

Rapid Opioid Detoxification - Guidelines

Summary The purpose of NSW Health Guidelines on Rapid Opioid Detoxification is to provide information on a procedure which may be conducted in private health facilities, licensed for Rapid Opioid Detoxification (ROD) as per the Private Health Facilities Regulation 2010 under the Private Health Facilities Act 2007. In accord with the regulation, Rapid Opioid Detoxification Class private health facilities must comply with the Drug and Alcohol Withdrawal Clinical Practice Guidelines—NSW.

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Audience Emergency departments;nursing;clinical staff;intensive care units

GUIDELINES FOR RAPID OPIOID DETOXIFICATION

PURPOSE

The purpose of *NSW Health Guidelines on Rapid Opioid Detoxification* is to provide information on a procedure which may be conducted in private health facilities, licensed for Rapid Opioid Detoxification (ROD) as per the *Private Health Facilities Regulation 2010* under the *Private Health Facilities Act 2007*. In accord with the regulation, Rapid Opioid Detoxification Class private health facilities must comply with the *Drug and Alcohol Withdrawal Clinical Practice Guidelines—NSW*.

KEY PRINCIPLES

ROD is not currently conducted NSW's public sector nor is it likely to be in the foreseeable future unless in the context of a clinical trial, thus the key principles of these guidelines are to ensure patients undertaking ROD procedures in a private health facility licensed for the purpose of ROD:

1. have been well informed of the treatment they are undertaking including potential risks and alternative treatment options;
2. have been advised verbally and in writing that rapid opioid treatment and naltrexone implants are still experimental treatments;
3. are advised verbally and in writing that naltrexone implants used in Australia have not been approved by the relevant regulatory authorities;
4. can competently provide signed, informed, consent to treatment;
5. have been satisfactorily assessed as appropriate for the treatment; and
6. are adequately monitored and supported during and post treatment.

The guidelines align with the *Private Health Facilities Regulation 2010* under the *Private Health Facilities Act 2007* which provides the recommended standards for the settings in which ROD is undertaken ensuring they are appropriately and adequately equipped. Refer section 4.1.7.

Further, the guidelines provide Public Hospital Emergency Departments and the like with appropriate recommendations on how to best manage patients who present post ROD treatment with complications and / or those who present in medical settings who are in continued treatment with naltrexone (including those with naltrexone implants).

USE OF THE GUIDELINE

As per the *Private Health Facilities Regulation 2010* (amended) under the *Private Health Facilities Act 2007*, compliance with the *NSW Health Guidelines on Rapid Opioid Detoxification* is a condition of a private health facility license for the purpose of ROD.

In addition these guidelines provide recommendations for clinical staff in medical settings such as Public Hospital Emergency Departments and the like for the management of patients who may present post ROD procedures with complications and /or patients presenting who are in continued naltrexone treatment (including naltrexone implants).

REVISION HISTORY

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| July 2011 (GL2011_009) | Deputy Director-General Strategic Development | Updates and Replaces GL2005_027 |
| February 2001 (GL2005_027) | Director-General | New guideline originally issued as Circular 2001/17 |

ATTACHMENTS

1. Guidelines for Rapid Opioid Detoxification



GUIDELINES
FOR
RAPID OPIOID DETOXIFICATION

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1 Purpose and aim of Guidelines

The purpose of *NSW Health Guidelines on Rapid Opioid Detoxification* is to provide information on a procedure which may be conducted in private health facilities, licensed for Rapid Opioid Detoxification (ROD) as per the [Private Health Facilities Regulation 2010](#) under the *Private Health Facilities Act 2007*.

Compliance with the *NSW Health Guidelines on Rapid Opioid Detoxification* is a condition of a private health facility license for the purpose of ROD. These guidelines supersede the *NSW Health Rapid Detoxification From Opioids – Guidelines (2005)* Document Number: GL2005_027.

ROD is not currently conducted in NSW's public sector nor is it likely to be in the foreseeable future unless in the context of a clinical trial. Private practitioners conducting ROD procedures in NSW must refer to the [New South Wales drug and alcohol withdrawal clinical practice guidelines \(2007\)](#), Chapter 5 and to the Commonwealth [Clinical Guidelines and Procedures for the Use of Naltrexone in the Management of Opioid Dependence \(2003\)](#) for more specific information pertaining to ROD procedures.

The aim of these guidelines is to ensure that:

1. patients have been well informed of the treatment they are undertaking including potential risks and alternative treatment options;
2. patients are advised verbally and in writing that rapid opioid treatment and naltrexone implants are considered experimental treatments;
3. patients are advised verbally and in writing that naltrexone implants used in Australia have not been approved by the relevant National regulatory authorities;
4. patients can competently provide signed, informed, consent to this treatment;
5. patients have been satisfactorily assessed as appropriate for the treatment;
6. patients are adequately monitored and supported during and following treatment;
7. the settings in which ROD is undertaken are appropriately and adequately staffed and equipped; and that
8. Public Hospitals (including Emergency Departments) and other comparable centres have appropriate guidelines on how to best manage patients who present with complications post ROD treatment and / or those who present in medical settings who have naltrexone implants.

2 Introduction

2.1 Benefits of opioid treatment

“Rapid Opioid Detoxification” (ROD) may be defined as the administration of one or more opioid antagonists (naltrexone and / or naloxone) to a person for the purposes of accelerating opioid withdrawal and rendering the person opioid free.

