03 July 2020
No.11

# Drugs of Abuse and the implications for Anaesthesia and Critical Care

**MA Balkisson**

**Moderator: Dr K Allopi**

UNIVERSITY OF
KWAZULU-NATAL

INYUVESI
YAKWAZULU-NATALI

**School of Clinical Medicine**
**Discipline of Anaesthesiology and Critical Care**

## Contents

## INTRODUCTION

Through history, mankind has sought out many and varied ways of manipulating the body and mind through the “powers” of chemical compounds.

This love affair with altering our perception of reality has produced some of the best pharmaceutical agents in the armamentarium of the anaesthetist today.

Over time, lines have been drawn separating licit from illicit substances and these distinctions have been adopted by law makers and governments world over.

Unsurprisingly many of the substances we know to be prohibited today started off as the latest “wonder drug” before precipitously falling from grace.

Given the indivisible bond between man and “recreational drugs”- it is expected that the abuse of them will be encountered in the peri-operative or critical care setting.

“When planning anaesthetic care, it is important for anaesthesiologists to understand the effects of these agents, including various drug interactions, to predict tolerance to some anaesthetic agents, to recognize drug withdrawal signs and symptoms, and to be prepared to manage all these factors in the perioperative period.” [1]

### Outline

1. The one-time innocent origins of illicit drugs
2. The history of drug scheduling and regulation
3. An overview of the commonly abused drugs in Durban and South Africa
    a. The extent of the burden
    b. Classification, description, and street names
    c. Pharmacodynamics and dose profiling
    d. Symptoms and signs of intoxication and/or withdrawal
    e. Impact on Anaesthesia

### The one-time innocent origins of illicit drugs

It is interesting to consider a world in which the drugs that we know today to be illegal and socially unacceptable were freely prescribed and marketed to the general public.

In truth most of the drugs now firmly in the Schedule 1 (US Controlled Substance Act) category of narcotics was developed by pharmacists attempting to cure the most pressing physical and mental health ailments of the day.

In today’s context we see the “Opioid Epidemic”. This term was first introduced in the early 1990s to describe a sudden increase in the number of deaths related to overdose of opioid type drugs in relation to the rise in prescription of opioids for non-cancer type pain. [2]

Most recently, in 2016, the biggest increase in mortality has come from the abuse of Fentanyl in the United States. The source of the Fentanyl in this instance is thought to be from its illegal manufacture rather than improper prescription. [3]

No drug, however, is more central to the cause of the opioid crisis than tea. This harmless beverage has a somewhat dark past.

“The earliest reference to opium growth and use is in 3,400 B.C. when the opium poppy was cultivated in lower Mesopotamia (Southwest Asia). The Sumerians referred to it as Hul Gil, the "joy plant." The Sumerians soon passed it on to the Assyrians, who in turn passed it on to the Egyptians. Opium was one of the products traded along the Silk Road”[4]

“It was known to ancient Greek and Roman physicians as a powerful pain reliever [and] was also used to induce sleep and to give relief to the bowels. It was even thought to protect the user from being poisoned. Its pleasurable effects were also noted.”[4]

By the 1800s – many countries were cultivating, and processing opium and it formed an essential commodity in international trade. The British, through the powerful East India Company, was a major producer of opium from its Indian colony. [4]

“China controlled the production of tea until well into the 19th century. Britain couldn’t produce its own tea, and for a time depended on poor quality leaves imported to Europe via the Netherlands .[5] Historical accounts have it that, to satisfy the country’s demand for tea, Britain exhausted its reserve of silver and changed instead to trading tea for opium. This led to widespread addiction to opium amongst the Chinese upper class which lead to the opening of so-called “opium dens”. This practise filtered down to the lower economic classes until the region was consumed, leading to the “opium wars” of the mid-19th century. Chinese migrant labourers working in the Americas were thought to have been the factor which introduced opium to the far west. [4]

Later in the 19th century, Laudanum was a popular opium based analgo-sedative in use. It contained various imaginative combinations of up to 10% powdered opium (equivalent to 1% Morphine) and mercury, hashish, cayenne pepper, ether, chloroform, belladonna and whisky, sherry, wine and brandy[6]. Its common indications were respiratory illness, diarrhoeal disease, non-specific agues, and rheumatism and was frequently prescribed to women for abdominal pains, anxiety, ‘nervousness’ and as a soporific. It became popular amongst lower income groups as it was cheaper than alcohol and available for purchase as a home remedy. The abuse of Laudanum is strongly suspected among poets of the Romantic era like Byron and Shelley. The use of Laudanum or “opium tincture” was regulated from the early 20th century and its popularity faded with the introduction of the synthetic opioids. It is produced today in limited quantities and remains a Schedule 2 drug. In the US and UK it is indicated for treatment of diarrhoeal illnesses.[7]

**Morphine**

Friedrich Sertürner is credited with the discovery of Morphine in 1803. He isolated it from opium resin, and it is thought to be the first alkaloid to be derived from a plant source. His discovery was prompted by the inter-variability in potency and adverse effects caused by differing sources of opium. The emetic effects and sub-therapeutic analgaesic effects were undesirable. He wanted to isolate the active ingredient which would be delivered in a safe, effective and reliable dose. The name of the drug comes from the Greek god of dreams “Morpheus” and the conventional naming of alkaloids to give the name Morphine.[6]

**Heroin**

By the mid-1800s – physicians had noted a problem with Morphine. Its propensity for causing addiction and physical dependence was becoming apparent. The invention of the hypodermic needle meant that more of the drug was being delivered parenterally. Chemists were looking for better version which eliminated this quality.

