrenia is 18.5% (Harrison et al, 2008).

Taking these findings into account, everyone should avoid cannabis, especially those with a family or personal history of schizophrenia.

An amotivational syndrome has been described in long-term cannabis use. There has been uncertainty as to whether this is a legitimate condition – but, there is at least partial scientific support (Lac and Luk, 2018).

There is a strong cross-sectional association between heavy cannabis use in adolescence and discontinuation of education, and job instability in adulthood. However, complicating this finding is that heavy cannabis users have lower aspirations and lower school performance prior to cannabis use.

Cannabis use may precede “harder” drug use. There is a selective recruitment into cannabis use of non-conforming adolescents, who already have a propensity to use illegal drugs. Once recruited to cannabis use, familiarity and access increases the likelihood that individuals will use other drugs.

Treatment – a recent study has suggested the use of long acting injectable naltrexone (Notzon et al, 2018).
HALLUCINOGENS
(lysergic acid diethylamide, LSD)

Illustration: When the author was at school (half a century ago), it was discovered that spiders on LSD performed very poorly (straight spider’s web on the left, LSD using spider’s web on the right). This was taken as evidence that LSD seriously reduced functional ability, and was used to discourage LSD use. In subsequent years it was found that even caffeine could impair the spider’s ability, so the “web performance” evidence lost persuasive value. Nevertheless, LSD remains a dangerous drug and use for any purpose is strongly discouraged.

LSD was synthesised during medical research for a benign ergot derivative. The substance is taken by mouth. Injection is unnecessary and rarely practiced.

Hallucinogens alter perception and mood without disorientation or memory disturbance (Abraham, 2000). They bind strongly to the serotonin-2A receptor and act as partial agonists.

The use of hallucinogens is frequently said to be increasing, however, there is evidence the use of LSD among US university students has been decreasing since a peak in 1978 (Pope et al, 2001). In 1997, the lifetime use of LSD prevalence of American high school seniors was 13.6%. Germany and Denmark report similar figures. As LSD lacks the addiction potential of alcohol, cocaine, or opiates, use typically declines in the mid 20s.
Acute effects of LSD include autonomic arousal, mydriasis, and modulation of sensory experience, particularly visual. Objects appear distorted, and geometric images rise and fall before one's eyes. Ordinary objects take on a new emotional meaning. There is loss of cognitive, perceptual and affective control. This may result in panic: a “bad trip”. As the effects subside there may be a sense of wellbeing or paranoid delusions.

Adverse effects include “bad trip” (panic), hallucinogen persisting perception disorder, and prolonged psychosis.

Panic reactions can be rapidly aborted with benzodiazepines, particularly diazepam and clonazepam. (This observation suggests the GABA receptor plays a role in modulating the effects of hallucinogens.)

Hallucinogen persisting perception disorder (“flashbacks”) are visual disturbances which occur sporadically for days or weeks following LSD use. Recovery may occur over months or years following the last substance use, but approximately half of all afflicted individuals have permanent problems (Orsolini et al, 2017). Symptoms include geometric hallucinations, false perceptions of movement, and ‘tails’ on images as the object moves across the visual field. Coloured pin-point dots may be seen in the bright sky. Neurophysiological studies demonstrate disinhibition of the cortical regions which process visual information (Abraham, 1983). It may be that LSD excitotoxically stimulates and destroys serotonin-2A receptor bearing inhibitory neurons. As only a sub-group of those who use LSD develop hallucinogen persisting perception disorder, this disorder may depend on genetic vulnerability. Support and continuous assessment are necessary to prevent and provide help should comorbid disorders (major depressive disorder, alcohol dependency) develop. Clonidine may be helpful (Learner et al, 2000).

Post-LSD psychosis remains a topic of debate. Clinically the picture resembles schizophrenia, but with more retention of affect and less thought disorder. Visual hallucinations like those of hallucinogen persisting perception disorder are a frequent feature and there may be mystical preoccupations. Some patients describe delusions and auditory hallucinations. The relationship of this disorder to schizophrenia remains to be elucidated.
GAMBLING DISORDER

Gambling disorder (GD) appeared as a psychiatric disorder in the DSM-5 (2013). Some psychiatrists still hold doubts about whether such ‘behavioural addictions’ are true psychiatric disorders.

