

## Taking stock: New Substances

Sedqa Drug Treatment Clinic

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Reader in Addiction Science

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## Taking Stock

- Use of illicit substances
- Identification
- Sought after and adverse effects
- 'New' illicit substances
- Recommended intervention/treatment

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## Agenda

- Mind-altering substances (cannabis, Ketamine, designer drugs, magic mushrooms)
- Opioids (heroin, methadone, buprenorphine)
- Stimulants (cocaine, khat)
- Steroids
- ANY THING MISSING?
- Plan to talk for 45 mins happy to take questions as we go

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## Cannabis

- A generic term used to denote several psychoactive preparations of marijuana (hemp) plant, *Cannabis sativa*
- *Cannabis* is defined as the "flowering or fruiting tops of the cannabis plant", from the traditional Indian term *ganja*
- *Cannabis resin* (separated resin, charas)
- The leaves are referred to as *bhanga*

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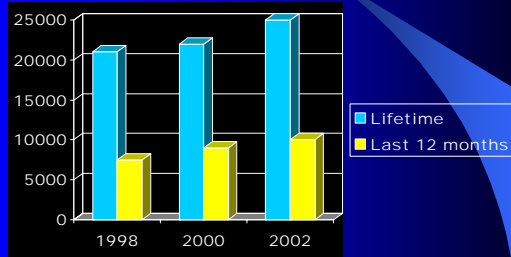
## Cannabis

- Cannabis contains at least 60 cannabinoids
- The most active constituent is  $\Delta^9$ -tetrahydrocannabinol (THC)
- As smoked wide variability in effects:
  - THC content
  - Puff volume, puff rate and duration breathhold

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## Lifetime and 12-month use of cannabis - U.K. 1998, 2000, 2002



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## Cannabis: marihuana

- New more potent forms; high THC
- 90% of all drug offences (rarely/never custodial)
- growth of police cautioning
- 8% of men, 3-4% of women used in last year
- Dependence syndrome :
  - Withdrawal symptoms include (Tennant 1996)
    - Sweating, mood disturbance, sleep disruption and gastrointestinal upset

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## Cannabis: Acute intoxication

- Acute intoxication:
  - Euphoria and exhilaration
  - Sense disinhibition (increased laughter)
  - Increased talkativeness (volubility)
  - Hyperactivity
  - Heightened hunger and thirst
  - Dreamlike state, calm and relaxed

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## Cannabis: sensory effects

- Light-headed, floating sensation
- Visual and auditory perception enhanced
- SLOWING of time passage
- Cognitive decrements – poorer problem solving
- Illogical thinking, impaired short-term memory
- Tendency to be side-tracked

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## Cannabis and Mental Health

- Evokes several types psychopathological reactions
- Strong feelings of anxiety & panic
- Paranoid reactions
- High doses: cannabis-induced psychosis

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## Psilocybin: Magic mushrooms

- Hallucinogen
- Cause auditory and visual hallucinations
- Seasonal

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## Recreational use of ketamine

- First reported 1971USA
- Linked to returning Vietnam veterans (experience on the battlefield)
- Intellectual hedonism with ketamine was popularized in the 1970-1980s
- Abuse by healthcare professionals gradually appeared.
- BENEFITS?
  - ketamine has the advantage of being easy to consume; the clear dose response effect and relatively short half-life reportedly making the effects easier to titrate than LSD.

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## Ketamine and the dance scene

- Appearance ketamine reported since the early 1990s and has taken two forms.
  - In its own right under various pseudonyms: *Super k*, *Vitamin K*, *Green*, *Mean Green*, *Jet*, *K* or *Special K* as tablets or capsules specifically sold with ketamine as its marketable content.
- Elsewhere appeared as a constituent of tablets purporting to be ecstasy often in combination with a stimulant drug such as ephedrine.
  - The surprise of experiencing immobility or hallucinations when empathy and euphoria were expected must come as a shock to unassuming ravers.

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## Pharmacodynamics Ketamine

- Almost unique anesthetic in its ability to produce a “dissociative” state
- That is, the higher brain centres being prevented from perceiving auditory, visual or painful stimuli leading to ‘a lack of responsive awareness’.
- Described as somato-aesthetic sensory blockade with amnesia and analgesia.
- NMDA receptors thought to underlie ketamine’s analgesic, dissociative and neuroprotective qualities
- Clearly outside clinical settings, such effects are potentially hazardous with injuries being masked and the risk of accidents increased.
- However, anesthesia is short lived and persists for only 5 to 10 minutes frequently requiring re-administration through an infusion to maintain the clinical effect.

