



Physical Co-morbidities

Methadone 101-2100

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Disclaimer

In the past two years I have received no payment for services from any agency other than government or academic.

OBJECTIVES

After this talk the participant should be aware of:

- Common opioid induced side effects and comorbidities.
- Common life style related comorbidities
- Increased mortality inherent in addictive disease
- Methadone's impact on that mortality.

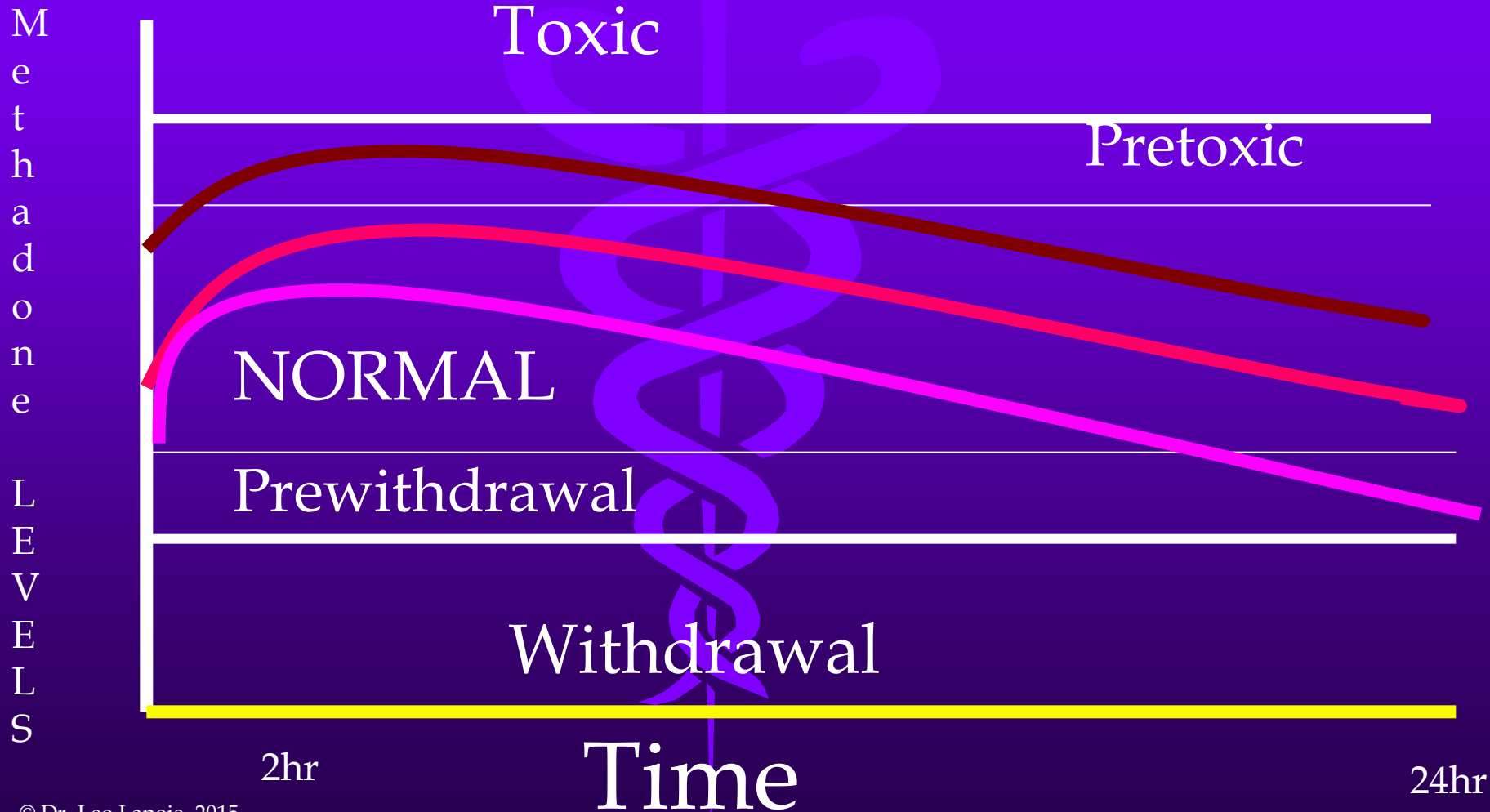
Opioid induced – side effects

- Sweating
 - Clonidine 0.1mg tid
 - Ditropan 5mg bid or tid
- Constipation → Bowel obstruction
- Dental carries
 - Opioids have anticholinergic properties
 - Tang
 - Meticulous oral hygiene

Treatment issue

- Fatigue
 - Nodding – Normal for a day or two after dose increase.

