Propofol Abuse

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Winchester 2019

Definitions

DSM V - Diagnostic Statistical Manual

~~Use~~
~~Abuse~~
~~Dependence~~
~~Addiction~~

=

Substance Use Disorders (SUDs)

"Addiction is a primary, chronic disease"
WHO, ASAM etc

Addiction is characterised by…….

- Inability to control – use >intended
- A strong compulsion to take the substance
- Craving
- Preoccupation with substance
- Persistent use despite negative consequences
- Progressive neglect of hobbies or interests

- Physical withdrawal state when intake ceased or reduced
- Tolerance

Saying in Alcoholics Anonymous

“If alcohol is costing you more than money, then you have a problem”

Addicts v chronic pain patients

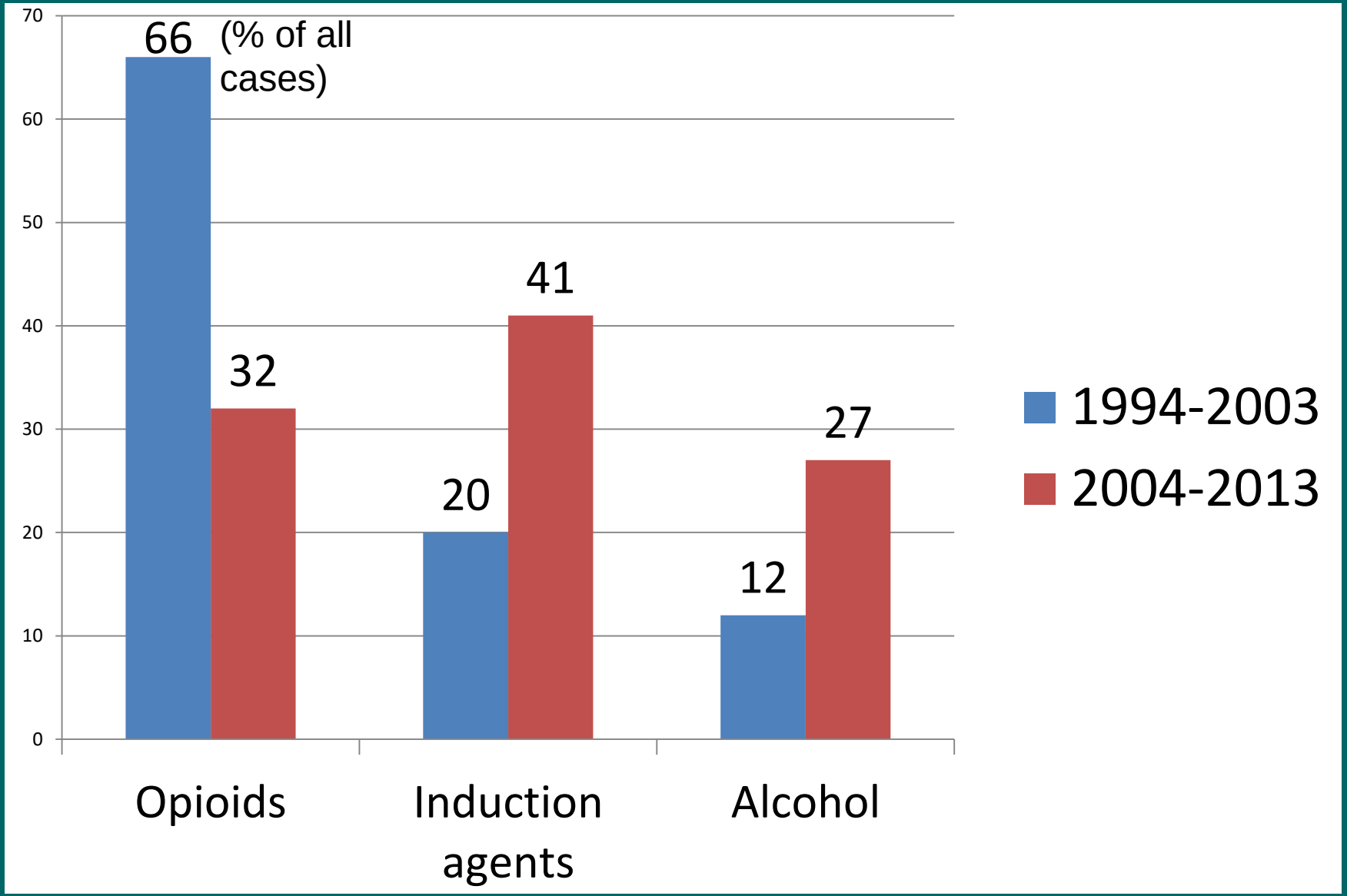
- ~~A strong *compulsion* to take the substance~~
- ~~*Craving*~~
- ~~*Inability to control*~~
- ~~*Preoccupation* with substance~~
- ~~*Persisting* with substance use despite negative consequences~~
- ~~Progressive neglect of hobbies or interests because of substance use~~
- Physical withdrawal state when intake ceased or reduced
- Tolerance