In 1862 Augustus Matthiessen was a lecturer in chemistry at St Mary’s Hospital Medical School in London. His area of research involved the opium alkaloids.

He partnered with Charles Wright in experimenting with esters of morphine by bubbling hydrochloric acid through morphine in a sealed tube. In 1874, Charles Wright, continuing the work of his mentor, synthesised acetyl-codeine, acetyl-morphine, and diacetylmorphine . [8]

In 1898, Bayer was a up and coming German pharmaceutical company. Bayer was looking to expand its market share through its novel pharmaceutical research department. They employed Heinrich Dreser, a chemist with an interest in the acetylation of codeine, and Felix Hoffman, a German chemist. During his research in adding an acetyl group to various molecules he "discovered" 2 drugs: Acetylsalicilc acid (Aspirin) and diacetylmorphine. [8]

Aspirin became a very popular drug for pain relief and put Bayer on the map. They proceeded to test the other compound diacetylmorphine on Bayer employees.

The name Heroin comes from the term *Heroisch* which was how the Bayer employees who tested the drug reported that it made them feel."[9]

Heroin use was promoted vigorously to physicians of the time. Due to the inability of Bayer to patent the drug – they relied on cornering the market through advertising. The claims of the company were that Heroin had all the best characteristics of Morphine without the addiction. It was a revolutionary cough-suppressant in a time when respiratory illnesses like Tuberculosis were widespread in the community. It was even described as a "cure" for Morphine addiction.[9]

Its popularity continued to rise amongst the physicians of the time. It was considered a wonder drug. However, some began to be aware of growing levels of addiction amongst both the patients it was administered to and the physicians prescribing it. Numbers of admissions related to heroin abuse began to rise and Bayer was forced to acknowledge its addictive potential. Bayer stopped producing Heroin in 1913. In 1914 the US banned its use without prescription. In 1920, the House of Delegates of the American Medical Association adopted a resolution "that heroin should be eliminated from all medicinal preparations and prohibited in the United States. [9] Under the name diamorphine, heroin is a legal prescription drug in the United Kingdom.

Today, Heroin abuse is still responsible for drug overdose deaths in the US rising from 1,960 in 1999 to 15,469 in 2016.[3] Since 2016, the number of deaths has remained steady with 14,996 deaths reported in 2018. A study by Plüddemann et al. in 2003/4 estimated that there were between 12 000 and 18 000 heroin users in Cape Town alone.

**Cocaine**

The coca plant is thought to have originated in South America and was the favoured traditional remedy of the Inca people. Its use in their religious ceremonies and burial rights is evidenced by archaeological findings.[10]

At the time of the Spanish invasion of South America native silver miners working in the northern Andes chewed the coca leaf to help overcome pain, fatigue, and the respiratory problems common at high altitudes. The practise of chewing the leaves with alkali substances (like lime) and holding in the mouth to promote the release of the active CNS stimulants is what has been passed down through the generations of people native to the region. [10] European and North American physicians did not take much interest in coca until about 1860. [11]

In a paper by Weil in 1978 he describes the actions of the Coca leaf.

"Traditionally, coca is considered an excellent restorative that combats physical fatigue and stimulates cardiac and respiratory functions in a useful way. For this reason, many Indians use it as an aid to physical work. In Andean towns coca is still regarded as the best treatment for the nausea, dizziness, and severe headache of altitude sickness (soroche), and tourist hotels routinely serve

hot-water infusions of the leaves to new arrivals from the lowlands. They are believed to promote healing of oral lesions and they are used both to relieve toothache and as a prophylactic to keep teeth white and resistant to decay".

Erythroxylum coca of the family Erythroxylaceae is native to the Andean slopes of South America. The cocaine alkaloid was first extracted from the leaves in the 1840s as one of around 14 different alkaloids. "The concentration of cocaine in the leaves varies from about 23% to 85%, depending on the species and growing conditions". [10]

The main alkaloid in the leaves of the coca plant was extracted in 1859 by Albert Niemann, a German scientist, who gave it the name cocaine. In 1884 cocaine became commercially available from Merck & Co.[12]

Cocaine found its way into many tonics and restoratives in the 1860s. It had many proponents including Sigmund Freud who was enthusiastic about its ability to treat the "nervous hysteria", morphine and alcohol addiction afflicting many amongst his patient group. He extolled its virtues and even used it on himself and his fiancé. [10]

**Cocaine in Coca-Cola**

The histories suggest that an entrepreneur named John Pemberton heard about cocaine as the latest "wonder-drug". After "testing" it on himself extensively he sought to make his fortune by improving upon the French cocaine wine, Vin Mariani, and creating a version for sale to the American public. When prohibition came to Atlanta in 1889 however, he found a drink containing alcohol to be less lucrative. He then developed a soft drink which still contained the coca extract which made it so popular. Combined with the caffeine rich Kola nut this syrup became Coca-Cola. [13]

Coca-Cola was marketed exclusively to professional, white middle class people. It was the drink for the fashionable and intellectual and this was accompanied by aggressive advertising[10]. However, the public opinion on cocaine turned when the extent of the addictive potential of cocaine was revealed. This prompted the onset of regulations on prescription and manufacture. In 1904 the cocaine was removed from the Coca-Cola syrup. In 1906 the Pure Food and Drug Act was enacted to stop the sale of patent medicines containing substances such as cocaine. (Before that date, manufacturers were not required to list the ingredients of their patent medicines) The 1906 act made truthful labelling of patent medicines sold across state borders mandatory, but it did not stop the sale of cocaine products. New York State tried to curtail cocaine sales by passing a law in 1907 that limited the right to distribute cocaine to physicians.[13]

The cocaine drug problem continued to rise until 1914, when the Harrison Act was passed.[14] [10] Its use largely dwindled in the 1960s partly due to the limitations of its sale and distribution and partly because of the rise in popularity of Amphetamines.