GD is similar to substance use disorder on clinical grounds. GD demonstrates ‘loss of impulse control’ (repeated unsuccessful efforts to control, cut back or stop gambling), ‘craving/withdrawal’ (needs to gamble with increasing amounts of money), ‘neglect of other areas in life’ (preoccupied with gambling, lies to family members to conceal the extent of gambling, has lost relationships or jobs because of gambling) (Romanczuk-Seiferth et al, 2014).

Some treatments of substance use disorders (e.g., naltrexone) are helpful in GD. Heritability of GD is estimated at around 50%, similar to some substance use agents 60%; Nestler, 2013). GD and substance use disorders commonly occur together.

The neuroimaging changes in GD are complicated and not the same as substance use disorder. One study (Koehler et al, 2013) found increased grey matter volumes in the PFC and the striatum. Another (Jousta et al, 2011) found changes in white matter tracts.

‘Loss of control’, ‘craving/withdrawal’ and ‘neglect of other areas in life’ have all been associated with different brain region changes (Romanczuk-Seiferth et al, 2014).

Of particular interest has been mesolimbic dopamine transmission – the major component of the brain reward system – which is markedly disrupted in substance use disorder. Abnormalities have been described in (GD), but there is divergence from the classic picture of drug addiction (Clarke, 2014).

DSM-5 Diagnostic criteria

A. Persistent problematic gambling leading to impairment or distress, as indicated by the individual exhibiting at least 4 of the following in the last year.
1. Needs to gamble increasing amounts of money in order to achieve the desired excitement.
2. Is restless/irritable when attempting to cut down or stop
3. Has made repeated efforts to cut down or stop
4. Often preoccupied with gambling, planning next venture, thinking of ways to get money
5. Often gambles when feeling distressed (helpless, guilty, anxious)
6. After losing, returns another day to get even (chasing one’s losses)
7. Lies to conceal extent of gambling
8. Has jeopardized or lost a significant relationship/job through gambling
9. Relies on others to provide money to relieve desperate financial situations

B. Gambling behaviour not explained by a manic episode.
References
Chester D, De Wall C. Aggression is associated with greater subsequent alcohol consumption: a shared neural basis in the ventral striatum. Aggressive Behav 2018 [Epub ahead of print]


Orsolini L et al. The “Endless Trip” among the NPS users. Front Psychiatry 2017; 8: 240.


Robinson T, Kolb B. Alterations in the morphology of dendrites and dendritic spines in the nucleus accumbens and prefrontal cortex following repeated treatment with amphetamine or cocaine. European Journal of Neuroscience 1999; 11:1598-1604.


Chapter continues on next page.
## Alcohol withdrawal protocols

General hospitals have standard alcohol withdrawal protocols. The Royal Hobart Hospital (Tasmania Department of Health and Human Services) has a satisfactory approach, and has given permission for their documents to be attached to this chapter.