Propofol abuse

- Incidence increased 5 x in 10 yrs to 2007
- 18% residents programmes 1 or more reports
- Australia – 41% of SUD cases involved propofol

Wischmeyer Anesthesia & Analgesia 2007
Fry Anaes Int Care 2005, 2015

Fry – 2 studies (All grades)



Propofol

- Early life trauma
- Females*
- Anxiety states
- Insomnia
- Stress

- Multiple doses over the day
- Indwelling cannula
- Sometimes part of polyabuse picture

- Trauma, RTAs ++

*Earley 2011

Mortality

- Maier 2017
  Survey of Forensic Medicine depts Germany, Austria, Switzerland

- 67% response rate
- 39 deaths – anaesthesia, ICU, EM, ODPs
  85% propofol major cause of death

- 11 - suicide
- Others ‘unintentional respiratory arrest’

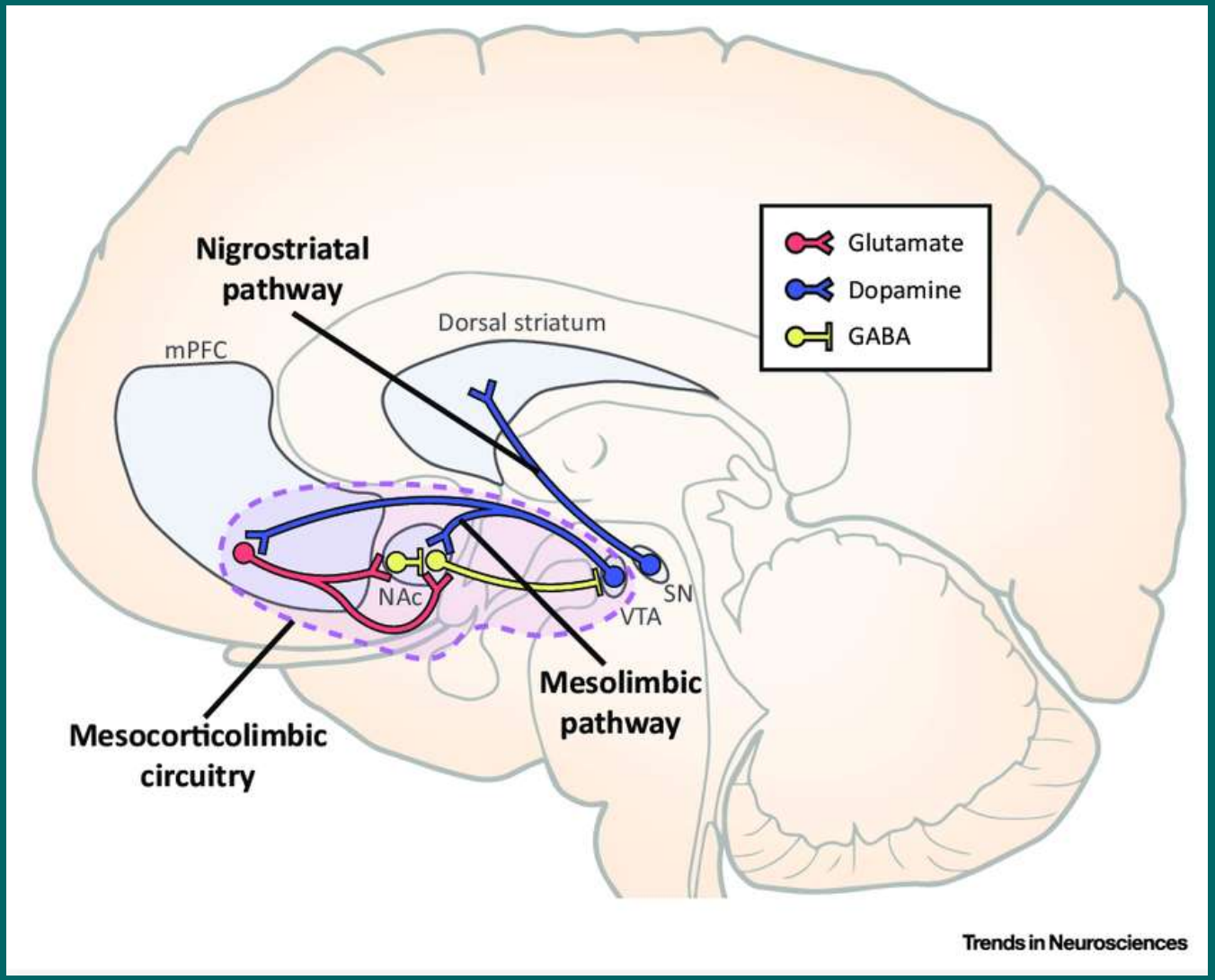
Mortality

- Wischmeyer 2009
  - 28% died using propofol

- Fry 2015 Australasia
  - 45% mortality in propofol users

- Warner 2013
  - 7.3% (of > 44,000 trainees died during training - all deaths were related to SUD in general