**Amphetamines and Methamphetamine**

"When biochemist Gordon Alles developed beta-phenylisopropylamine in 1927 (later to be known as Amphetamine) he was looking to create a decongestant and bronchodilator to substitute for Ephedrine"[15]. (Ephedrine was the alkaloid derived from the plant Ephedra used commonly for the treatment of asthma, coughs and congestion.) [16]

Following his studies, the pharmaceutical company SKF (Smith, Kline, and French) patented the base form of amphetamine. They marketed it as "Benzedrine": an inhaler containing 325mg of amphetamine to be inhaled every hour to treat congestion.

In 1935, the American Medical Association approved the production of Benzedrine Sulphate tablets for such indications as narcolepsy, post-encephalitic Parkinsonism, and minor depression[17] [17]. The popular theory was that minor depression was simply “anhedonia” caused by a lack of impetus to action. With this view, amphetamines were the ideal cure. [15]

Concurrently, in 1893, the Japanese Chemist Nagayoshi Nagai created methamphetamine by combining iodine and phosphorous with the precursor chemical, ephedrine, to enhance endurance and alertness and ward off fatigue [16]. The commercial drug however only became popular after oral amphetamine tablets had already taken over the market.

During World war 2 amphetamines had gained traction as a prescription antidepressant. There were some reports of misuse but by 1945 the industry was worth $2 million.[15]

Historical reports demonstrate that the US military were supplying Amphetamines to servicemen as a matter of routine and in medical supply kits as 5mg tablets. This practise was repeated by British military and among Japanese and German Military methamphetamine distribution was allegedly common practise.[15] The was to stave of exhaustion, increase alertness and provide troops who could march further for longer.

In parallel, amongst civilians, amphetamines were increasingly being taken for the off-label indication of weight loss.

Amphetamine sales continued to grow from strength to strength well into the 1950s. Most prescriptions (85%) in the early 1960s were aimed at women.[15] with support from authorities like the AMA for the advertising of drugs like “Dexamyl™, which was a combination of drugs dextroamphetamine and amobarbital which is a barbiturate sedative.

The competition from other companies produced many more iterations of amphetamine and methamphetamine salts. Its widespread use exposed the adverse effects like psychotic episodes, which were initially attributed to schizophrenia unmasked by the drug. But these episodes were too common amongst a variety of personality types to deny a common exogenous cause. By 1960, though it was initially postulated that amphetamines were being used habitually (like one would use caffeine), it became evident that they were in fact addictive.[15] In a placebo controlled double blind trial, physicians in Britain established that, those patients regularly taking amphetamines, were physically dependent.[15]

It took until 1970 for the legal production, marketing, and distribution of amphetamines to slow down. This was a direct result of the Comprehensive Drug Abuse Prevention and Control Act. [15] Today it is restricted to South African Schedule 6 for the indications of ADHD and narcolepsy but remains a popular drug of abuse.

**LSD, Methaqualone and Phencyclidine**

The Ergot fungus that grows on Rye and other grains caused by C. Purpurea is responsible for the condition called Ergotism which is manifested in humans and livestock if the infected grain is ingested. The symptoms included convulsions, hallucinations, miscarriage and dry gangrene. [18]

In 1917 Arthur Stoll, a swiss chemist, identified the compounds in the Ergot that caused the physiological effect: ergotamine and ergobasine. [19] The discovery of these compounds has led to the manufacture of 2 important pharmaceuticals for medical purposes: treatment of obstetric haemorrhage and treatment of migraines.

A third compound found in ergot is lysergic acid. 12 years after Stoll made his discoveries – Albert Hoffman tried combining Lysergic acid with a variety of organic compounds to create a drug that could stimulate respiratory and circulatory systems.

He reacted lysergic acid with dimethylamine. He called it LSD 25. Its effect during animal testing raised no particular interest and the compound was ignored for 4 years. During inadvertent contact with the compound (followed by self-experimentation) he experienced the hallucinogenic effects for himself. In his memoir he described the “extraordinary shapes with intense, kaleidoscopic play of colours.” That he experienced [19]

LSD became a popular drug of the 1960s “hippie” culture characterised by people like, Harvard Professor, Timothy Leary, also a known fan of LSD, forming the “psychedelic movement” called the League of Spiritual Discovery. He coined the phrase “tune in, turn on, drop out” [20] Many suspect the Beatles song: “Lucy in the Sky with Diamonds.” to be an ode to LSD. The US government did not outlaw LSD until 1968.

**Methaqualone**

“Known as Mandrax in South Africa, it was created by chemists in India in 1951 while they were trying to create a better drug for combating malaria.” It was found to be a powerful hypnotic and sedative and thought to be non-addictive. [21].