Naloxone and naltrexone are not currently registered by the Therapeutic Goods Administration (TGA) in Australia for use in rapid detoxification. Research is currently being conducted nationally and internationally on naltrexone use in the treatment of opioid dependence and practitioners are obliged to keep themselves up to date with this research if they are using naltrexone in clinical practice.

ROD in Australia

There is variable consumer demand for rapid opioid detoxification. ROD as a stand-alone treatment shares many of the same limitations as other treatment approaches providing opioid withdrawal. The vast majority of patients relapse to dependent opioid use following withdrawal unless they are linked in with ongoing treatment such as:

- residential rehabilitation programs;
- counselling programs;
- continuing naltrexone treatment; or
- re-engaged with opioid maintenance treatment.

One of the greatest risks of relapse to opioid use following detoxification and loss of tolerance to opioids, is an increased risk for non-fatal and fatal overdose.

The use of ROD has waned in the past decade for the following reasons:

1. Use of buprenorphine:
Buprenorphine management of withdrawal has become more available and it can avoid the need for ROD. Initiation of naltrexone while ideally deferred for 3-5 days post buprenorphine in OPD settings may be commenced in an inpatient unit within 1-2 days of ceasing buprenorphine
2. The safety and adverse event profile of ROD:
ROD can be associated with a range of complications, mainly related to precipitated opioid withdrawal and / or sedation. These complications may include severe dehydration, renal failure and delirium and require hospitalization. While the extent of this risk still uncertain, there have been several deaths in Australia associated with ROD and a number of admissions to hospital of critically ill patients.
3. Cost to services:
The cost and resources required to provide rapid detoxification, namely inpatient hospital admission with intensive medical and nursing staffing, has made ROD less attractive.
4. Decreased use of oral naltrexone:
Greater clinical experience and research with oral naltrexone demonstrated its limited role in treating opioid dependence, with high relapse rates (fewer than 10% retention at 6 months). As such, a detoxification approach that was largely oriented towards inducting patients onto oral naltrexone became less widely used in Australia.

While demand for ROD as a treatment option has waned in the past decade, naltrexone implant devices have been widely used in recent years, often in conjunction with ROD. The vast majority of ROD procedures currently performed in Australia are within this context.

2.2 Naltrexone implants

Naltrexone implants are sustained release devices that are inserted subcutaneously, typically in the abdominal wall, under local anaesthesia. The implants are claimed to release therapeutic plasma levels of naltrexone for up to 3 to 6 months with more recent devices claimed to be effective for up to 12 months. However, therapeutic plasma levels of naltrexone are poorly defined by research studies. In addition, the lack of a naltrexone implant approved by the Therapeutic Goods Administration means that no guarantee can be given of consistent blood levels achieved by a specific device.

In standard practice a person undergoing ROD is required to be opioid abstinent for a period of 7-10 days before an implant is inserted to avoid a precipitated withdrawal. However, opioid dependent people often find it difficult remaining abstinent for this period of time given the severity of the symptoms associated with opioid withdrawal. For this reason, ROD is one approach for initiating naltrexone implants as the detoxification process can be completed under sedation and within 6 – 12 hours from short acting opioids. However, ROD from long acting opioids such as methadone may take up to 12, 24 or even 72 hours.

Naltrexone implants are manufactured both in Australia and overseas, but are not currently registered for the treatment of heroin dependence with the TGA in Australia or in any other country with a comparable regulatory process. In Australia, these devices are used by a small number of private practitioners. In Australia naltrexone implants are used under the TGA's Special Access Scheme (SAS). Practitioners using naltrexone implants must comply with the requirements as stated in the Commonwealth's ['Access to unapproved therapeutic goods via the Special Access Scheme'](#) (2009).

As the Royal Australasian College of Physicians (RACP) position statement on the use of naltrexone implants highlights, few patients meet the 'Category A' criteria of the SAS, of which the requirement is to have a "...seriously ill from which death is reasonably likely to occur within a matter of months". The RACP's statement indicates most opioid dependent patients can be effectively treated with a range of existing treatment approaches. Further, it should be emphasized that the role of naltrexone implant treatment remains unclear. A small number of controlled trials have demonstrated some benefits of the implant over placebo or oral naltrexone. These studies highlight high levels of relapse to opioid and other drug use as seen with other treatments such as methadone and buprenorphine.

At the time these guidelines were being reviewed, the National Health and Medical Research Council (NHMRC) was reviewing the evidence for efficacy and safety of naltrexone treatments for opioid dependence.

It is recommended that medical practitioners providing ROD or considering referring patients for naltrexone are cognizant of the NHMRC statement when it is released. Please refer to: <http://www.nhmrc.gov.au/>

2.3 Opioid withdrawal and ROD

The *New South Wales drug and alcohol withdrawal clinical practice guidelines* (2007), Chapter 5 provide the most relevant guidance on opioid withdrawal. The severity of opioid withdrawal symptoms are somewhat unpredictable, but influenced in part by three factors:

1. Firstly, the psychological state of the patient undergoing opioid withdrawal. Higher levels of anxiety and psychological distress are often associated with more severe withdrawal symptoms;
2. Secondly, the greater the dose of opioid (and the longer the half-life of the opioid) being administered regularly, the more severe the withdrawal syndrome on discontinuing; and
3. Thirdly, the more rapid the rate at which the opioid is withdrawn, the more severe the withdrawal syndrome.

The administration of opioid antagonists (such as naloxone or naltrexone) in ROD procedures to opioid-dependent people precipitates an immediate abstinence syndrome, often of considerable severity.