A bit about neurotransmitters

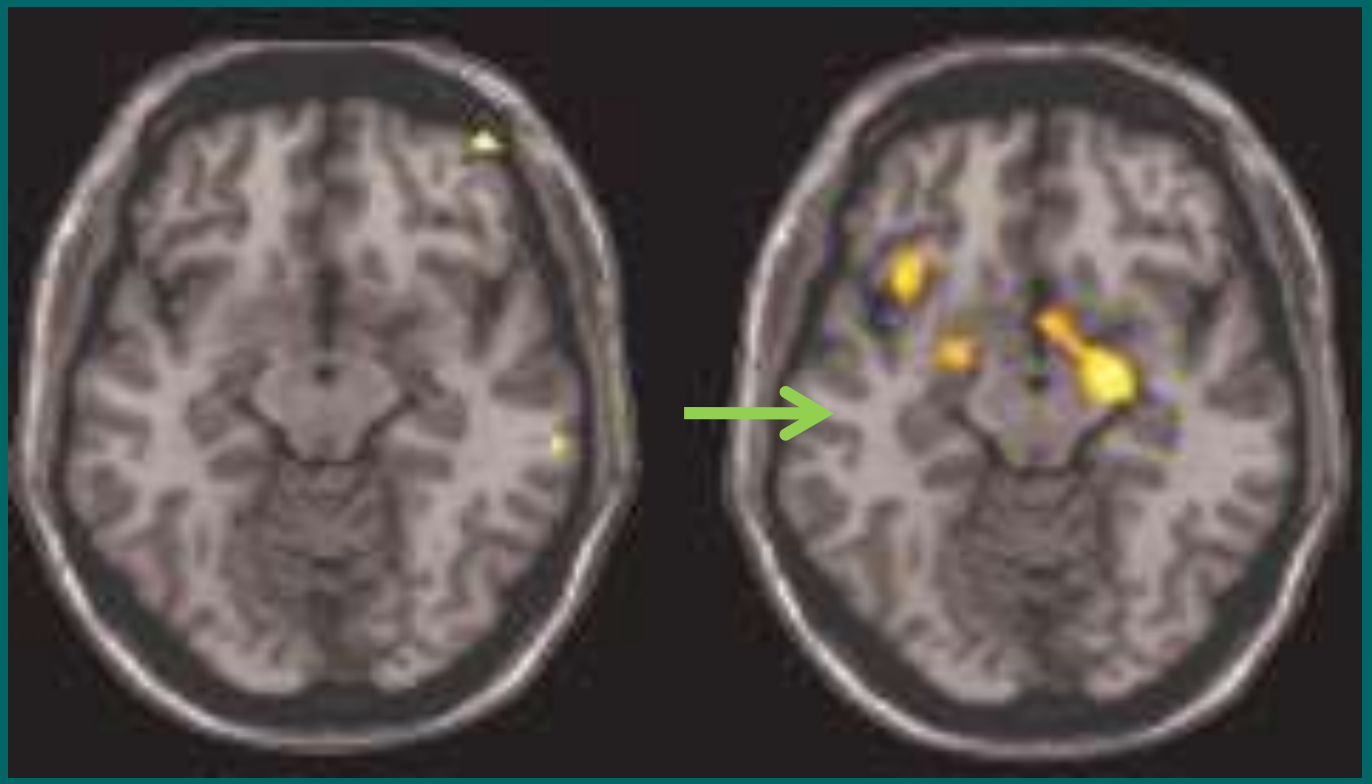


Stanton 2019 Trends in Neuroscience

Propofol

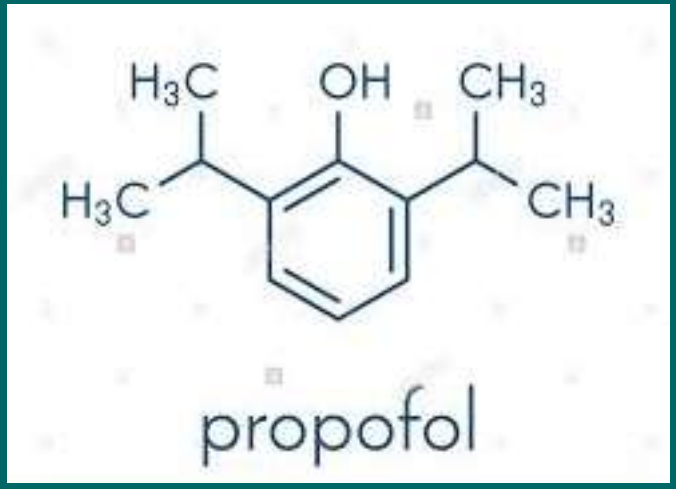
- Causes dopamine release VTA & NAccumbens
  (in anaesthetic & subanaesthetic doses)
- Distinct effects on $GABA_A$ receptors
  (also effected by alcohol, barbiturates & benzos)
- Increases endogenous cannabinoids (mice)
- Affects mesolimbic reward system in same way as opiates, amphetamines, cocaine
- Result – anxiolysis, relaxation, feeling of wellbeing, sleep