It found great popularity in the 1970s under the trade-name Quaalude in Japan, Germany, the UK, and the US where it was widely “prescribed” by stress clinics with impunity. Its abuse was rampant and earned it the nickname “disco-biscuits” but its hypnotic effects made it the original “date-rape” drug. By 1984 it was a Schedule 1 drug in the US. Today it continues to be a common drug of abuse in South Africa as the world's largest producer and consumer of methaqualone. [22]

**Phencyclidine (PCP)**

Phenyl cyclohexyl piperidine was originally created as an anaesthetic drug in the 1950s. It is a potent dissociative agent acting as a glutamatergic NMDA receptor blocker . In 1957 it was released under the trade name Sernyl. It was problematic in that it caused significant post-operative psychosis, anxiety and dysphoria [23]

By 1965 it was discontinued and limited only to use in veterinary medicine and remains a common animal tranquiliser. However, PCP became a popularly abused drug in the 1960s. It was distributed in tablet form and was called “The PeaCe Pill," shortened to “PCP”. In the 1970s, use became more prevalent including use by snorting by 1978. [24]

**MDMA**

“Methylsafrylaminc” was the name given to 3,4 – methylenedioxymethamphetamine. It was created in 1912 as a drug to stop bleeding but was discovered to have psychoactive properties. Merck patented the drug in 1914. Its therapeutic use was never realised but it was allegedly diverted into “weapons development” during the infamous MK-Ultra projects carried out by the CIA. [25]

Though it was classified as a Schedule 1 drug in 1984 – MDMA (now commonly known by the names Molly or Ecstasy) had become a staple part of the “rave” scene. Despite its definitive illegal status – researchers are looking into the role of MDMA in the treatment of post-traumatic stress disorder. [26]

**CANNABIS**

In South Africa, laws concerning the consumption of cannabis for both medical and recreational purposes are under reform. Its use was first restricted in this country in 1922 in keeping with the mandates set forth in the International Opium convention. Cannabis is thought to have come to South Africa through Arab and Indian traders. Oral histories describe its use by the indigenous peoples well before South Africa's "discovery" by European Settlers in 1652. The khoi-san people referred to it as "dacha" which could be the origin of the colloquial term "dagga". Provincially, the drug was starting to be regulated between 1850 and 1910 and in certain provinces outlawed.

In 2018, the South African Constitutional Court decriminalised the use and cultivation of cannabis in a private space. The buying and selling of cannabis and its seeds remains illegal. It can, however, no longer be categorised as an illicit substance.

**Whoonga/ Nyope/ Sugars**

This drug is a South African concoction which, at its base, contains low grade heroin in powdered form which can be mixed with any combination of compounds. "Nyaope is a fine brown powder due to its mixture with soil, sand or in some cases cement powder done to mask its identification as an illicit drug"[27] The true contents of Nyaope were the subject of study by Khine et al in 2015.

"[In] A Cross-sectional, qualitative and descriptive pilot study on samples purchased from various sources of 12 townships in Northern Gauteng Province, the constituents consistently detected in all samples were caffeine, drugs of abuse such as opiates, codeine, morphine, methyl-dioxy amphetamine (MDA) and heroin. Some samples contained antibiotics (citroflex) and antiretroviral drugs (zidovudine). Central nervous system (CNS) depressants such as phenobarbitone and benzodiazepines, benzitramide, moramide intermediates and thiofentanyl and stimulants such as Pipradol, and fenethyline were detected"[27]

In KZN, this drug is mainly sold in the southern township of Umlazi and other towns north and south along the freeway where it goes by the name "Sugars". The Albert Park in the Berea in Durban has the moniker "Whoonga Park" as being a popular location for sale and consumption of the drug.

It has a high propensity to addiction with only one use. The withdrawal from this drug is acute and characterized by severe abdominal pain, salivation, nausea, muscle spasms, seizures, and psychosis. The user will often seek another 'hit' of the drugs for the sole purpose of taking the discomfort away.

Sugars are relatively low-cost compared to other street drugs on the market at around R30 a hit. This makes it attractive amongst poorer communities. The users are usually young men – some still school-going age – who adopt multiple small day jobs in the hope of earning enough to buy a few hits. They are known in the community as "Amphara" and Ukuphanta – refers to the daily "hustle" for small jobs that can fund the drug habit. [28]

The main positive effects of Whoonga come from the heroin component which gives the characteristic euphoria and feeling of wellbeing. This effect can be produced from intravenous injection, but most heat the drug on aluminium foil and inhale the fumes. The effects can last 6 to 24 hours before the withdrawal begins.

**The History of Drug Scheduling and Regulation**

A *psychotropic drug* is any drug capable of affecting the mind, emotions, and behaviour.

A *narcotic drug* – a drug which in small doses "dulls the senses", "relieves pain", and brings on sleep but in larger doses has dangerous effects and most often causes addiction. [29]

The first example of international cooperation on drug regulation was in 1909. Named the "International Opioid Convention". The united states and 13 other countries collectively agreed to impose restrictions on the manufacture and trade of morphine and cocaine.[30]

It was the first of many versions of similar kinds of treaties and conventions. Each one attempting to improve on the other in extent of substances included in the convention and the degree to which illicit substance production could be criminalised.