<table>
<thead>
<tr>
<th>Nausea and vomiting</th>
<th>Tactile disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No nausea and no vomiting</td>
<td>0: None</td>
</tr>
<tr>
<td>1: Mild nausea with no vomiting</td>
<td>1: Very mild itching, pins and needles sensations, any burning, any numbness or do you feel bugs crawling on or under your skin?</td>
</tr>
<tr>
<td>2: Intermittent nausea, with dry retching</td>
<td>2: Mild itching, pins and needles, burning or numbness</td>
</tr>
<tr>
<td>3:</td>
<td>3: Moderate itching, pins and needles, burning or numbness</td>
</tr>
<tr>
<td>4:</td>
<td>4: Moderately severe hallucinations</td>
</tr>
<tr>
<td>5:</td>
<td>5: Severe hallucinations</td>
</tr>
<tr>
<td>6:</td>
<td>6: Extremely severe hallucinations</td>
</tr>
<tr>
<td>7: Constant nausea, frequent dry retching and vomiting</td>
<td>7: Continuous hallucinations</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Tremor</th>
<th>Auditory disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No tremor</td>
<td>0: Not present</td>
</tr>
<tr>
<td>1: Not visible, but can be felt with idea finger tip to finger tip</td>
<td>1: Very mild sensitivity</td>
</tr>
<tr>
<td>2:</td>
<td>2: Mild sensitivity</td>
</tr>
<tr>
<td>3:</td>
<td>3: Moderate sensitivity</td>
</tr>
<tr>
<td>4:</td>
<td>4: Moderately severe hallucinations</td>
</tr>
<tr>
<td>5:</td>
<td>5: Severe hallucinations</td>
</tr>
<tr>
<td>6:</td>
<td>6: Extremely severe hallucinations</td>
</tr>
<tr>
<td>7: Severe, even with arms not extended</td>
<td>7: Continuous hallucinations</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Paroxysmal sweating</th>
<th>Visual disturbances</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No sweat visible</td>
<td>0: Not present</td>
</tr>
<tr>
<td>1: Barely perceptible sweating, palmer moist</td>
<td>1: Very mild sensitivity</td>
</tr>
<tr>
<td>2:</td>
<td>2: Mild sensitivity</td>
</tr>
<tr>
<td>3:</td>
<td>3: Moderate sensitivity</td>
</tr>
<tr>
<td>4: Beads of sweat obvious on forehead</td>
<td>4: Moderately severe hallucinations</td>
</tr>
<tr>
<td>5:</td>
<td>5: Severe hallucinations</td>
</tr>
<tr>
<td>6:</td>
<td>6: Extremely severe hallucinations</td>
</tr>
<tr>
<td>7: Drenching sweats</td>
<td>7: Continuous hallucinations</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Anxiety</th>
<th>Headache, fullness in the head</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: No anxiety, at ease</td>
<td>0: Not present</td>
</tr>
<tr>
<td>1: Mildly anxious</td>
<td>1: Very mild</td>
</tr>
<tr>
<td>2:</td>
<td>2: Mild</td>
</tr>
<tr>
<td>3:</td>
<td>3: Moderate</td>
</tr>
<tr>
<td>4: Moderately anxious or guarded; so anxiety is intense</td>
<td>4: Moderately severe</td>
</tr>
<tr>
<td>5:</td>
<td>5: Severe</td>
</tr>
<tr>
<td>6:</td>
<td>6: Very severe</td>
</tr>
<tr>
<td>7: Equivalent to acute panic states as seen in severe delirium or acute schizophrenic reactions</td>
<td>7: Extremely severe</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Agitation</th>
<th>Orientation and clouding of sensorium</th>
</tr>
</thead>
<tbody>
<tr>
<td>0: Normal activity</td>
<td>0: Orientated and can do serial additions</td>
</tr>
<tr>
<td>1: Somewhat more than normal activity</td>
<td>Ask person to perform serial addition of 3’s up to 30 eg: 3000...</td>
</tr>
<tr>
<td>2:</td>
<td>1: Cannot do serial addition or is uncertain about date</td>
</tr>
<tr>
<td>3:</td>
<td>2: Disoriented by date by no more than 2 calendar days</td>
</tr>
<tr>
<td>4: Moderately agitated and restless</td>
<td>3: Disoriented for data by more than 2 calendar days</td>
</tr>
<tr>
<td>5:</td>
<td>4: Disoriented for place and/or person</td>
</tr>
<tr>
<td>6:</td>
<td></td>
</tr>
<tr>
<td>7: Rapid and flighty during most of the interview or constantly threatens about</td>
<td></td>
</tr>
</tbody>
</table>
# Alcohol Withdrawal Form

## Tasmania Department of Health and Human Services

### Southern Region

**Nursing Management** - Nurse in a quiet, evenly lit environment. Provide reassurance and explanation. Re-orientate the person if confused. Ensure adequate hydration.

## Observations

<table>
<thead>
<tr>
<th>Date</th>
<th>Time</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Breath Alcohol Reading</th>
<th>Temperature (per axilla)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Pulse</th>
<th>Respiration Rate</th>
<th>Blood Pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Alcohol Withdrawal Assessment Score

<table>
<thead>
<tr>
<th>Time</th>
<th>Nausea and Vomiting</th>
<th>Tremor</th>
<th>Paroxysmal Sweats</th>
<th>Anxiety</th>
<th>Agitation</th>
<th>Tactile Disturbances</th>
<th>Auditory Disturbances</th>
<th>Visual Disturbances</th>
<th>Headache, Fullness in Head</th>
<th>Orientation and Clouding of Sensorium</th>
<th>Total Score</th>
<th>Medication Given</th>
<th>Time Given</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
VITAMIN ADMINISTRATION
- Thiamine 100 mg and multivitamins daily.
- Give thiamine orally unless parenteral administration indicated (e.g. malnutrition, acute Wernicke's Syndrome).
- Persons receiving intravenous dextrose or glucose should first receive parenteral thiamine to prevent acute Wernicke's Syndrome.
- If AWS score rises to 17 or more recommence diazepam loading after further medical assessment.