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## Pharmacodynamics

- With sub-therapeutic dosing a trance-like cataleptic state with amnesia is produced
- Without depression of respiration or cardiac function
- Typically the eyes tend to remain open with a disconnected stare and nystagmus (irregular eye movement) can be observed
- The recreational drug user may appear to be awake but is dissociated from the environment, immobile and unresponsive to pain
- Problematic emergence phenomena and other unpleasant experiences appear maximal in early adolescence.

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## Recreational use of Ketamine: Cognitive effects

- One-off sub-anaesthetic doses of ketamine leads to:
  - Disrupted attentional performance
  - Impaired performance on tests of vigilance
  - Recognition memory, verbal fluency
  - Working and episodic memory (a deficit seen in schizophrenia)
- Tests of higher executive function (Wisconsin Card Sorting Test): preferentially disrupts delayed word recall, sparing immediate recall and post-distraction recall.
- Indeed the acute amnesiac effects can be so marked that they can make it difficult for subjects to describe to researchers attempting to record the episode

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## Cognitive effects

- The perceptual and mood changes observed are highly sensitive to: Age, Dose, Route
  - Previous experience (expectations, personality, motivation and mood)
  - Setting (social, physical and emotional environment)
  - Low dose stimulant effects predominate and environmental conditions are significant
- High dose psychedelic effects become the primary experience
- Some users report taking issues of set and setting into careful consideration prior to using ketamine
- Experiences of ketamine may be perceived quite differently (bizarre, intense, extreme or vivid imagery) by different individuals.

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## Gay Dance Scene

- Ketamine appeared at first in UK in the gay dance scene during the early 1990s
- Gay media observers noted that with many early users an adherence to strict set and setting rituals led ketamine to be considered by some as an elitist drug.
- More recently, with Gamma Hydroxy Butylate (GHB) ketamine has become the latest addition to a thriving 'poly-pharmy' of club-land drug abuse.

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## Adverse effects

- Variability in effect are also influenced by constitutional differences and other drugs consumed.
- Recreational use may lead to overdose which has occasionally been life threatening.
- Ketamine unlike LSD also induces feelings of aggression
- The commonest complaints in an American case series of 20 patients:
  - Anxiety, chest pain, and palpitations
  - Sympathetic over activity with tachycardia most common
  - Most frequent complications reported after ketamine overdose was severe agitation and rhabdomyolysis

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## Intoxication & Overdose

- The symptoms appear to be short-lived
- Discharged A&E within 5 h of presentation.
- In children, inadvertent overdose 5-100 times the recommended clinical dose.
- Adverse effects were reported to include brief respiratory depression and no residual effect
- **Wide margin of safety in overdose.**
- Risks of cardiac over stimulation and respiratory depression are potential consequences of combining ketamine with stimulants and CNS depressants respectively.

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## Gamma-hydroxybutyrate (GHB)

- GHB has emerged as a recreational disassociative anaesthetic
- Developed as an anaesthetic but not effective
- Became popular in 1977 when Japanese research showed released Human Growth Hormone
- Weightlifters & body builders used as GHB that impact on HGH increased strength and endurance
- Used in clubs as mild intoxicant

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## Gamma-hydroxybutyrate (GHB)

- GHB has a very short half life
- GHB produces amnesia
- Implicated as an agent in drug-facilitated sexual assault
- May see mild agitation and excitement
- Short-term high linked to poly drug use

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## Anabolic Steroids

- Androgenic hormones that include or are derivatives of testosterone (nandrolone, methenolone, ethyltestosterone)
- Long associated with competitive athletes, weigh lifters and body builders
- Thought to enhance shape & performance
- Hidden group

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## High dose use: Anabolic steroids

- Endocrine effects:
  - Females: hirsutism, coarsening of voice, male pattern baldness and acne = Irreversible
  - Adolescents: stunting of growth, feminizing, gynecomastia (growth of breasts in men)
  - Males: Increase in balding, testicular atrophy (emaciation).