Cocaine visual stimulation in addict



Kilts, Gross et al Am J Psychiatry 2004

Who is at Risk?



Nature or Nurture ?

guardian.co.uk

Specialty Factors

Anaesthesia, Emergency Medicine

Attract those liking high risk, high intensity environment

Younger, risk takers

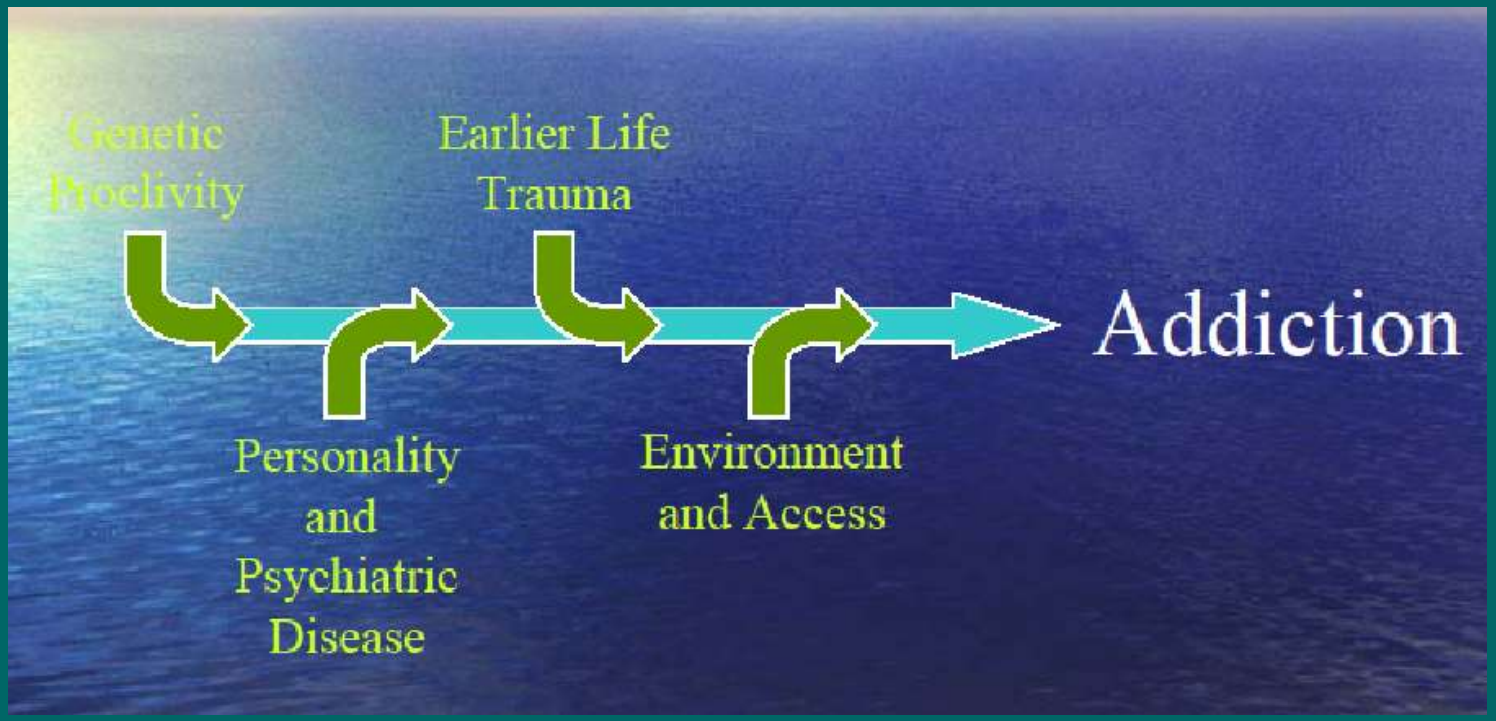
Psychiatrists – introvert, introspective, dysphoric

Surgeons

Confident, aggressive individuals with few inhibitions

little social anxiety or guilt, competitive & low addiction rates

Hughes et al. J. Addictive Diseases Vol18 (2) 1999



Paul Earley, Atlanta, Georgia

Genetic proclivity

- Addicted/alcoholic parents
  - biggest predictor in all SUDs

- Reward Deficiency Syndrome (RDS)*
  - manifest as behaviours or conditions due to a genetic dopamine deficiency state
  - or depletion of/resistance to dopamine in SUDs

Are there addiction genes??