Methadone and Fatigue



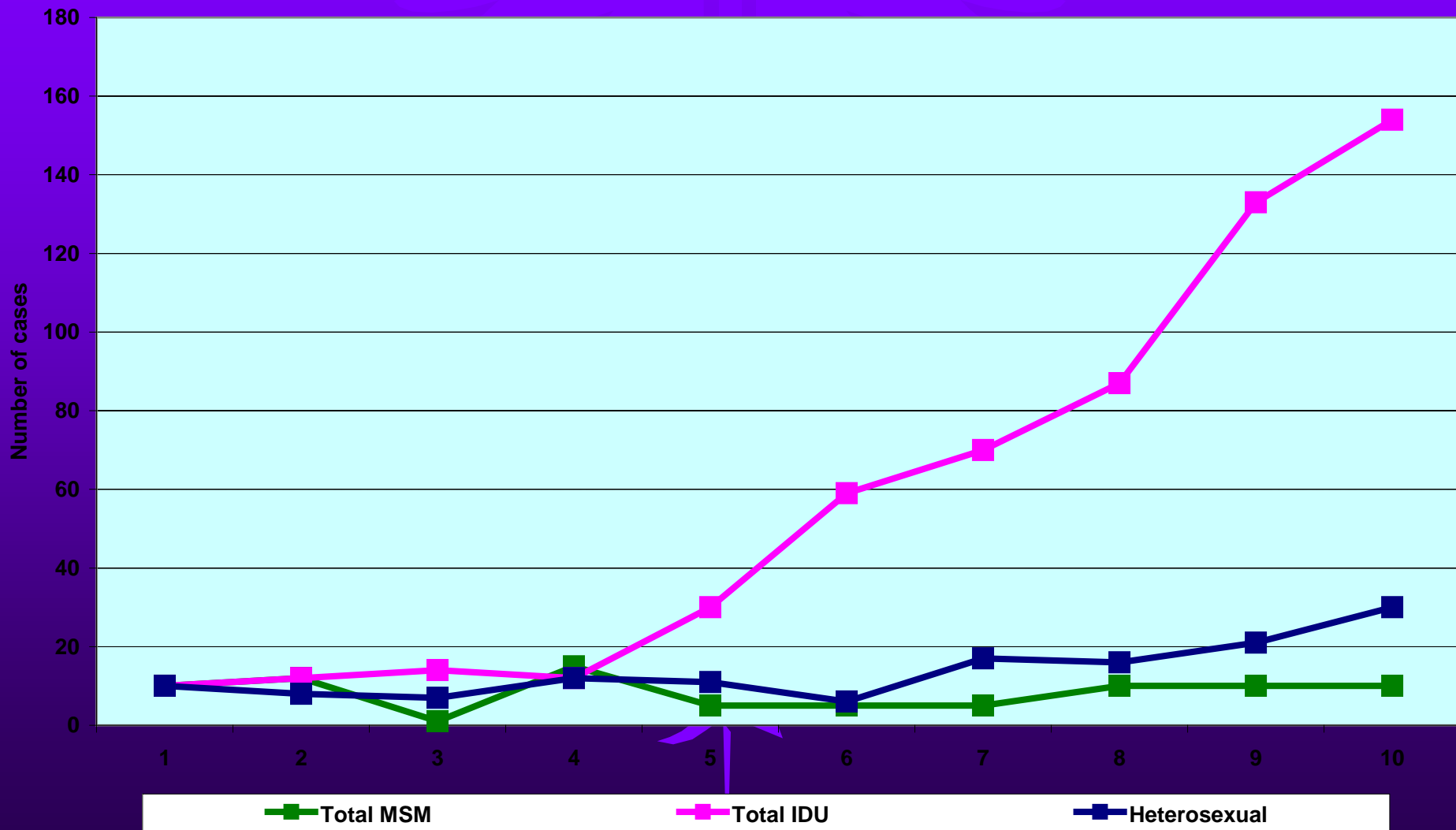
Sleep Disorder

- Insomnia almost universal in addicted population.
- Methadone aggravates Central Sleep Apnea