The 1961 Single Convention sought to place greater control over the plants and precursors from which the illicit substance was derived. [30]

"The Single Convention created four lists or Schedules of controlled substances and established a process for including new substances in the Schedules without the need to modify the text of the treaty's articles. The Convention's four Schedules contain more than one hundred substances, which are classified according to the different degrees of control to which they must be subjected."[30]

In 1988, the United Nations convened another conference to negotiate what would become the Convention Against Illicit Traffic in Narcotic Drugs and Psychotropic Substances. The treaty obliged countries to impose criminal sanctions to combat all aspects of illicit drug production, possession, and trafficking. The control of illicit substances and their precursors is essentially monitored by 3 bodies:

- The International Narcotics Control Board
- The Commission on Narcotic Drugs
- The World Health Organisation

"As the treaty enforcement body under the 1961 Convention and the 1971 Convention, the CND decides – based on WHO recommendations – on the classification of the narcotic drugs and psychotropic substances under international control. Thus, the CND and the WHO (as explained below) are the two bodies with the power to add or remove drugs from the lists of controlled substances and move them from one Schedule to another" [30]

"The International Narcotics Board is an "independent and quasi-judicial monitoring body, established by treaty, which is responsible for ensuring that the international drug control conventions are implemented."[30]

There are five different schedules of controlled substances, numbered I–V. The Controlled Substances Act describes the different schedules based on three factors: (US)

- Potential for abuse:
- Accepted medical use:
- Safety and potential for addiction

| Schedule | Potential for Abuse | Medical Use | Potential for Addiction |
|---|---|---|---|
| I | High | None | Not safe to use even with medical supervision |
| II | High | Yes – with severe restrictions | Abusing the Drug can cause severe mental and physical addiction |

| | | | |
|---|---|---|---|
| III | Medium | Yes | Abusing drug can cause severe mental addiction and moderate physical addiction |
| IV | Moderate | Yes | Abusing the drug may lead to moderate mental and physical addiction |
| V | Lowest | Yes | Abusing the drug may lead to mild mental and physical addiction |

[30] [31]

The misuse of drugs regulations 2001 in the UK uses a very similar 5 tier scheduling system.

"In South Africa, section 22A of the Medicines and Related Substances Act, 1965 (Act 101 of 1965) provides for a graduated system of control over sale and supply of substances, ranging from access via any retail outlet, at one extreme, to outright prohibition, at the others" .[32] There is an 8 schedule system. Drugs like Heroin, cocaine and methaqualone belong to schedule 7. Schedule 8 is described as a strictly controlled substance and has 3 drugs: Amphetamine, dexamphetamine and nabilone. "These are drugs which can be used for very limited indications and only by approval of the Director-General to medical practitioners who have obtained special permission from the South African Health Products Regulatory Authority for such use and prescription" [32]

**An overview of the commonly abused drugs in Durban and South Africa**

**The extent of the burden**

SACENDU (South African Community Epidemiology Network on Drug Use) released a 2018 update on drug trends in SA. They note that alcohol and cannabis abuse remain the most common primary drugs for which patients seek treatment. The table below summarises the findings of the report.

| | |
|---|---|
| Cannabis | 30 – 55% |
| Methamphetamine | Most common primary drug in Western Cape. 30% prevalence compared to 1% in KZN. |
| Cocaine | 12% primary or secondary drug use in KZN, and 4% in WC. Proportion of admissions low and not rising. |
| Heroin | Smoking use has overtaken injection use. More prevalent in WC. |
| Nyope/ Whoonga | KZN reported 11% as primary drug of abuse. Gauteng 4%. National number rising. |
| OTC drugs | Codeine abuse is most common, other analgaesics, benzodiazepines and cathininones (stimulant) abuse on the rise. |
| South African Community Epidemiology Network on Drug Use (SACENDU) – Phase 43 | |

The United Nations Office on Drugs and Crime reported on South Africa that

"Prior to 1994, cocaine and heroin were not readily available in the society. Following South Africa's re-integration into the world-wide community in the 1990s, its developed transportation, or in trafficking of many commodities, including drugs" (UNOCD, 2002)

South Africa's general trade routes, geographical relationships to "at-risk" countries and sub-optimal border security make it the ideal location through which to traffic and market illicit substances.

South Africa is both the world's largest producer and consumer of methaqualone in the form of counterfeit Mandrax. "In November and December of 2001, 5.8 tons of methaqualone and Mandrax powder were seized from drug manufacturing operations in Johannesburg and Port Elizabeth. The December raid alone, which represented 3.3 tons, had a street value of 550 million rand ($49.05 million USD) and was the largest seizure to date by South African authorities".

"In January 2002, South African police confiscated 1.5 million Mandrax tablets worth an estimated 1,5 million rand ($133,779.00 USD)." [33]

In a 2018 paper by Peltzer et al a survey amongst south African youths "an increase of any past 3-month drug use from 3.7% in 2008 to 4.4% in 2012 was observed in South Africa. Prevention and intervention activities targeting drug use, in particular in identified risk groups, need to be strengthened in South Africa." [34]

**Impact on Anaesthesia**

Drug Abusers have contact with hospital services either to treat direct consequences of the drug use like overdose or poisoning, withdrawal and assist in detoxification, or they require medical intervention for the indirect consequences. These include an increased risk for trauma, parasuicide, complications of IV administrations like infections, emboli and limb ischaemia, acute myocardial ischaemia, cardiac, liver, or renal failure and HIV co-infection. Additionally, illicit drug users undergoing elective surgery may experience withdrawal during their inpatient admission. The literature regarding specific interactions of anaesthetic drugs and illicit drugs and reviews around the management of the drug abuser coming for an anaesthetic is necessarily non-specific since many of the factors are related to the type, dose and duration of drug concerned.