Variations associated with SUDs found in:

- mu opioid receptor gene (*OPRM1*)
- dopamine receptor gene *DRD2*
  - deficiency → craving, impulsive behaviours
  - excess removal from synapse (polymorphism)
  - enhanced DA transcription - ↑ synaptic clearance
- & many others

- Degree of expression varies with drug exposure, environment etc.

Personality, psychiatric disease

Personality - addicts v controls*

- Novelty seeking higher
- Harm avoidance lower

Psychiatric co-morbidity – bipolar

Affective temperament – strong assoc^{n} between SUDs, mood & anxiety disorders

**Herman et al., 2003*

Early life trauma

- Emotional, physical, sexual abuse
- Parental death or maternal separation at early age
- Lack of parental warmth
- Lack of rewards & affirmation, negative messages

- AA – abuse, low self-esteem, shyness, anxious
  - just ‘not fitting in’

- All related to Dopamine dysfunction, RDS

Role of stress - multifactorial & complicated!

Work/home life

- CRF may decrease dopamine release in the NAc.
- Addicts given GC exhibit craving

- Stress reduces dopamine receptor production

- Catecholamines & other stress-induced inflammatory changes disrupt dopamine synthesis

Result = low dopamine state = alleviate with drugs

Environment & access

Access

- Is anaesthesia chosen for access – along with A&E, all other doctors give drugs by proxy
- Is it the access dictating choice of drug ?
- Different drug of choice if not in anaesthetics
- ? Why me when friends drank more than I did ??!!

Addiction

- genetics - load the gun
- psychology, personality - aim
- environmental factors - pull the trigger

Bray GA. 1998

Propofol

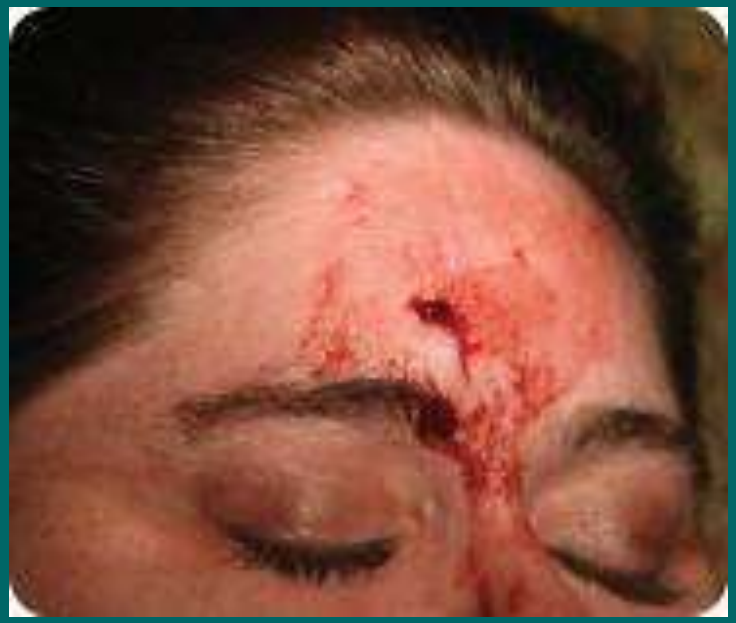
How much ?

20 - 50mg x10 per day up to
100mg over 20 times per day
Indwelling cannula

- Notable for intense craving
- Compulsion to use even in high risk situations (driving) & risk of discovery (at work)

- Probably $GABA_A$ mediated effects

‘The Propofol face’