Lifestyle Related Comorbidity

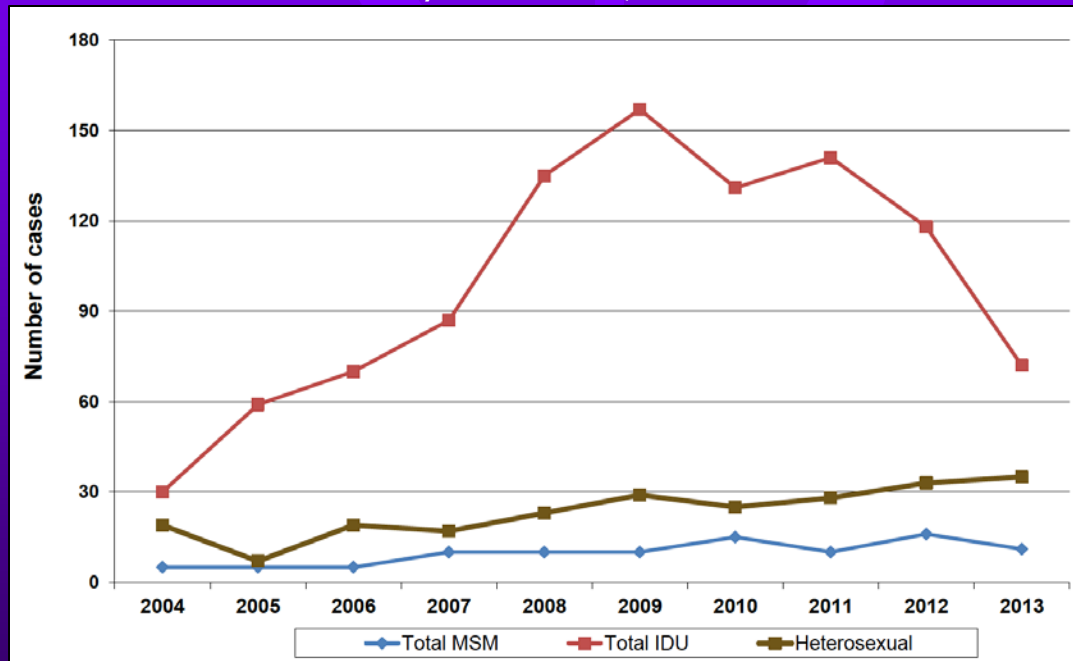
- Hepatitis B, Hepatitis C, HIV, Syphilis, STDs
- Hepatitis C infection present in $\pm 85\%$ of our patients.
 - Now curable
 - ALCOHOL ABUSE is disastrous
- HIV – Treatable but no curable