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## High-dose anabolic steroids

- Cardiovascular risks:
  - Accelerated atherosclerosis
  - Coronary artery disease
  - Thrombembolism disorders (High BP)
  - Cerebrovascular accidents (blood clots)

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## Psychoactivity & Abuse potential

- Known to alter sexual and aggressive behaviour
- Likened to alcohol-related behaviour
- Excessive cheerfulness, increased libido
- Severe mood lability
- Withdrawal symptoms include:
  - Irritability, anxiety, insomnia, hot flushes, anorexia, myalgias (muscle pain)

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## Anabolic Steroids: dependence

- Dependence reported in some
- Chronic use; more cycles of use; obsession with training, aggression
- Symptoms of craving
- Dissatisfaction with body image
- TREATMENT:
  - Education, relapse prevention
  - Psychological intervention

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## Cocaine

- An alkaloid obtained from coca leaves or synthesized from ecgonine
- Cocaine HCl used in ENT as a local anaesthetic (vaso- constrictive action)
- Powder is sniffed (snorted), effects 1-3 mins lasting 30 mins
- Powerful Central Nervous System stimulant

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## Crack

- “Crack” or “rock” is alkaloidal (free-base) cocaine, beige in colour
- Intense high 4-6 seconds after crack is inhaled
- Euphoria lasts about 5-7 seconds

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## Cocaine & Crack

- CNS stimulant
- Increase Serotonergic activity – risk seizure
- 30-50% Increase HR, BP
- Dilated pupils
- Hyperactivity
- Up for it!

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## Cocaine and crack

- Cocaine availability has decreased to be replaced by crack
- Crack is extracted from cocaine
- High risk sexual behaviour
- Violence, criminality
- Cardiovascular problems

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## Cocaine and crack

- Physical effects
  - Large doses taken by those not used to it can cause hypertension, cardiac arrhythmias and convulsions
  - Death due to cardiac or respiratory arrest
- Psychological
  - Anxiety and restlessness
  - Visual or tactile hallucinations

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## Cardiotoxicity

- Cardiovascular morbidity has been specifically linked to the use of cocaine or crack
- Constriction of coronary arteries causes reduced blood flow to heart
- Risk myocardial infarctions

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## Chronic cocaine users

- Psychiatric evaluation shows that:
- Most suffer from concurrent mental disorder
- Major depression, anxiety disorder
- personality disorder (anti-social)
- Childhood history ADHD
- Reason: self-medication of disorder?

- Emerging evidence that Disulfiram reduces cocaine use especially amongst heavy drinking patients

## Cocaine behavioural therapies

- Relapse prevention
- Contingency management

## Treatment & Intervention

- Pharmacotherapy:
  - Dopaminergics amantadine (releases DA)
  - Antidepressants (5-HT uptake inhibitor) Fuoxetine (Prozac)
  - Other
    - Buprenorphine (suppresses Cocaine use in monkeys)
    - No universal agreement

## Khat in the UK – rising concern



## What is khat?



- Leafy twigs chewed as a stimulant
- Several commercial varieties
- Obtained from *Catha edulis* (Celastraceae – the Spindle Tree family)
- Grows in Eastern Africa
- Used as a stimulant in Ethiopia
- Imported for use by Ethiopian, Somali, Yemeni, bangladeshi etc communities in UK

## Khat in the UK

- Not illegal in most other W. European countries
- Cathinone (considered major active ingredient) is illegal
- Imported several times each week– has to be fresh
- Used within immigrant communities especially by men in 'coffee shops'
- Concern over associated psychiatric illnesses and other toxicity aspects
- Concern about use by schoolchildren, possible widening of use by wider society

## Khat in the UK

Use amongst Somali population

- Estimated at least 45,000
- Many refugees with complex problems
- Close association with depression and psychiatric problems
- Tension between adverse and beneficial aspects
- Parents prefer children to use khat rather than alcohol or tobacco

## Pharmacology of cathinone and khat

Peripheral effects include:

- Increased blood pressure
- Increased heart rate (tachycardia, palpitations)
- Mydriasis (dilated pupil)
- Dry mouth – thirst
- Fall in urinary flow rate – adrenoceptor-mediated contraction of bladder neck