General principles in the recognition of drug abuse would be to check the unconscious patient for needle track marks, nasal septum destruction, paraphernalia of drug use such as the heroin spoon and filter, the glass pipe for smoking amphetamines, or sandy, soil like substances on the patient's clothes.

Physical signs such as mydriasis, diaphoresis, hypertension, hyperthermia, tachycardia and mental disturbances such as paranoia, anxiety and aggression are common to the index effects of stimulant type drugs but can also be the manifestation of withdrawal from such drugs as Heroin, Mandrax, benzodiazepines and barbiturates.

Respiratory depression, somnolence, hypotension and or bradycardia is common to opioid overdose and the acute effects of benzodiazepines amongst others.

Collateral history is important in identifying doses, timings, and long-term use of the drug. Poly-pharmaceutical abuse is common, alcohol being the most common accompaniment, and the anaesthetic provider should be wary of drug interactions with common anaesthetic agents. Serotonergic drug abuse puts the patient at risk of serotonin syndrome.

Lastly – chronic drug abusers usually have a poor nutritional status and can frequently present with moderate to severe dehydration and pre-renal impairment.

"The intraoperative management of an addicted patient should focus on three areas:

- Managing intoxication (if the patient is still intoxicated, especially in emergency surgery),
- Preventing or treating withdrawal
- Achieving adequate recovery and effective analgesia. For the latter, multimodal analgesia and/or regional anaesthesia are strongly advocated techniques" [1]

Toxicology screening is a routine component of trauma assessment and stratification. It is less practised in admissions to medical ICUs and literature on guidelines for the rational use of drug testing in ICU is lacking.

**Drugs commonly tested on urine screening include**

Amphetamines, Barbiturates, Benzodiazepines, Cannabinoids, Cocaine, Methadone, Opiates and Phencyclidine.

Drugs of abuse which are not amenable to urine assays are: fentanyl, methadone, oxycodone, meperidine, buprenorphine and GHB (gamma hydroxybutyrate)

"Substances that are not similar to the defined classes can produce negative results even though they are present. Some drugs may be difficult to detect with the standardized assays, either because the test is not set up to detect the drug, such as methylenedioxy-methamphetamine (MDMA, also known as Ecstasy or Molly), fentanyl, methadone, oxycodone (Oxycontin), meperidine, or buprenorphine, or because the drug does not remain in the body long enough to be detected, such as gamma-hydroxybutyrate (GHB)"[35]

**Drug information by class**

| **Amphetamines** | |
|---|---|
| Known as: | Ice (Crystal Meth), Tik, Speed, Fast, Up, Whiz, Crystal |
| Medications | Ritalin, Dexedrine, Concerta, Adderall |
| Routes of Administration: | ORAL, IV, INHALED, INSUFFLATED |
| | Effects usually felt immediately when smoked or injected and within 30minutes when ingested. |
| | Contents vary by manufacturer. Can also contain caffeine, ephedrine, phenypropolamine. Can be combined with benzodiazepines and heroin. Can be combined with bath salts (synthetic canthinones) |
| MOA | Release of Dopamine from nerve terminals and prevention of its reuptake and metabolism. Inc release of Noradrenaline and Serotonin. |
| Psychotropic effects: | Increased focus, concentration, increased ability to stay awake, paranoia, auditory/ visual hallucinations, agitation, anxiety, grandiosity, pressured speech, euphoria |
| Physical effects: | Pyrexia, tachycardia, mydriasis, dry mouth, tremor of small muscles. Rhabdomyolysis, seizures, Arrythmias, Acute MI, cerebral haemorrhage. Chronic use can lead to Dopamine depletion. |
| Kinetics | A single dose will have effect for up to 4 hours. Peak concentration at 3 hours. Half-life of 10 hours enteral and 12 hours for parenteral. Cyp2d6 metabolism. No active metabolites. Methamphetamine is metabolised to amphetamine. |
| Withdrawal | Long term use at high doses leads to tolerance and physical dependence. Some studies suggest catecholamine depletion. Symptoms can persist from 5 days to 3 weeks. Fatigue, insomnia, psychomotor agitation |

[36, 37]

| **Cocaine/ Crack Cocaine ((benzoyl methyl ecgonine)** | |
|---|---|
| Known as | Blow, Snow, Rocks, Klippe, Crack, Coke, Charlie, C, Line, Bump, Yayo, Llelo. |
| Medications | Still used as topical anaesthetic in some ENT/ Dental procedures |
| Routes of admin: | Snorted, smoked, IV, Rectal,<br>Crack – free base cocaine: smoked. |
| MOA | Enhances activity of Dopamine by blocking reuptake into the nerve terminal. Possibly also prevents reuptake of serotonin and noradrenaline. |
| Psychotropic effects | Stimulant, Euphoria, (Similar to amphetamines) |
| Physical | Vasoconstriction of superficial vessels, "increased energy and alertness", tachycardia, hypertension, angina, seizures, Sexual dysfunction |
| Kinetics: | Peak effect in 5 to 10 minutes following IV use or inhaled use. Intra-nasal route peak effect in 60 mins.<br>Offset can occur in 1 hour. Much shorter than amphetamines. |
| Withdrawal/ Toxicity | 3 phases "Crash" "Continued" "Extinction" – and can last up to 6 months. Depression, insomnia, irritability, lack of energy |