**Fig. 8 Saskatchewan HIV Cases by Selected Risk Factors,
Saskatchewan 2000-2009**



HIV in Saskatchewan: Incidence and risk factors

Count of new HIV cases by risk factors, SK 2004-2013



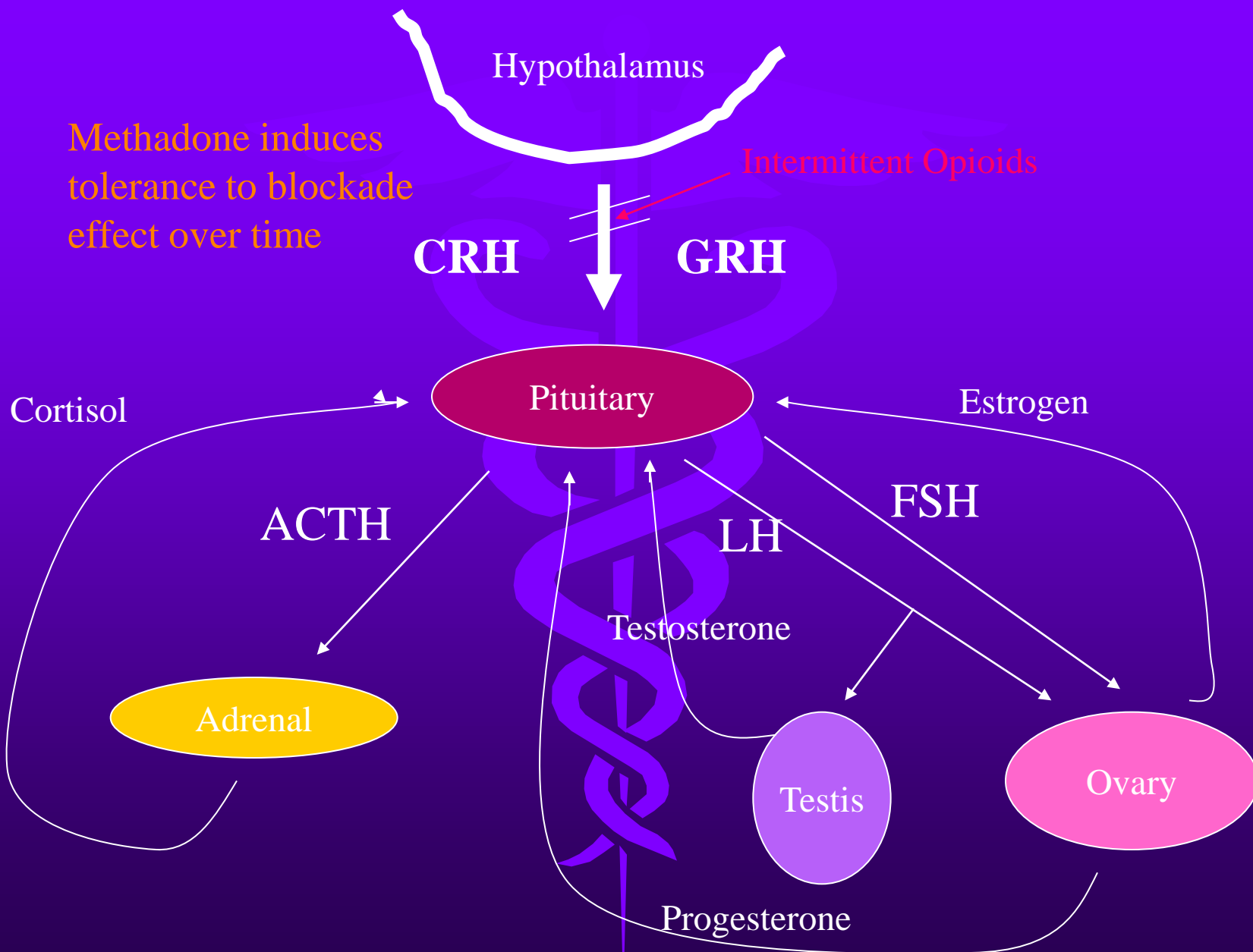
Saskatchewan Ministry of Health, Dec 1 2014. *HIV and AIDS in Saskatchewan 2013.*

Lifestyle Related Comorbidity

- Hepatitis B, Hepatitis C, HIV, Syphilis, STDs
- Staphylococcus aureus
 - Endocarditis – Tricuspid
 - Osteomyelitis – Spinal
 - Epidural Abscess
- Pregnancy

Sexual Dysfunction

- Opioids (and many other drugs including cannabis) block the Hypothalamic Pituitary Axis.
- Release of Gonadotropin Releasing Hormone is blocked.
- Corticotropin Releasing Hormone also blocked – reduced tolerance to stress
- Prolactin Inhibiting factor = gynecomastia
- Tolerance to this effect develops when patient on constant dose of long acting opioid.



Immunodeficiency

- Blocking hypothalamic pituitary axis release of corticotrophin impairs responsiveness to stress.
- That, poor nutrition, and perhaps the drugs themselves impair the patients immune response.
- Addicted persons often do not handle infection as well as non addicted person
- Methadone transiently inhibits killer lymphocyte

Hypogonadism

- Ask about *libido* as opposed to erectile dysfunction.
- If clinically indicated do CBC, TSC, Prolactin, FSH, LH, total and free (bioavailable) Testosterone.
- Should replace if deficient

Methadone Related Death

- Methadone deaths rarely occur in isolation.
- Most common other drug found is a benzodiazepine.
- Remember the phenomenon of **tolerance**.
- Don't initiate two psychoactive drugs at the same time.

Methadone Related Death

- Death is seven time greater in a patient initiating methadone therapy than in a heroin addict.
- It is 97.8 times greater than in the patient who has been on methadone for 2 weeks or more.
- Old study suggested that death occurred 16-18 hours after ingestion.
- LoVecchio et al 2006 found that all overdose symptoms were obvious within 9 hours (average 3.4 hrs post ingestion)