## Toxic effects associated with Khat chewing

- Dental problems
  - Bad gum inflammation
  - Loss of teeth
- Cancer
  - No increase in oral cancer
  - High incidences of oesophageal cancer (Yemen) and stomach cancer (UK)

## Toxic effects associated with Khat chewing

- Psychiatric aspects
  - Memory and decision-making impaired
  - Agitation and depression
  - Moderate but persistent psychic dependence
  - Possible link with psychosis

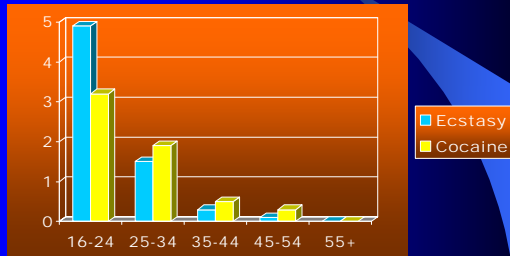
## Ecstasy (MDMA)



## Different 'brands' of ecstasy tablet



## Typical age-related prevalence of ecstasy and cocaine use in the UK



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## MDMA - Fatalities

- Been number of high profile deaths
- 60-100 in GB in last decade
- BUT risk factors unclear?
- Adverse psychiatric consequences
- Adverse Physiological consequences

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## Physical effects

- Powerful stimulant
- Acute risk of over heating - hyperthermia
  - Affects sympathetic nervous system
  - Increase HR, Pulse, BP
  - Risk dehydration
  - Cerebrovascular events

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## Excessive intake of hypotonic fluids coupled with an increase in plasma vasopressin (AVP) may cause lethal hyponatraemia

(Cherney *et al*, 2002; Budisavljevic *et al*, 2003; Brvar *et al*, 2004; Wolff *et al*, 2006)

Excess water  
Report from The Times, Nov 22, 1995

LEAH BETTS DIED OF DRINKING WATER TO COUNTER DRUG'S EFFECT

By Jeremy Lawrence, Health Correspondent

<http://www.independent.co.uk>



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## Metabolic effects

- Effects peak at 1 h and last up to 6h
- High profile deaths associated with hugely elevated temperature
- Hyperpyrexia – Temp above 42°C will bring about death

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## Designer Drugs

- Definition of the term designer drug:
- “A synthetic version of a controlled substance (MDMA) that is produced with a slightly altered molecular structure to avoid being classified as an illicit drug” (Merriam-Webster, 2008)

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## Piperazines

- Broad class drugs used in medicine (antipsychotics, antidepressants, impotence, motion sickness and anti-angina)
- Manufactured for recreational use often mimicking effects of MDMA or LSD (hallucinations, euphoria, intensification of tactile sensations)
- The most common reported piperazine based drugs are:
  - BZP, TFMPP, mCPP, Olanzapine

## Designer Drugs

- Australia several fatalities related to para-methoxy amphetamine (PMA), which shares not only the stimulant and hallucinogenic effects of MDMA but also its risk of hyperthermia.
- Tablets containing 4-methylthioamphetamine (4-MTA, flatliners). A derivative of amphetamine, has been associated with at least six deaths since it was identified in Europe in 1997.
- Di( $\beta$ -phenylisopropyl)amine (DPIA) one of the impurities found in illicitly manufactured amphetamine.

## Some effects of Designer Drugs

- Effects: blurring of vision, clumsiness, crawling or tingling feeling of the skin, fever; irregular, twisting movement, especially of the face, arms, and legs
- Joint pain, skin rash or itching, abdominal or stomach cramps or pain
- Diarrhea, dizziness, drowsiness, headache, muscle weakness, nausea or vomiting, and tremors.

## Methamphetamine (crystal ice)

- Smokable “ice” a pure form (+)-methamphetamine HCl
- Methamphetamine becomes “ice” when crystallised out of a saturated solution
- Solvent used trapped in crystal – volatile = rapid crystallisation (oral use)
- Less volatile (methanol) large crystal = smoking

## Crystal meth (“ice”)

- “Ice” epidemic has never occurred here!
- Worldwide: only drug used more than amphetamine = cannabis (Condon 2007)
- Smoking or IV use rather than insufflation (intranasal use) common route
- Becoming more widely available
- Further info: See Addiction 2007; 102 supplement