Opioid antagonists, naloxone and naltrexone, have a higher affinity for opioid receptors than common opioids such as morphine, methadone, codeine, oxycodone and heroin, and thus displace opioids such as these from mu receptors. This displacement causes a rapid and severe opioid withdrawal syndrome. In effect, the use of opioid antagonists in withdrawal increases the severity of withdrawal but reduces its duration.

Severity of withdrawal is also dependent on the type and the amount of opiate or opioid last used. Withdrawal severity may also be determined by the duration since last opioid use (shorter half life drugs such as heroin are associated with an earlier onset of withdrawal symptoms) as well as the physical and mental characteristics of the individual. The manifestations of precipitated withdrawal differ from the usual opioid withdrawal being more sudden in onset and perhaps more severe.

There is substantial evidence that ROD treatment can produce severe physiological and psychological distress. If untreated, the acute phase of precipitated withdrawal involves two major clusters of symptoms:

1. *gastrointestinal*, comprising unremitting vomiting and diarrhoea, often with cramping abdominal pain, lasting many hours. Without supportive treatment, patients may become dehydrated and develop electrolyte, acid/base disturbances and / or acute renal failure.
2. *significant psychological disturbances*, comprising agitation, dysphoria, and delirium. Delirium can last for more than 24 hours .

Some aspects of antagonist precipitated withdrawal appear to be of shorter duration than the process of spontaneous withdrawal. For example, in anaesthetised patients given a bolus dose of naloxone, signs of physiological withdrawal resolve in 4-6 hours. Once acute withdrawal signs have subsided, further administration of naloxone evokes no further withdrawal signs, and this has been taken as definitive evidence that acute withdrawal is complete.

However, while acute signs of withdrawal subside, many patients remain ill for considerably longer.

The major factor associated with severity of precipitated withdrawal is recency of opioid use as the severity of withdrawal is proportional to the amount of drug still circulating ie. the greater the interval between opioid use and administration of naltrexone, the less severe is the precipitated withdrawal.

Heroin is a relatively short-acting drug and thus heroin-dependent patients who receive naltrexone within 12 hours of their last use of heroin experience more severe withdrawal reactions than subjects in whom administration of naltrexone is delayed 24 hours. This same severe reaction may be experienced in methadone users up to 10 days after last use of this drug. In most patients on methadone however, signs of significant withdrawal are evident at 72 -96 hours at which time ROD may be considered.

The severity of precipitated withdrawal is also influenced by the level of neuroadaptation ie those patients with a high opioid tolerance experience more severe precipitated withdrawal.

Patients maintained on methadone are more likely to have more severe precipitated withdrawal when given an antagonist than persons using street heroin. This reflects two factors:

1. long term exposure to a high dose of opioid and thus a high degree of neuroadaptation to opioids; and the
2. long half-life of the drug means methadone may be circulating up to 80 hours or longer after the last dose.

3 ROD approaches and procedures

3.1 Approaches to ROD

Published descriptions of ROD often involve a wide variety of medications and approaches resulting in a lack of consistent data on the efficacy of any regimen.

However, it is possible to identify 3 broad approaches for ROD including:

1. *General anaesthesia* with intubation protects the airway, but obviously requires an operating theatre or high intervention unit (eg Intensive Care Unit) with staff capable of administering general anaesthetic and monitoring intubated patients. Patients must have no anaesthetic contraindications and should be warned of the risk of general anaesthesia and intubation.
2. *Deep sedation* without airway protection involves a risk of aspiration; and
3. *Light (minimal) sedation*. The problem with performing ROD in lightly-sedated subjects is the risk of agitation, delirium, vomiting and diarrhoea.

ROD under general anaesthesia is generally not undertaken in Australia now as only those procedures involving minimal sedation can be carried out in low-level medical settings. The small number of private practitioners undertaking ROD procedures in NSW do so using light to deep sedation.

3.2 ROD procedures

3.2.1 Medications and risks

The major symptomatic medications used during ROD include:

- Clonidine: a centrally acting alpha-2 agonist, to reduce sympathetic over activity, agitation, and withdrawal distress.
- Midazolam: used to induce sedation and amnesia for the procedure.
- Hyoscine butylbromide (Buscopan®) may be useful for abdominal cramps.
- Octreotide: a synthetic somatostatin analogue, is often used for controlling gastrointestinal symptoms of diarrhoea. It also aids in the management of nausea, and vomiting.
- Metoclopramide or ondansetron, (a 5HT antagonist): are used to suppress nausea.

NOTE: IV fluids may be used for individuals not tolerating oral fluids.

There have been several documented fatalities associated with ROD that relate to the administration of multiple medications. In essence, the more drugs used to ameliorate symptoms, the greater the risks of drug interactions and potential for cardiovascular and respiratory toxicity.

- Clonidine can produce significant hypotension and bradycardia. In the context of dehydration, this can contribute to acute renal failure.
- Benzodiazepines can contribute to worsening of delirium, and to depression of consciousness, respiration and gag reflex and risk of aspiration.
- Octreotide, metoclopramide and ondansetron are relatively safe in doses used in this procedure.

3.2.2 Minimizing risks

The longer the opioid free period prior to ROD the less the opioid withdrawal symptoms following ROD. The duration of this period should be longer if the opioid used has a longer half life. Hospital admission may be needed to achieve this.