| **Heroin (diacetylmorphine)** | |
|---|---|
| Known as | Horse, Junk, Hairy, Harry, Thai White, Skunk, Smack, The Dragon |
| Medications | None |
| Routes of admin: | Oral, Intravenous, Inhaled, "chasing the dragon" Snorting, Suppository, Subcutaneous |
| MOA | Agonist at CNS opioid receptors. Metabolises to 6-MAM (monoacetylmorphine) |
| Psychotropic effects | Euphoria, "Rush" |
| Physical | Flushed skin, miosis/ mydriasis, itching skin, nausea |
| Kinetics: | A typical dose is 100mg. Oral – slower onset due to first pass metabolism. IV – 1 to 2 minutes. Crosses the blood brain barrier more rapidly (20sec). More lipid soluble. More analgaesic potency (2.5x). Difficult to detect in blood because of rapid hydrolysis to 6-monoacetylmorphine<br>Plasma T1/2 = 3 minutes. Renal Clearance 90% |
| Withdrawal/ Toxicity | Heroin is considered a short-acting opioid. Withdrawal can begin as soon as 6 – 12 hours after the last dose. The peak time of withdrawal is at 2 – 3 days and can last 5 – 10 days in total.<br>Medical detox is undertaken with drugs like Suboxone – a partial opioid agonist and long - acting, Methadone, Naloxone and Naltrexone (a longer acting opioid antagonist).<br>Minimum lethal dose 200mg. Addicts may tolerate 2g. |

[38]

| **LSD** | |
|---|---|
| Known as | Acid, microdots, blotter, hippie, zen, Kool-Aid, Golden dragon |
| Medications | No current medical indication. Research in progress |
| Routes of admin: | Oral. 25mcg – minimum dose to produce effect. (75–150 µg p.o) |
| MOA | Predominant mechanism of Action appears to be at Serotonin receptors in the Raphe Nucleus and Locus Coerelus (inhibits)<br>Strong assoc. with 5HT2 receptor for hallucinogenic effects. |
| Psychotropic effects | Euphoria, perceptual changes, synesthesias, |
| Physical | Impaired coordination and reaction time, Dec. attention and concentration, at 0,5 – 1 mcg/kg: ANS sympathomimesis – tachycardia, hyperthermia, mydriasis. Respiration unchanged, increased. |
| Kinetics: | Oral onset 30 – 45 mins. Peak effect 1 – 2.5 hours.<br>Duration of action: 9 – 12 hours. Half life of 175 mins. Elim half life of 3.6 hours. Detectable in urine for up to 4 days post ingestion.<br>Hepatic metabolism, inactive metabolites. Renal Excretion, also skin and lungs. |
| Withdrawal/ Toxicity | Risk of toxicity is low. Psychosis, hyperthermia, suicidal ideation poses risk of morbidity and mortality. No physical dependence proven. Withdrawal symptoms uncommon. |

[39]

| **Methaqualone** | |
|---|---|
| Known as | Mandrax, Quaaludes, Mandies, Buttons, MX, White Pipe and Cream |
| Medications | No current medical indication |
| Routes of admin: | Oral (300mg tabs), inhaled (smoked) |
| MOA | Barbiturate like central nervous system depressant. Suspected to work on GABA receptor |
| Psychotropic effects | Euphoria and Sedation, anxiolysis, disinhibition |
| Physical | Headache, dizziness, somnolence, respiratory depression, sweating, bradycardia. |
| Kinetics: | Onset of action within 30 minutes of ingestion of 300 to 600mg for “strong sedation” Tolerant users can take up to 2000mg daily.<br>Lethal dose is 8 – 20g. Duration of action: 4 – 8 hours.<br>Detected in urine up to 72 hrs after last dose. |
| Withdrawal/ Toxicity | 12 – 24 hours since last dose. Nausea, vomiting, tremors, anxiety, delirium, diaphoresis, convulsions, seizures.<br>Dose exceed 8 grams can be fatal. |

[40]

| **MDMA** | |
|---|---|
| Known as | Ecstasy (E), Molly (M), ADAM, |
| Medications | Use in some psychological research |
| Routes of admin: | Orally ingested tablets (E) or powdered form for snorting or filling into capsules (M). Usually “cut “with other drugs e.g. ketamine, heroin, synthetic cathinones. |
| MOA | Serotonergic agonist: inc. transport of serotonin into the nerve terminal |
| Psychotropic effects | Inc sense of wellbeing, increased confidence, increased energy, reduced anxiety, amplified reactions to colours, lights. |

| | |
|---|---|
| Physical | Hyperthermia, dehydration, if user also taking SSRI then increased risk of developing serotonin syndrome. Teeth clenching. Blurred vision |
| Kinetics: | Onset in 30 – 60 minutes of ingestion. Duration of action varies between 2 – 8 hours. Offset of effects around 6 hours. |
| Withdrawal/ Toxicity | Up to 8 hours after a single dose: symptoms more psychological than physical. Anxiety, depression, insomnia, and decreased concentration. “Severe crash” in mood, energy levels. Can last days to weeks. |

[41]

