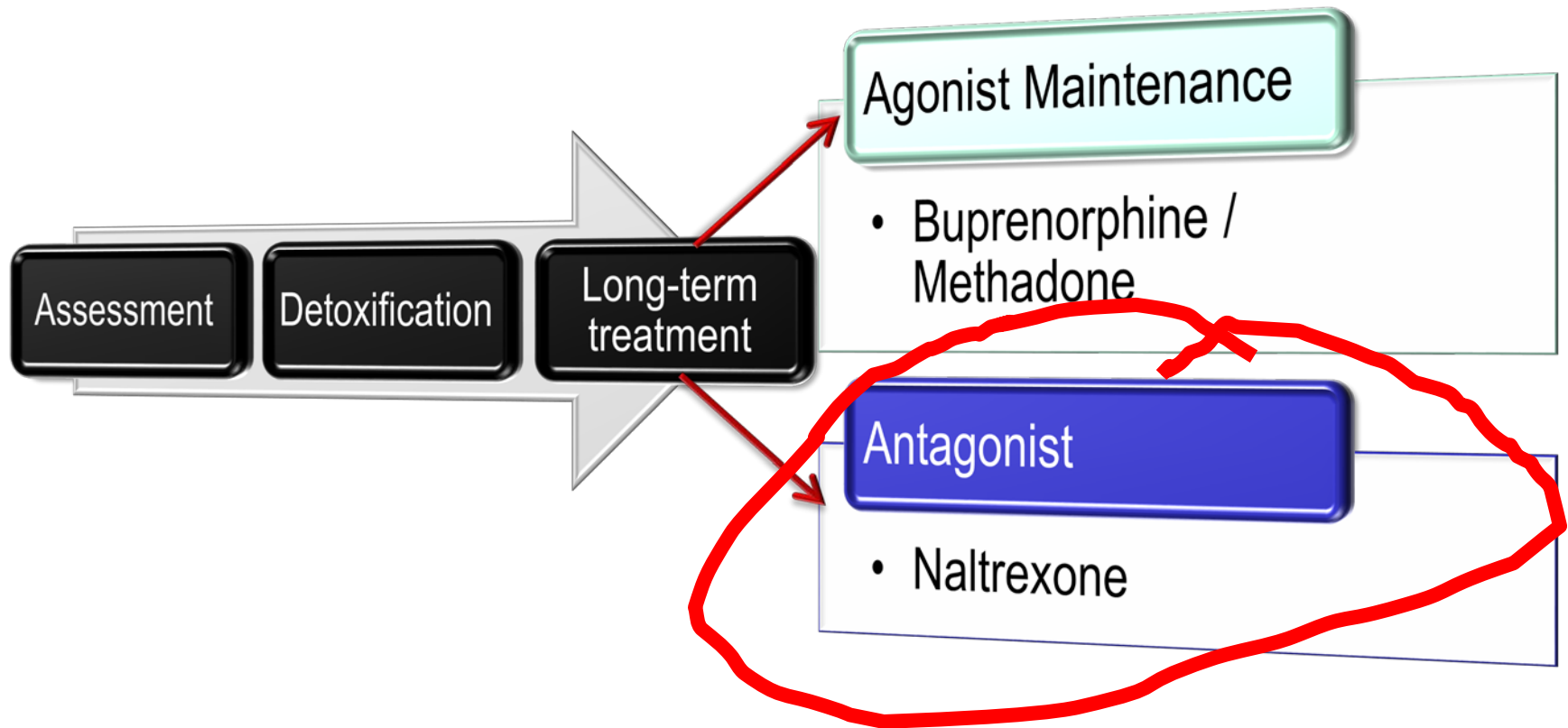


Long term treatment for opioid
dependence – Antagonist
therapy

Treatment of Opioid Dependence



Antagonist treatment – Naltrexone

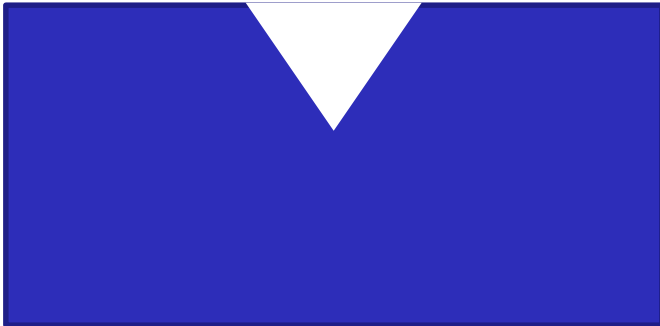
- Naltrexone (NTX) synthesized in 1965
 - ✓ Eliminate drug craving and prevent relapse
- Approved for this purpose by US FDA in 1984
- Approved for treatment of alcohol dependence in 1994

Naltrexone – Mechanism of action

- Naltrexone acts as “Antagonist”
 - ✓ A drug, which by itself does not produce any effect,
 - ✓ but prevents the action of agonist by blocking the receptors
- Pure μ antagonist



Opioid
Antagonists

A dark blue rounded rectangular box containing the text "Opioid Antagonists" in white, sans-serif font. The text is arranged in two lines, with "Opioid" on the top line and "Antagonists" on the bottom line.