4 Protocols for ROD

4.1 Patient protocols

The risks of this procedure can be further minimized if, in addition to careful use of medications for symptom relief, the following protocols are complied with.

4.1.1 Suitability and assessment

In general terms, patients with good social supports (employment, relationship, family), with few psychological difficulties who are committed to abstinence appear to be most likely to benefit from ROD.

Careful assessment prior to treatment is essential including the screening of patients for underlying medical or psychiatric conditions.

Assessment must include the patient's:

- substance use;
- drug and alcohol and medical treatment history;
- medical condition;
- psychiatric and cognitive conditions;
- psychosocial circumstances;
- willingness and capacity to engage in ongoing psychosocial treatment; and the
- perspectives of other relevant health professionals engaged in the patient's care.

Refer Appendix A - ROD Assessment Criteria.

Absolute Contraindications

- pregnancy
- a history of significant cardiac disease, or evidence of heart disease on clinical examination
- acute or chronic renal impairment
- decompensated liver disease – jaundice and/or ascites, hepatic encephalopathy
- history of significant mental illness including psychosis.

Relative contraindications

- those with chronic pain who are unable to be treated without opioids
- current dependence on benzodiazepines, alcohol, or stimulants
- History of treatment for depression (patients may require psychiatric assessment prior to ROD)
- Unstable social circumstances – patients who are homeless or in highly unstable social circumstances require a comprehensive plan to stabilize their circumstances prior to undergoing ROD.

4.1.2 Information for patients

Written information on the procedure must be provided to patients. Practitioners must identify and address any barriers to the patient understanding the information provided including non-English speaking, low literacy or a form of disability. Practitioners must confirm with the patient that they are able to understand the information that has been provided and provide an opportunity for questions to be asked.

Practitioners have a responsibility to ensure that informed consent can be obtained by providing patients with all relevant information pertaining to ROD procedures including the following:

- Other treatment options available to patients for them to consider prior to undertaking ROD including clear details of the range, usual outcomes and adverse events of conventional treatment approaches for opioid dependence;
- Statement that naloxone and naltrexone are not currently registered by the Therapeutic Goods Administration (TGA) in Australia for use in rapid detoxification;
- Statement that the safety and effectiveness of naltrexone implants is not proven, , thus patients undertaking ROD as a prelude to naltrexone implants must also be informed that they are undergoing treatment of uncertain effectiveness and safety, and provide written consent acknowledging this and specific consent to any treatment involving unregistered naltrexone implants;
- Clear and concise information on the manner of physiological and psychological risks associated with ROD including a risk of hospitalisation for complications and high overdose risks (which may prove fatal) post ROD procedure.
- Contra-indications of treatment and possible courses of action that will be taken in the eventuality of an adverse event during the procedure;
- Information on the range of potential adverse events and other consequences (e.g. impaired opioid analgesia) associated with long-acting naltrexone products, and how these will be addressed in the event that they occur (e.g. need for surgical excision); and
- Full details of the costs of treatment, frequency of appointments, and availability of support services incorporated into treatment plans.

4.1.3 Competent and informed signed consent

Opioid dependent persons are often marginalized and vulnerable. These individuals often feel desperate about their situation and are subject to intense pressure to undertake treatment from family or authorities. Thus, many patients are unable to make an immediate decision as to whether or not they wish to participate in ROD. It is important to allow patients time to think about their treatment options. Patients should not be pressured into making a decision.

After providing all relevant information pertaining to ROD treatment, signed consent to treatment must be obtained from a 'competent patient' (meaning the patient has capacity at the time of treatment consent).

Refer Appendix F - Consent for Rapid Opioid Detoxification Treatment

4.1.4 Treatment plans

As it is evident, ROD alone is not an effective treatment, ROD must be offered as part of a comprehensive management plan that should be explained to the patient with consent signed by the patient prior to commencing ROD.

Patients should be encouraged to participate in a relevant continuing aftercare program and should be encouraged to engage with a GP and receive treatment of any existing physical and / or mental co-morbidity. Treatment must incorporate coordination with relevant service providers (for patients seeking to withdraw from opioid treatment pharmacotherapy such as methadone, the patients planned ROD must be discussed with their prescribing doctor and for patients with significant medical or psychiatric conditions, the treatment plan must be discussed with their health practitioners).

Treatment plans must detail the costs of treatment and details pertaining to aftercare including ongoing treatment costs (naltrexone, counselling), frequency of appointments and coordination with support services.

4.1.5 Discharge

Nursing, medical and psychosocial support during and after the acute phase of withdrawal is essential. The patient should be monitored as an inpatient until assessed as fit for discharge. Given the acute nature of ROD procedures, discharge should not generally occur within 24 hours post acute withdrawal phase. In some instances discharge within this 24 hour period is acceptable if, but must only occur if the 'Discharge Criteria as provided in Appendix B – ROD Discharge Criteria has been met.

In the instance of an adverse event during or post ROD procedure, transfer of care to public hospital emergency department or intensive care unit may be indicated. In these instances, the private health facility must use the ISBAR tool (as below) as part of clinical handover:

Introduction

Situation

Background

Assessment

Recommendation

4.1.6 Aftercare

Vigorous attempts to follow patients are indicated after ROD. Generally, patients should be seen daily for the first 3 to 5 days after the procedure (according to patient's clinical condition and supports), then at regular (e.g. weekly to monthly) intervals over subsequent months.