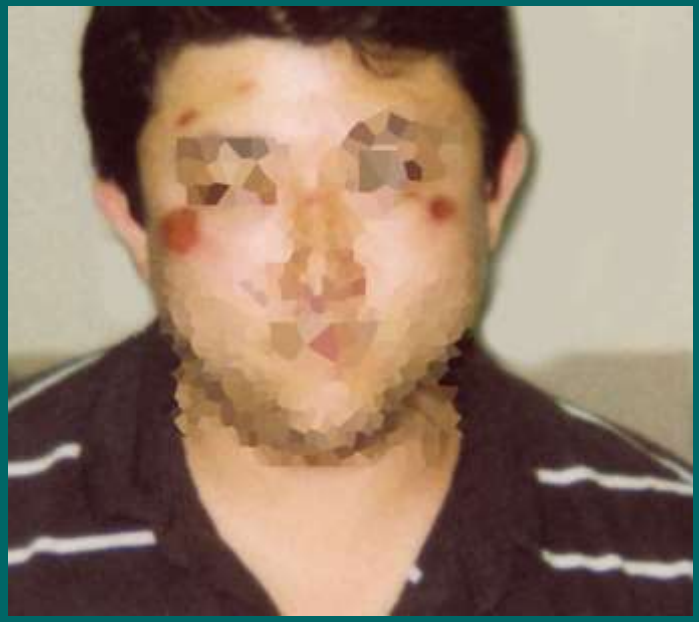


Photo Dr Paul Earley

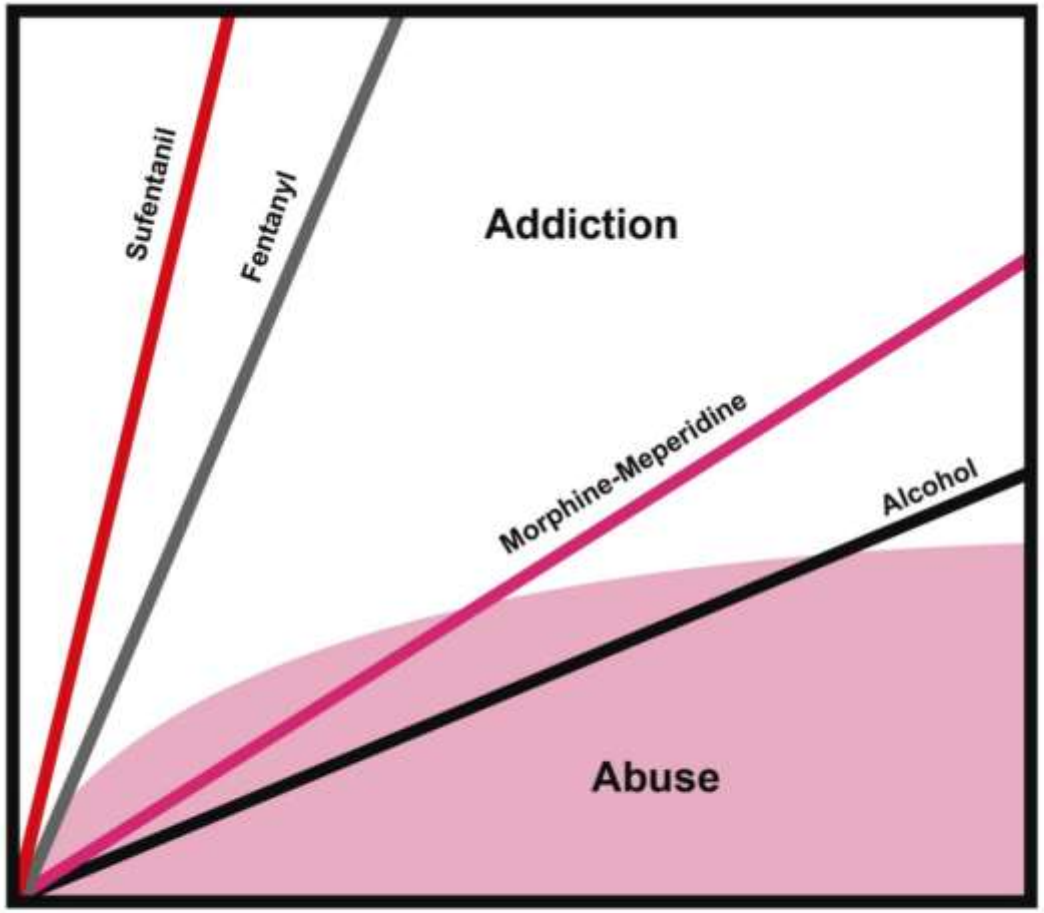
Age group

- Mostly younger doctors, trainees
- Discovery within 1 year, usually few months

- Probably more likely to be discovered at work rather than self-disclosure

- Prolonged use – take drug to avoid negative (low dopamine state withdrawal) effects rather than achieve original increased dopamine state or experience a ‘high’