Opioid Antagonists

Opium/
Morphine


Heroin

NALTREXONE

Buprenorphine

Naltrexone – pharmacology

- Competitive blockade of opioid receptors
 - ✓ Able to displace agonists from the opioid receptor
- Metabolised by liver
- Half life sufficient to permit daily dosing
- Patients do not develop tolerance to NTX
 - ✓ Not required to increase doses over days/months

- 
- Requires the patient to be free of opioids before administration of naltrexone

- ✓ 3 – 7 days for most opioids

- ✓ 10 – 14 days for methadone

OTHERWISE → Risk of precipitating withdrawals

Rationale of NTX therapy

- Drug use is a reinforcing condition
- Number of cues associated with craving and drug seeking behavior
 - ✓ Environmental
 - ✓ Emotional state
 - ✓ Physical state
- Can precipitate conditioned withdrawal and craving days to months after stopping opioid use → leading to relapse

Naltrexone breaks this cycle

Naltrexone: practice guidelines

- Available as 50 mg tablets
- Oral administration
- Appropriate patient selection
 - ✓ Motivated, educated, professionals
 - ✓ Strong family support system
 - ✓ No major complications in occupational/social spheres, i.e. homeless, unemployed, etc.
- Compliance
 - ✓ Supervised administration → involving F/M in treatment improves retention in treatment

Naltrexone: practice guidelines

- Regimen:

- ✓ 50 mg Once / day

- ✓ 100 mg / alternate day

- ✓ Thrice a week

- Monday – 100 mg

- Wednesday – 100 mg

- Friday – 150 mg

- Added advantage:

- ✓ Anti-craving agent for alcohol

■ Steps in initiation

Initial assessment

- Detailed history
- Examination of patient
- Baseline LFT
- Explain the rationale of NTX treatment

Detoxification

- Can be done on inpatient or outpatient basis

Opioid free

- After detoxification, patient to maintained opioid free for 3 – 5 days
- Adjuvant medications (NSAIDs, Sedatives) can be given

Naltrexone initiation

- Confirm patient is 'opioid free'
- Administer half tablet of NTX and observe for one hour
- If no withdrawals precipitated, administer the other half of NTX
- From next day onward, administer NTX once a day, or other dosing schedule

Naltrexone: practice guidelines

■ Side effects

- ✓ Infrequent, minor
- ✓ Nausea, gastritis, sleep disturbances, drowsiness, skin rashes → disappear within 1 – 2 weeks of treatment
- ✓ ? Elevated liver function tests
 - Product labelling: contraindicated in acute hepatitis and liver failure
 - Can be safely administered in minor liver abnormalities
 - Monitor LFT on a quarterly basis

Naltrexone: practice guidelines

- Duration of treatment: at least 6 – 12 months
 - ✓ Patients would have tried to use opioids on naltrexone → no euphoria → extinction of drug use behavior
 - ✓ Learnt to deal with stressors/life events without resorting to drug use

Naltrexone: practice guidelines

- Retention is important issue in Naltrexone – hindering factors
 - ✓ No direct relief of unpleasant/protracted withdrawal symptoms
 - ✓ Stopping/skipping NTX doses does not lead to withdrawals
 - ✓ Effect of opioids can be felt within 1-2 days of stopping NTX

Recommended in strongly motivated individuals with strong support systems

Naltrexone: practice guidelines

- Naltrexone alone is not sufficient...
 - ✓ Adjuvant assessment and treatment of comorbidities
 - ✓ Counselling
 - ✓ Family therapy
 - ✓ 12 step programs

To conclude...

- Opioid dependence is a chronic, relapsing disorder
- No single approach is likely to work for ALL patients
 - ✓ Patients must have access to a MENU OF OPTIONS to choose from
- Antagonist therapy is a good option for strongly motivated patients with a strong support system

To conclude.....

■ Naltrexone – characteristics

- Once-daily or less frequent oral administration.
- Blocks the euphoric high of opioids.
- No psychotropic or reinforcing effects.
- Nonaddicting, with no withdrawal symptoms on cessation.
- No increasing tolerance to its opioid-antagonist actions.
- Absence of serious adverse reactions or toxicity, even in long-term use.
- Essentially no abuse potential.
- No “black market” resale value or potential for diversion.
- Easy availability at reasonable cost.