There are many approaches to the delivery of aftercare including;

- Medical monitoring – regular review with the prescribing doctor, with monitoring of compliance, review of drug use, sometimes with urine testing to confirm self-report;
- Counselling – regular scheduled counselling sessions have frequently been used;
- Supervised dosing – a family member or friend supervises the daily administration of naltrexone, sometimes administering the tablet crushed to minimize the risk of the patient spitting it out; and
- Self-help groups may be a valuable adjunct to people trying to maintain abstinence.

These approaches to enhancing compliance are not mutually exclusive and there is no clear evidence as to which approach is most effective. But what is clear is that vigorous follow-up and support enhance the effectiveness of treatment.

For those patients undergoing continued oral naltrexone treatment, recommendations for the monitoring of these patients is contained in the National Drug Strategy [Clinical Guidelines and Procedures for the Use of Naltrexone in the Management of Opioid Dependence](#).

Patients treated with naltrexone should be issued with a card that can be provided to medical practitioners in case analgesia is required following illness or injury.

4.1.7 Facilities for ROD procedures

The *Private Health Facilities Regulation 2010* under the *Private Health Facilities Act 2007* provides the licensing standards for private healthcare facilities generally and the specific requirements for Rapid Opioid Detoxification Class private health facilities.

5 Adverse events

5.1 Post ROD

Private health care facilities licensed for the purpose of ROD are responsible for any adverse events that may occur during and post ROD procedures. If the facility is unable to provide appropriate treatment in response to an adverse event, the facility is responsible for referral and appropriate clinical handover to an appropriate treatment provider.

In the acute phase of precipitated withdrawal, two major clusters of significant symptoms may be experienced: gastrointestinal; and psychological disturbances. It is evident these symptoms can persist for a number of days after the ROD procedure as detailed below.

5.1.1 Gastrointestinal (GI) and related autonomic disturbances

Most notably:

- Nausea
- Vomiting
- Diarrhoea,
- Urinary frequency; and
- Excessive sweating

These symptoms are likely to persist in those patients who were dependent on long action opioids such as methadone and in patients who have had a naltrexone implant inserted.

Persistent diarrhoea, vomiting, urinary frequency and sweating can lead to significant fluid and electrolyte disturbances (dehydration, hyponatremia, hypokalemia and acid base disturbances). In patients not tolerating oral rehydration, IV fluids and specific treatment to re-establish electrolyte balances is required. This may be achieved in the Private facility or it may require transfer to a Public Hospital.

5.1.2 Central Nervous System (CNS) disturbances

Most notably:

- Agitation;
- Anxiety;
- Disturbed sleep;
- Muscle tension.

Severe symptoms can include confusion and delirium. These may be exacerbated by excessive -use of benzodiazepines to manage agitation and sleep problems. Symptoms may persist for several days

5.1.3 Overdose

Patients post ROD procedures are at significantly high risk of overdose and clinicians must ensure this has been discussed with patient and appropriate aftercare has been incorporated into the patient's treatment plan to minimize the risk of overdose.

5.1.4 Existing pain conditions

Some patients when opioid free may experience pain from existing conditions previously masked by opioid analgesia. These conditions may include dental pain resulting from poor dental hygiene. Patient treatment plans should detail any existing pain conditions that may be problematic post ROD.

5.2 Post naltrexone implant

Those who have had a naltrexone implant inserted may experience complications after the procedure as detailed below.

5.2.1 Localized adverse events

Most notably:

- Local wound sepsis and subsequent systemic infections;
- Immunoreactivity; and
- Autolysis of the implant.

These complications may require antibiotics and / or surgical management.

5.2.2 Difficulties with subsequent analgesia

Patients with naltrexone implants may experience difficulties in achieving opioid analgesia due to the blocking effects of naltrexone. Difficulties arise in not knowing whether naltrexone implant inserted some time before are still providing therapeutic levels of naltrexone (estimated at between 1 to 2ng/ml), as there is considerable variation in available naltrexone implant brands, and there also appears to be wide variability between individuals.

It may be that the naltrexone implant has 'worn off', and indeed the patient may be overly sensitive to opioid doses. As such, it is recommended that clinicians proceed cautiously with opioid analgesia – with initial test doses that are carefully monitored, and subsequently titrated. Non-opioid analgesic approaches should be considered. Consultation with acute pain and addiction medicine teams is recommended.

5.2.3 Overdose

Cases have been reported where patients who have undergone ROD and then had a naltrexone implant inserted later presented with an overdose – either through the use of opioids (it is thought due to the naltrexone implants wearing off prematurely), or through the use of other sedative drugs (e.g. benzodiazepines, alcohol, antidepressants and neuroleptic medications).

Patients presenting with overdose in these cases should have toxicology performed (urine, blood, breathalyzer) to assist in identifying the substances used.