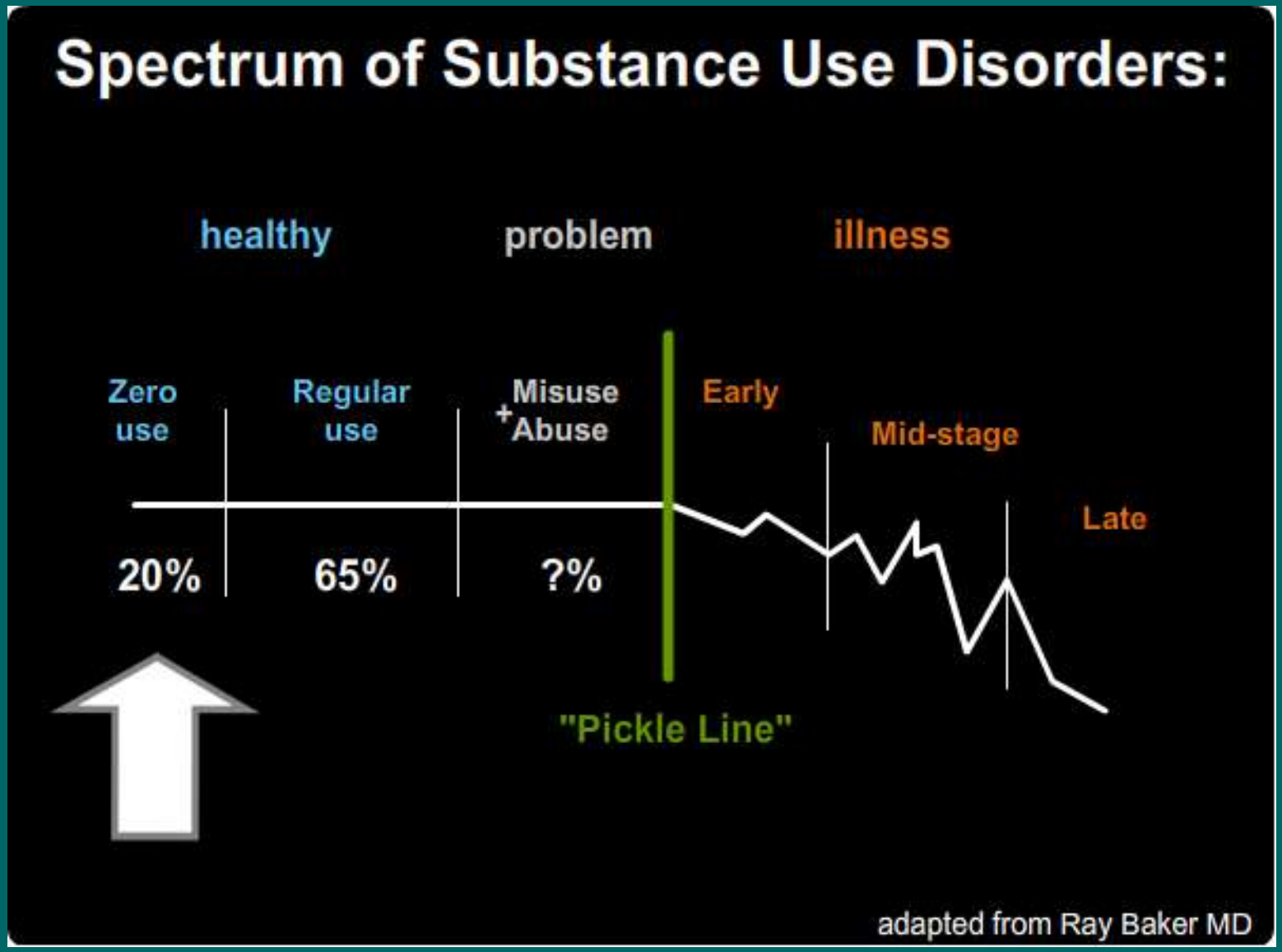
- Withdrawal - hyperhidrosis, tachycardia, anxiety & insomnia (similar to Benzodiazepines)



Time course of addiction

Graph from WP Arnold ASA & Elsevir

The slippery slope



Chemical testing for Propofol

Propofol Glucuronide Urine (or hair)

- Shaved head
- Bleached hair, internet shampoo
- Buy clean urine on internet
- Poppy seed cake excuse
- Catheters
- B vitamins v visible dilution

Hair testing etc

15% relapses were not using initial drug of choice

Relapse risk factors*

1. Family history
2. Dual diagnosis
3. Opiates

4. Previous relapse

*(Domino 2005)

Other addictions/behaviours

All mesolimbic reward system & dopamine related

Opioid tablets cause as many problems & withdrawal symptoms as iv opiates

Signs someone has SUD issue

Behaviour

- Alcoholic takes lots of sick days
- If work is source of drug, will ***not*** take sick leave
- Volunteer for extra shifts especially nights & weekends when less chance of being observed
- CHANGE in behaviour is important
  - from previous pattern
  - over course of the day

Intervention

- **the process of demonstrating to sick doctor that they have problem which requires urgent attention**
- Phone treatment centre ahead
- Have list of helpful numbers
- Take someone with you
- Prevent going ‘home alone’ afterwards
- Non-judgemental
- Badly conducted intervention may results in bad outcome
- Diffuse difficult situation: offer assessment rather than insist they have a problem
- Reporting to the police causes all sorts of problems
- These doctors are sick, not criminals
- Addiction an illness – it’s ok to be ill