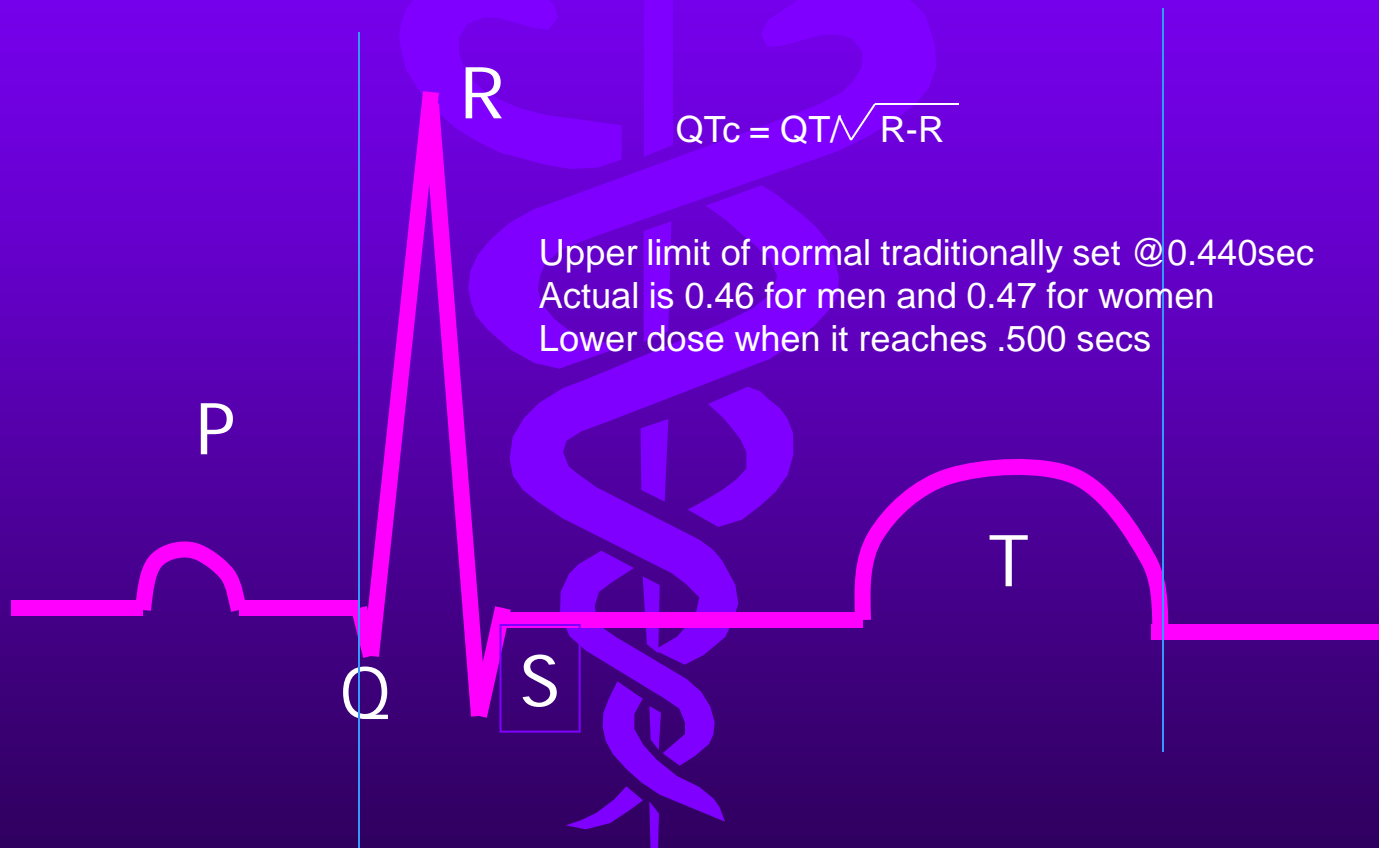
Isomers

- l-methadone (R enantiomer) is a potent mu receptor agonist

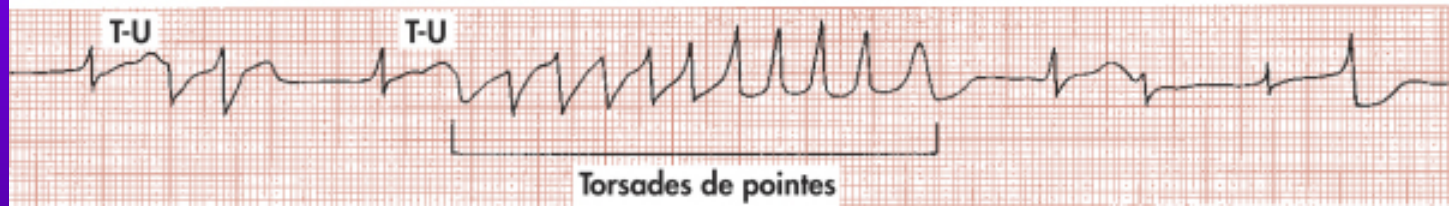
Isomers

- d-methadone (S enantiomer) little mu receptor effect but moderate NMDA receptor antagonist
- Preferentially metabolised by Cyp 2B6 which has six different genotypes
- Interferes with hERG potassium channel – prolonged QTc