Appendix A – ROD Assessment Criteria

| Criteria | Operational criteria & method of assessment |
|--|--|
| 1. Opioid dependent individuals. | 1.1 DSM IV criteria checklist 1.2 Examination for signs of drug use 1.3 Self-report 1.4 Urine drug screen (optional) |
| 2. Less than 18 years of age. | 2.1 Proof of identity Patients who are less than 18 years old must be assessed by 2 practitioners. |
| 3. If in opioid treatment, discuss with prescriber or clinic. | 3.1 Self-report 3.2 Confirmation from Pharmaceutical Services |
| 4. Not dependent upon, intoxicated or withdrawing from alcohol, BZD or amphetamines. Dependent cannabis use is not an exclusion criteria. | 4.1 Clinical history & examination 4.2 Drug use history |
| 5. Not pregnant or breast feeding. | 5.1 Urine bHCG test at assessment using rapid urine test kits |
| 6. Social environment suitable | 6.1 Assessment of social environment (in particular, patient not homeless) |
| 7. No active or unstable medical condition | 7.1 Medical assessment 7.2 Blood tests if indicated |
| 8. No significant psychiatric or cognitive condition | 8.1 Psychiatric assessment |
| 9. Able to give informed and voluntary consent to ROD procedure and ongoing treatment and commitment to abstinence | 9.1 Addiction Medicine Specialist Assessment 9.2 Specific enquiry to exclude coercion by family, peers or community or legal agencies. 9.3 Consideration of the risks and benefits of the proposed treatment in relation to other treatment options. Explanation of treatment process, expectations. 9.4 Informed Financial consent. 9.5 Signed patient consent form |

Appendix B – ROD Discharge Criteria

Patients may only be discharged when they meet ALL of the following criteria:

1. Ability to tolerate oral fluids;
2. Are not experiencing persistent vomiting and or diarrhoea with signs of volume depletion (Pulse >100, BP <100 systolic;
3. Do not exhibit significant cognitive impairment, including sedation, confusion or disorientation; and
4. Do not score in the moderate to severe range (>13) of the Clinical Opiate Withdrawal Scale (COWS).

Appendix C – Managing Complications Post ROD

In a number of cases, patients who have undergone ROD presented to public hospital emergency departments with severe complications attributed to ROD. The table below provides some suggestions on how such complications may be managed. Most of these presentations can be managed in the ED or an associated observation ward. However, as noted, resources must be available to supply one-to-one nursing and security personnel if required.

Recommended Emergency Department Management Post ROD

Antagonist Accelerated Withdrawal: GI Predominance

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|------------------------------|---|
| <u>First-line Treatment</u> | Nil by mouth with IV fluids |
| Vomiting | Metoclopramide 10 mg IV or Prochlorperazine 12.5 mg IV |
| Diarrhoea | Loperamide 2 mg orally |
| <u>Second-line Treatment</u> | |
| Vomiting | 5-HT ₃ antagonists, e.g., ondansetron 4 mg IV |
| Diarrhoea | Octreotide 50 -100 microg SC |
| Abdominal pain / cramps | Hyoscine butylbromide 20 mg IV |
| Sympathetic stimulation | Octreotide 50 microg SC Clonidine ** 75–150 microg IV or orally; maximum 900 microg /day |

Antagonist Accelerated Withdrawal: Fluid and electrolyte disturbance predominance

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| Significant fluid and electrolyte disturbances (dehydration, hyponatremia, hypokalemia, acid base disturbances) | Use of intravenous fluids selected to correct specific imbalances identified. Patients may require several litres of fluid over 24-48 hrs |
|---|---|

Antagonist Accelerated Withdrawal: CNS Dominance

| | |
|------------------------------|--|
| <u>First-line Treatment</u> | |
| Agitation | Midazolam 5 mg IV prn* or Diazepam 5 mg IV prn* |
| Departmental resources | One-to-one nursing Security staff |
| <u>Second-line Treatment</u> | |
| Evidence of dystonia | Consider benztropine 1 mg IV prn; maximum 2 mg |
| Airway compromise | Rapid-sequence intubation Propofol infusion |
| Sympathetic stimulation | Clonidine ** 75–150 microg IV or orally; maximum 900 microg /day |

*Large doses may be required. Close monitoring of respiratory function is mandatory and advanced airway management may be required.

** Monitor pulse and blood pressure if providing large, up to maximum dose.

GI: gastrointestinal; IV: intravenously; SC: subcutaneously; CNS: central nervous system; prn: as needed, mg: milligram, microg: microgram

Appendix D - Managing Patients Currently Treated with Naltrexone

Patients with naltrexone implants or currently taking oral naltrexone medication may present at emergency departments or in other medical settings requiring the administration of pain medication. Medical professionals treating such patients should first consider that naltrexone is an opioid antagonist and that inadequate pain management is likely to occur if opioid analgesics such as morphine and fentanyl are used. Secondly, there can be significant variances between implant types, and individual responses to naltrexone leading to difficulties in knowing whether a naltrexone implant inserted is still providing therapeutic levels of naltrexone.

Early consultation with a toxicologist, specialist pain and/or addiction medicine consultant is advised in this setting. Provision of opioids to patients taking opioid antagonists (such as naltrexone) can be dangerous and only should occur with appropriate monitoring, ready access to resuscitation equipment and staff.

Analgesia

It is recommended that effective analgesia for patients on oral naltrexone and with naltrexone implants is more likely to be achieved with non-opioid treatment.

For mild pain

- consider oral paracetamol and/or NSAIDs (including parenteral NSAIDs such as ketorolac).

For more severe pain:

- consider addition of oral tramadol or ketamine infusion.

It is also important to recognise that despite prescription of naltrexone, many patients are not abstinent from opioids in the days prior to hospital presentation and that a naltrexone implant, even if in situ, may not provide effective opioid blockade. Moreover, naltrexone is a competitive antagonist whose action may be overcome by a higher dose of opioid medication. Thus, parenteral opioids can provide effective analgesia in this clinical setting, and should be considered for acute severe pain. However, this can be dangerous and should only be considered in a hospital setting where toxicity can be monitored appropriately.

The initial dose should be within the usual range for the condition being treated but higher doses may be considered. It is recommended a lower dose is used initially titrating up slowly.