Practitioner Health Programme PHP

020 3049 4505 www.php.nhs.uk

- 2008 - doctors & dentists in London area
- Now nationwide
- Assessed, +/- referral to treatment centre.
- NHS funded – provides whole care package
- Multi-disciplinary & rigorous follow-up
- Co-morbidity addressed

Resources

Sick Doctors Trust 0370 444 5163

- Helpline 24 hours, national cover
- Manned by addicted doctors in recovery
- Advice, referral to detox centres etc
- - free assessment at most
- Not a diagnostic service, more signposting &
- network of contacts

British Doctors & Dentists Group BDDG

Support group

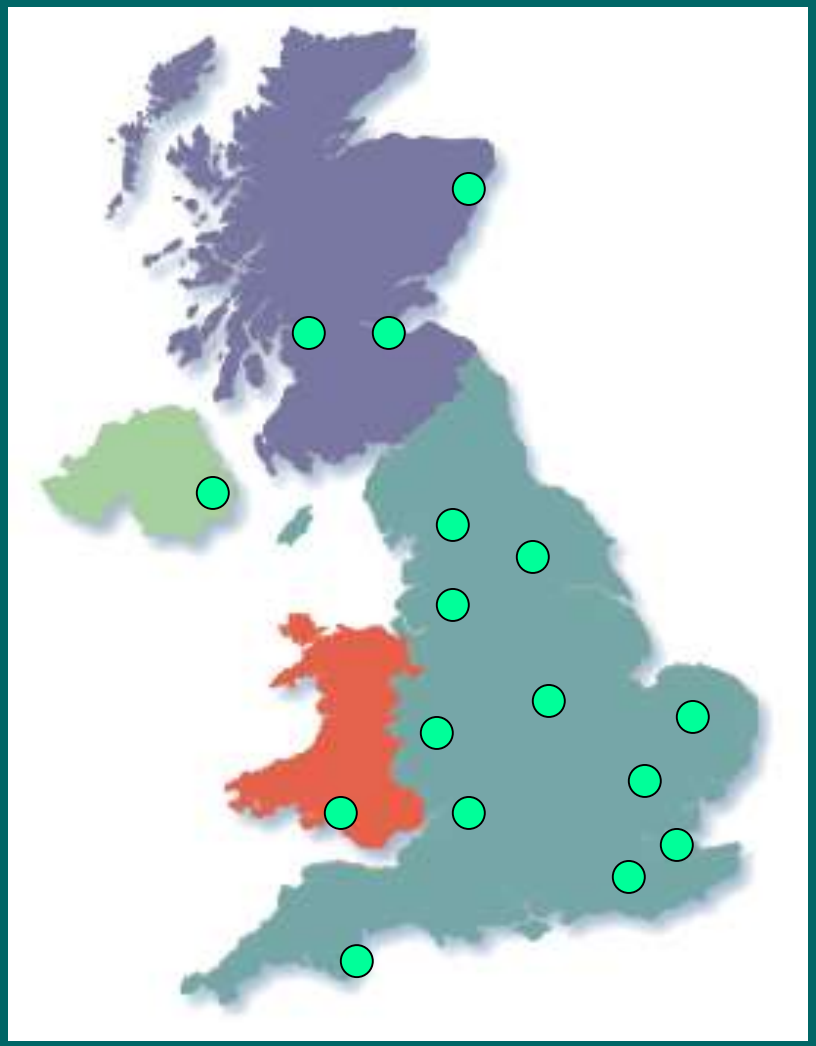
18 groups nationwide

Alcoholics & addicts

Monthly meetings

Students welcome

GMC etc discussed



Recipe for good recovery

- In-patient management 4- 6 weeks
- Naltrexone for opiate addicts
- Relentless monitoring - > 2yrs
- Regular hair/urine testing
- Not off work for > 1 year
- 12-step group attendance & a good sponsor
- BDDG attendance
- Dept. allows time for appts & group attendance

The GMC

Like 3 things:

1. Honesty
2. Insight
3. Taking of remedial steps

- Self-referral quite common these days – not such a bad thing
- Recommend AA, NA (Narcotics Anonymous) BDDG attendance
- Manage uncomplicated addiction as a health not disciplinary issue
- (don’t let your HR dept go down disciplinary route)

Future approaches

Oxytocin

- prevents naloxone-induced withdrawal symptoms
- blocks amphetamine-induced increases in dopamine levels in the nucleus accumbens

Baclofen

$GABA_B$ agonist reduces drug seeking & self administration of propofol (rats)
ie ? elevated DA levels satisfy desire

PET scans

Dopamine dysfunction resolution – monitor progress
Detect relapse risk

Find out how to get a handle on the problem, get help, and get better

Addiction & Recovery

FOR DUMMIES®

Brian F. Shaw, PhD
Paul Ritvo, PhD
Jane Irvine, DPhil
Clinical scientists and psychologists

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