## CONCLUSION

Narcotics are an indelible part of the collective history of mankind. Their discoveries have often been made in good faith with the intention of helping people and progressing medicine. Their indiscriminate prescription to the public in conjunction with an unwillingness of physicians to accept the truth of their addictive potential have contributed to the prevalence of drug addiction. Although international efforts have curtailed the sale and distribution of narcotics, the economic gains of the illicit drug trade keep these substances in circulation and ensure that addicts have a route back to abuse. In modern times we are seeing a resurgence in opioid abuse with Fentanyl overdose responsible for over 31000 deaths in the US in 2018. In South Africa, alcohol and drug abuse continue to rise due to shifting socio-economic divisions and a growing middle class. It is incumbent on the anaesthetist to familiarise themselves with the signs of illicit drug abuse to provide patient-specific, safe and wholistic perioperative care

## REFERENCES


1. Beaulieu, P., *Anesthetic implications of recreational drug use.* Canadian Journal of Anesthesia/Journal canadien d'anesthésie, 2017. **64**(12): p. 1236-1264.
2. Trickey, E., *Inside the Story of America's 19th-Century Opiate Addiction.* Smithsonian Magazine, 2018.
3. *History of the Opioid Epidemic*. 2020.
4. *Opium Poppy: History*. 2019.
5. Munsi, P., *How a Scottish Botanist Stole China's Tea and Changed Indian History | OZY.* OZY, 2019.
6. Hodgson, B., *In the arms of morpheus: the tragic history of laudanum, morphine, and patent medicines*. 2001: Firefly Books.
7. *Laudanum - Wikipedia*. 2020.
8. Sneader, W., *The discovery of heroin.* Lancet, 1998. **352**(9141): p. 1697–1699.
9. Palet, L.S., *The Deadly Drug That Used to Be a Popular Medicine | OZY.* OZY, 2015.
10. *Cocaine - History, Introduction To The West, Coca-cola, Early Drug Laws, After The 1960s*. 2016.
11. Weil, A.T., *Coca Leaf as a Therapeutic Agent.* Am. J. Drug Alcohol Abuse, 1978. **5**(1): p. 75–86.
12. *A Yale Drug Historian Sniffs Something Familiar in Today's Cocaine Craze*. 2020.
13. Cohen, M.M., *Jim Crow's Drug War*

*Race, Coca Cola, and the Southern Origins of Drug Prohibition.* Southern Cultures, 2006. **12**(3): p. 55-79.

14. *History of Cocaine in America: When Did It Become Illegal?* 2020.
15. Rasmussen, N., *America's first amphetamine epidemic 1929-1971: a quantitative and qualitative retrospective with implications for the present.* American journal of public health, 2008. **98**(6): p. 974-985.
16. *Who Invented Meth: History of Meth and its Links to WW II*. 2017.
17. Heal, D.J., et al., *Amphetamine, past and present--a pharmacological and clinical perspective.* Journal of psychopharmacology (Oxford, England), 2013. **27**(6): p. 479-496.
18. *ergot | Definition, Symptoms, & Ergotism*. 2020.
19. Shroder, T., *Acid Test: LSD, Ecstasy, and the Power to Heal*. 2014: Blue Rider Press.
20. Williams, H., *How LSD influenced Western culture*. 2020.
21. *Methaqualone | Encyclopedia.com*. 2020.
22. Low, H. and T. Heyden, *The rise and fall of Quaaludes.* BBC News, 2015.
23. *PCP Facts, History and Statistics | Dangers and Legality*. 2015.
24. *PCP | CESAR*. 2020.
25. On Drug Abuse, N.I., *MDMA (Ecstasy/Molly)*. 2020.
26. Editors, H.c., *MDMA*. 2020.
27. Khine, A.A., et al., *Identifying the composition of street drug Nyaope using two different mass spectrometer methods.* 1., 2015. **14**(1): p. 49–56.
28. Hunter, M., *Op-Ed: The work of whoonga, an epidemic on the move*. 2020.
29. *Medical Dictionary by Merriam-Webster*. 2020.
30. *The UN Drug Control Conventions*. 2015.
31. *Controlled Substances Act - Wikipedia*. 2020.
32. *Medicines and Related Substances Act: Schedules | South African Government*. 2020.
33. Peltzer, K., et al., *Illicit drug use and treatment in South Africa: a review.* Substance use & misuse, 2010. **45**(13): p. 2221-2243.
34. Peltzer, K. and N. Phaswana-Mafuya, *Drug use among youth and adults in a population-based survey in South Africa.* 1., 2018. **24**.
35. Jenkins, D.H., *Substance abuse and withdrawal in the intensive care unit. Contemporary issues.* Surg Clin North Am, 2000. **80**(3): p. 1033-53.
36. *Department of Health | Pharmacology of amphetamines*. 2020.
37. *Amphetamines | CESAR*. 2020.
38. *Heroin Withdrawal Timeline, Symptoms and Treatment*. 2020, American Addiction Centers, Inc. (AAC).
39. Passie, T., et al., *The pharmacology of lysergic acid diethylamide: a review.* CNS Neurosci. Ther., 2008. **CNS**(Neurosci): p. Ther.
40. *Methaqualone Withdrawal Symptoms And Signs, And Detoxification | Withdrawal*. 2011.
41. *Ecstasy (MDMA) Withdrawal: Symptoms, Effects, and Treatment*. 2020, American Addiction Centers, Inc. (AAC).