Implant site complications

Some patients with naltrexone implants may present many weeks after implantation with an infection or abscess at the implant site.

In most instances, infected implants respond to oral or parenteral antibiotic treatment but in other cases, surgical excision may be required.

It is recommended that pain associated with implants be treated with non-opioid analgesia such as non-steroidal anti-inflammatory drugs.

It is not uncommon for patients to present to the Emergency Department requesting removal of an implant. In such a case, consultation with Addiction Medicine specialists is advisable, at least by telephone if not available face-to-face. The patient's right to determine their treatment should be respected, and the implants may be removed under local anaesthesia by an appropriately skilled clinician. The patient should be encouraged to enter another form of treatment according to their desires and local availability of services.

Appendix E - Patient Information on Rapid Opioid Detoxification

What is Rapid Opioid Detoxification?

Rapid Opioid Detoxification (ROD) is a way of withdrawing from heroin, methadone or other opioid drugs in a short period of time using a drug called 'naloxone' (NARCAN) or 'naltrexone'. Naltrexone blocks the effects of opioids and when given to a heroin or opioid dependent person who has opioids in their system causes a severe withdrawal reaction. Withdrawal symptoms can last for many hours or days and can be very dangerous if not managed properly. These symptoms may include:

- vomiting;
- diarrhoea;
- cramping and abdominal pain
- dehydration and kidney failure in severe cases;
- agitation; and
- delirium (a severe state of confusion, being "out of it").

During ROD procedures people are sedated and given other drugs to try to lessen the severity of these symptoms. If you are planning to undertake ROD it is important that you discuss with your doctor what medications will be used to treat these symptoms and what risks (rare and not rare) are associated with this type of treatment.

A lot of people who've undergone ROD relapse back to dependent opioid use following withdrawal unless they are having ongoing treatment like naltrexone or counselling.

Why do people choose it?

Usually people wanting ROD treatment are having a naltrexone implant put in so they don't have to take naltrexone tablets each day to help them stay opioid free after the procedure.

It is important that you know naltrexone is NOT currently registered for use in ROD procedures by the Therapeutic Goods Administration (TGA) which is the Australian Government Department that regulates medicines and medical devices used in Australia.

The evidence for the safety and effectiveness of naltrexone implants is still emerging, but has not yet been proven and for this reason, naltrexone implants are NOT registered for use in Australia. They are currently used under the Special Access Scheme (SAS) Category A which allows for unapproved medical products to be used for a single patient on a case by case basis for as the scheme states

"persons who are seriously ill with a condition from which death is reasonably likely to occur within a matter of months, or from which premature death is reasonably likely to occur in the absence of early treatment"

Naltrexone tablets known by their brand name Revia® HAVE been registered in Australia by the TGA since 1998. However, they are only registered as an 'adjunct' or additional treatment for opioid dependence, meaning naltrexone tablets shouldn't be the only treatment you are having.

If you want to have a naltrexone implant put in or to start on naltrexone tablets, you need to be free from opioids such as heroin for a period of 5 days before hand and 10 days for methadone (less for buprenorphine).

Because it is often difficult to remain abstinent for this period of time, some people choose to undergo ROD because the procedure can be completed within in a day or two in most instances. However, research shows ROD is neither quick nor painless and withdrawal symptoms can last for several days after the procedure. The "Clinical Guidelines and Procedures for the Use of Naltrexone in the Management of Opioid Dependence" written by the Commonwealth (2003) indicate a significant number of patients who do ROD will relapse back to heroin addiction within 6 months. If you do take

heroin or medicines like methadone, morphine, OxyContin or MS Contin and then within 24 hours have naloxone or naltrexone, you will have very severe and unpleasant symptoms of opioid withdrawal. These symptoms are much more severe than any you have previously experienced from stopping heroin suddenly.

It is important to know too that you can get onto naltrexone tablets without undergoing ROD by taking medicines that ease the symptoms of withdrawal. Options include withdrawal treatment with buprenorphine (Subutex) or buprenorphine-naloxone or (Suboxone) or symptomatic medication such as clonidine (Catapres). Withdrawal symptoms usually last about 5 days. After 5-10 days without opioids, you can start taking naltrexone tablets.

You should make sure you talk to your doctor about these other options before deciding to go ahead with the ROD procedure.

Also you should know that some people experience pain i.e tooth pain, back pain after ROD because they have been on opioids which have stopped them from feeling pain from existing conditions. If you are aware of any pain you had before using opioids, discuss it with your doctor so the management of this pain can be incorporated into your treatment plan.

Consent for ROD

It is really important that you understand the procedure you are considering can be dangerous and uses medicines in ways they are not registered for. There is a risk of death associated with this procedure, although it is a small risk, you should know that there have been several deaths in Australia associated with ROD. If you sign the consent form agreeing to treatment you need to make sure you understand what the risks (rare and not rare) are and you should discuss these thoroughly with your doctor before agreeing to treatment.

Your doctor should provide you with written information and should discuss the information provided with you to make sure you understand. Your doctor should also allow time for you to ask questions.

If you agree to this treatment and sign the consent form you are also agreeing to the costs associated with ROD that may include the cost of the procedure and any costs associated with overnight accommodation in the facility, the cost of the implant and replacement implants if required or the costs of naltrexone tablets (taken daily) as well as the costs of ongoing counselling. You have the right to be informed how much this treatment will cost before agreeing to participate.