MEDICAL MANAGEMENT OF ACUTE ALCOHOL WITHDRAWAL
- Preferred drug treatment when indicated is:
  Diazepam 20 mg orally 2 hourly until score is 10 or less.
- Further medical assessment is required for doses beyond 120 mg.

WITHDRAWAL CONVULSION PROPHYLAXIS
- Preferred drug treatment is:
  Day 1  Diazepam 15 mg orally for 5 doses at 2 hourly intervals
  Day 2, 3  Diazepam 10 mg orally b.d.
  Day 4  Diazepam 5 mg orally b.d.

NOTE: If high AWS scores occur during the Day 1 loading phase, doses should be converted to 20 mg and continued 2 hourly until the score is 10 or less. Ensure that a minimum total of 75 mg diazepam has been given on Day 1 unless the patient is excessively drowsy.

COMBINED ALCOHOL AND BENZODIAZEPINE WITHDRAWAL
- Where a combined alcohol and benzodiazepine dependence exists, the minimum dose of diazepam given during Day 1 should be equivalent to the stated dose of benzodiazepine intake, to a maximum of 80 mg. This dose should be given at a rate of 20 mg per 2 hours until the total first day dose has been given.
- In the initial stages, more diazepam may be required to manage acute alcohol withdrawal symptoms or to prevent withdrawal convulsions. This should be given at a rate of 20 mg per 2 hours until the score has settled.
- During subsequent days, inpatient clients will require a continuous, gradual diazepam withdrawal regime in accordance with the recommended guidelines.
- Such regimes feature: QID doses of diazepam with the total daily dose decreasing by 5-10 mg per day over a period of 7-14 days.

GENERAL
- Symptomatic treatment (e.g. Paracetamol for headache, Metoclopramide for nausea or vomiting) may be useful.
OBSERVATION CHART

Average daily alcohol consumption during the past week ____ grams (follow chart below to calculate consumption)

Note:
1. Notify Medical Officer if on admission client reports a history of:
   - Daily alcohol use of 80 grams or more
   - Withdrawal seizures
   - Recent benzodiazepine use (this may affect the expression of alcohol withdrawal symptoms)

2. Seek medical assessment should one or more of the following occur:
   - Any convulsions
   - Total score of 11-19 (drug treatment is a matter for clinical judgement)
   - Total score of 20 or more (drug treatment is indicated)

3. Diazepam should not be given until the Breath Alcohol Reading is less than or equal to 0.10 g%.

4. Approximate alcohol content for different beverages in grams.

<table>
<thead>
<tr>
<th>Per Litre</th>
<th>Pint 425 ml</th>
<th>Bottle 750 ml</th>
<th>Echo, Can 375 ml</th>
<th>Schooner 285 ml</th>
<th>Wine Glass 120 ml</th>
<th>Port Glass 60 ml</th>
<th>Split Glass 30 ml</th>
</tr>
</thead>
<tbody>
<tr>
<td>Beer Light 2.5%</td>
<td>8.5</td>
<td>15</td>
<td>7.5</td>
<td>5</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beer Regular 5%</td>
<td>17</td>
<td>30</td>
<td>15</td>
<td>10</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Table Wine</td>
<td>100</td>
<td>60</td>
<td></td>
<td>20</td>
<td>10</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fortified Wine</td>
<td>200</td>
<td>120</td>
<td>60</td>
<td>40</td>
<td>20</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>Spirits</td>
<td>240</td>
<td>120</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>10</td>
</tr>
</tbody>
</table>

- Low Alcohol Beer
- Beer or Wine Cooler
- Wine
- Fortified Wine
- Spirits or Liqueurs

425 ml = 285 ml = 120 ml = 60 ml = 30 ml = 10 grams