## Physical & Mental effects

- Rapid onset action if smoked/injected
- Instantaneous euphoria, high
- Longer half-life than cocaine and MDMA (effect lasts longer)
- Cardiovascular effects
- Lack quality sleep is profound
- Increase physical activity, decreased fatigue and appetite

## Treatment for stimulant users

- Harm reduction strategies, social support
- 12-step approach (methamphetamine)
- Pharmacological support limited
- Psychological support, CBT, relapse prevention
- Alternative therapies (acupuncture?)
- Brief intervention - education

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## Properties of Opiates

- CNS depressant
- Pinned pupils
- Respiratory depressant
- Emesis
- Euphoria
- Analgesic
- Sleep

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## Heroin - extent of the problem

- Growth rate of addicts - 20% per year
- Between 1995 and 2005 the price of heroin halved in real terms
- £10 bag (wrap) sixteenth of gramme

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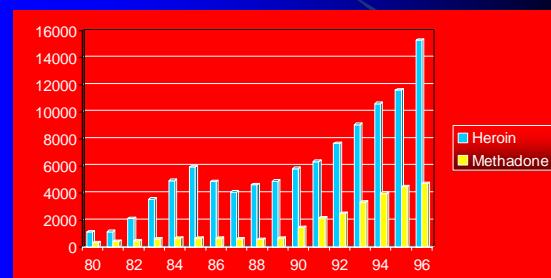
## Heroin (Diacetylmorphine)

- maybe 200,000 regular users
- Used by IV, skin popping, smoking, snorting or chasing
- Rapidly absorbed and metabolised into morphine
- Tolerance and dependence

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## New Notifications for Heroin Addiction U.K. (1980-1996)



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## Methadone

- Long acting opioid agonist
- Orally effective
- Constipation
- Sweating
- Respiratory depression

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## Impaired Liver

- Kreek (1980) excretion methadone slower in clients with chronic Liver disease
- Novick (1981/5) Methadone excreted more slowly with chronic severe liver disease (cirrhosis) not viral hepatitis
- Low peak plasma with severe alcoholic liver disease compared to current problematic alcohol use

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## Methadone dosing with Hepatitis

- Dosing as normal with acute viral hepatitis
- Lower doses for clients commencing methadone with Liver cirrhosis
- Clearance may slow down with Chronic active hepatitis and obstructive jaundice
- Long Term effect unknown

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## Methadone & Alcohol

- Alcohol use:
  - Bingeing (acute high intake) will induce methadone withdrawal symptoms
  - Educate client
  - Alcohol dependence – may need higher dose if liver enzymes affected
  - Not a good mix – poor prognosis

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## Signs of methadone OD

- Adult respiratory arrest with a pulse
- Pin point pupils (not universal especially in children)
- SNORING (shallow respirations rate <8/min)
- Bradycardic & hypertensive

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## Buprenorphine

Registered product for treating opiate dependence, Subutex®

Available in 0.4, 2 and 8 mg sublingual tablets

Standard therapeutic doses maintenance agent 8 mg to 24 mg per day.

Buprenorphine is also registered as analgesic in a preparation suitable for IV, IM or SC injection (Temgesic® 0.3 mg in 1 ml ampoules).

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## Buprenorphine

- **Buprenorphine** = partial opiate agonist
- registered in Europe, Australia management of opiate dependence  
Buprenorphine more effective than symptomatic medications (such as clonidine and benzodiazepines) in individuals undergoing short-term detoxification from heroin (Gowing et al 2000; Lintzeris et al 2002)  
Safe in overdose.

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## Buprenorphine: Mixed partial agonist-antagonist

- High affinity at both *mu* and *kappa* receptor sites (Lewis, 1985).
- Binds very tightly to the receptors and the slow receptor kinetics (Hambrook & Rance, 1976)
- long half life of 24 hours
- Less severe withdrawal syndrome when the drug is withdrawn
- Antagonist at the *kappa* receptors which essentially blocks the effects of other opiates if administered
- Results in the phenomenon of 'precipitated withdrawal' if sufficient time is not given between the last dose of opiate, and the time at which buprenorphine is administered.

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## Summary

- The field is always changing
- Be vigilant: listen to what you are being told
- Take a good drug or alcohol history
- Always take the opportunity to educate

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## Useful web sites

1. <http://samhsa.gov>
- <http://NIDA.gov>

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## Thank you

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