Sometimes people feel like they should undergo this type of treatment because their family, partner or a community agency thinks it is what they need and it is really important that you give your consent to this treatment because you want to do it and you are committed to being abstinent from opioids.

Your doctor should give you written information about what to expect before, during and after the procedure and this information should be discussed with you to make sure you understand and so you have the chance to ask questions.

Preparation for the Procedure

Once you have decided to go ahead with the procedure it is suggested that you:

1. minimise any drug use in the preceding days (you must not have any opioids in the 48 hours prior to the procedure).
2. minimise any alcohol consumption
3. contact your doctor if you develop any illness such as the flu which may impact on the safety of the proposed procedure.

make any necessary plans for aftercare, and to reschedule work or social commitments.

After ROD

It is best if you can get a friend or family member to be there when you are discharged and someone who can provide support for the first few days after the procedure.

Whilst you may be physically free of opioids after the ROD procedure, it tends to take a while for people to get used to being opioid free psychologically and it is really important that you have support in the form of ongoing counselling to help you adjust to an opioid free life.

Risk of overdose post ROD

There is evidence that shows a big risk for people who have undergone ROD is that of overdose. Once you have completed withdrawal you have low to no tolerance for opioids so if you 'use' there is a high chance that you will overdose. There have been a number of deaths in Australia attributed to a failure to take this into account. For this reason, it is important that you consider ongoing naltrexone treatment and counselling.

More information:

If you want to discuss this information further, you could make an appointment with your GP, or an alcohol and drug treatment service.

Alcohol and Drug Information Service (ADIS)

This is a 24 hour, 7 days a week telephone help line for people in NSW with an alcohol and drug problem or their family and friends. You do not have to provide your name and address or any identifying information.

The numbers are:

(02) 9361 8000 or 1800 422 599 (if you live outside of Sydney)

New South Wales Users and Aids Association (NUAA)

This is a not-for-profit, NSW-based organization (primarily funded by NSW Health) that provides education, practical support, information and advocacy to users of illicit drugs (particularly those who inject drugs), their friends and allies.

You can speak to your peers without having to provide your name and address or any identifying information.

The numbers are:

(02) 8354 7300 or 1800 644 413 (if you live outside of Sydney)

Methadone Advice and Conciliation Service (MACS)

The Methadone Advice and Conciliation Service (MACS) is a telephone helpline that provides opiate pharmacotherapy information (including methadone and buprenorphine), referrals, advice and a forum for pharmacotherapy concerns.

The line is open Monday to Friday from 9.30am to 5.00pm

Ph: 1800 642 428

Appendix F - Consent for Rapid Opioid Detoxification Treatment

It is suggested any consent forms for ROD treatment must as a minimum include the following.

Aims of Treatment

The aim of Rapid Opioid Detoxification (ROD) is to accelerate withdrawal from opioids by the administration of an opioid antagonist (naltrexone or naloxone).

Patient's Responsibilities

Those undertaking ROD must:

- Be aiming to achieve opioid abstinence;
- Be opioid free for a period of 48 hours prior to undertaking ROD;
- Understand the procedure itself and the risks involved during and after the procedure including a significant number of patients undergoing ROD will require hospital treatment after the procedure;
- Accept the costs associated with the procedure and any ongoing treatment costs; and
- Accept they are agreeing to a treatment that may involve the use of naltrexone and other medications in ways that are not registered with the Therapeutic Goods Administration (TGA) Australia including the use of naltrexone implants under the Special Access Scheme (SAS).

Service providers' Responsibilities:

It is the responsibility of service provider to:

- To identify and address any barriers to the patient understanding the information provided including non-English speaking, low literacy or some form of disability;
- Provide the patient with written and verbal information on ROD and alternative treatment options and provide further information as requested;
- Provide a statement and verbal explanation that naloxone and naltrexone are not currently registered by the Therapeutic Goods Administration (TGA) in Australia for use in rapid detoxification and naltrexone implants are currently an unregistered medical device.
- Provide the full details of the costs of treatment, frequency of appointments, availability of support services as part of a comprehensive treatment plan;
- Provide clear and concise information on the manner of physiological and psychological risks associated with ROD and complications post ROD such as overdose risks, complications with implants and impaired opioid analgesia and that whilst the risk of death is low, there have been several deaths associated with ROD in Australia;
- Provide the patient with an outline of the process itself and drugs to be used during the procedure and possible courses of action that will be taken in the eventuality of an adverse event during the procedure;
- Ensure accurate assessment that deems patients as appropriate for ROD including explanation of contradictions to treatment;
- Provide competent care and treat you with dignity and respect;

I understand the rights and responsibilities outlined in this agreement.

Name of patient (printed): _____ Date: _____

Signed: _____

I understand the rights and responsibilities outlined in this agreement.

Name of Facility (printed): _____ Date: _____

Medical practitioner (printed): _____

Signed (medical practitioner): _____

6 Acknowledgements

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Dr Alex Wodak

Anne Lawrance

Anna Keato

7 Acronyms

| | |
|-------|--|
| AChAM | Australasian Chapter of Addiction Medicine |
| CNS | Central Nervous System |
| GI | Gastrointestinal |
| MAC | Medical Advisory Committee |
| NHMRC | National Health and Medical Research Council |
| NSW | New South Wales |
| OTP | Opioid Treatment Program |
| RACP | Royal Australasian College of Physicians |
| ROD | Rapid Opioid Detoxification |
| SAS | Special Access Scheme |
| TGA | Therapeutic Goods Administration |

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