QT Interval

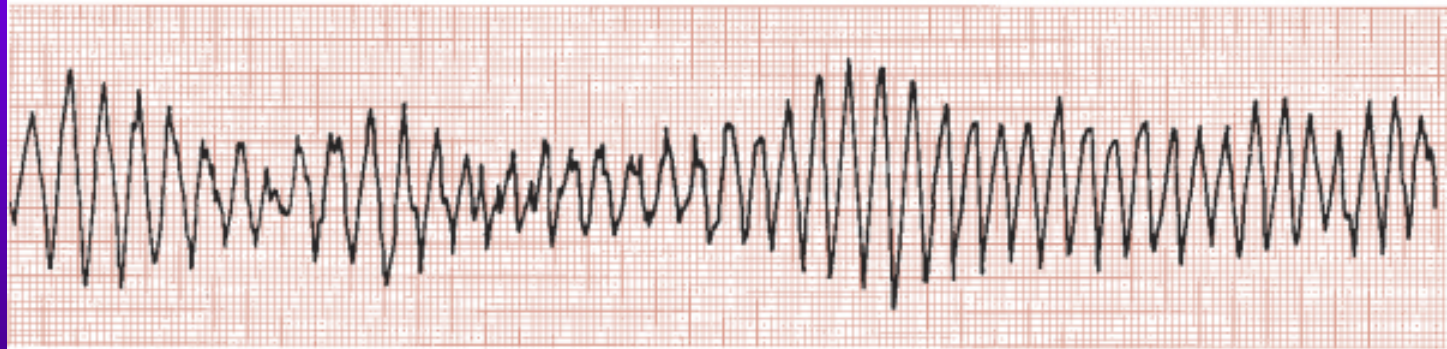


Torsades de Pointes: Nonsustained



Torsades de Pointes: Sustained

Monitor lead



Always

- Monitor ECG
- Other drugs that prolong QTc
- Caution patient re hypokalemia

Methadone blood concentrations in fatal cases overlap completely with those found in methadone maintenance program participants and in decedents where death is due to trauma and the presence of methadone simply an incidental finding... Given the degree of overlap of finding in cases where methadone is, and is not, related to the cause of death, it is simply impossible to distinguish between the two categories on the basis of toxicology testing alone.

Karch's Pathology of Drug Abuse Third Edition, CRC Press 2002

Relative Risk

- Methadone is a dangerous medication. Many deaths have been attributed to it, but:
- Untreated opioid addiction is so much more dangerous.

Buprenorphine related deaths

- Almost always in association with benzodiazepines when buprenorphine is injected.
- More frequent in Europe when buprenorphine is marketed as Suprex, with no naloxone.

The Sick Addict

- Is not Health care friendly
- Chaotic lifestyle that is addiction driven
- Does not find health care a friendly place

The Spanner in the Works

- Addicted patient often has a compromised endocrine and immunological system
- Patient is unable to increase cortisol levels in time of stress such as sepsis
- Immune system doesn't deal well with infection

The Spanner in the Works 2

- Withdrawal
- If this is not managed properly patient will leave because the withdrawal is causing greater distress than the illness itself

Withdrawal Management

- Opioid
 - Alcohol
 - Benzodiazepine
 - In hepatic failure
 - Nicotine
- Opioid
 - Benzodiazepine
 - Benzodiazepine
 - TAL –
Temazepam,
Alprazolam,
Lorazepam
 - Nicotine

Treatment Priorities

- Safety – patient and staff
- Treating the acute condition – doing what it takes to insure that the patient completes his or her course of treatment

Treatment Priorities

- Overcoming the addiction
 - This is a long term goal – not an immediate priority (unless the drug is harmful in the short term like alcohol or tobacco [but not nicotine])
 - Illness may present a “window of opportunity”
 - Generally speaking, an acute illness is not the time to “rehab” an addicted patient – it may be a good time to start laying the groundwork

SPAM

- S - stigma
- P - prejudice
- A - and
- M - misunderstanding