

**Long term pharmacotherapy of alcohol
dependence – approach and clinical
practice guidelines for disulfiram
therapy**

INTRODUCTION

□ Alcohol Dependence Syndrome (ADS) – Basic Facts

▣ Is a chronic disorder

Condition persists for a long period of time



Requires treatment for long duration

▣ Is a relapsing condition

Clients may resume drinking after stopping



Treatment should be provided such that relapse can be prevented

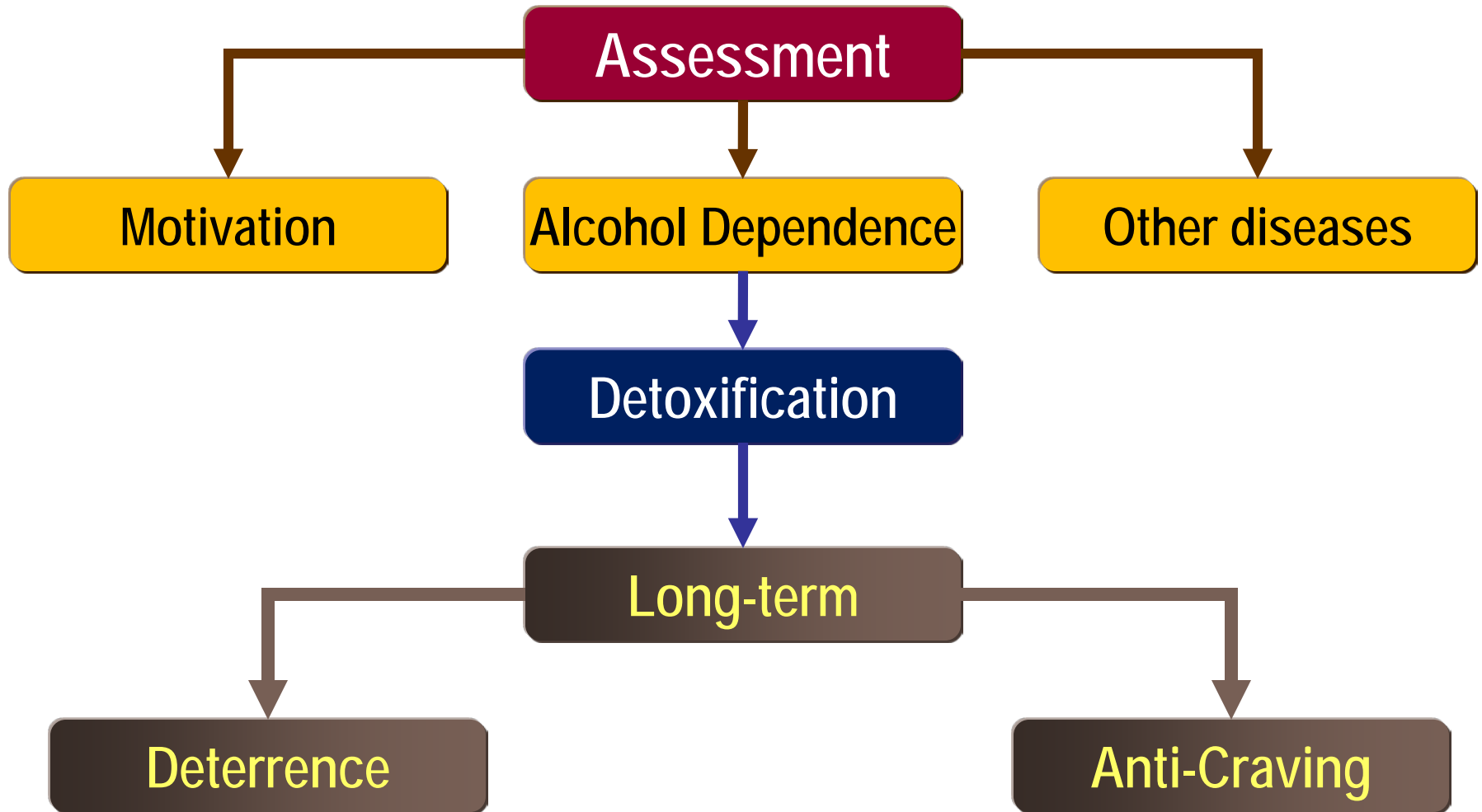
▣ Is a disorder of the brain

Changes at brain level occur due to long term use of alcohol

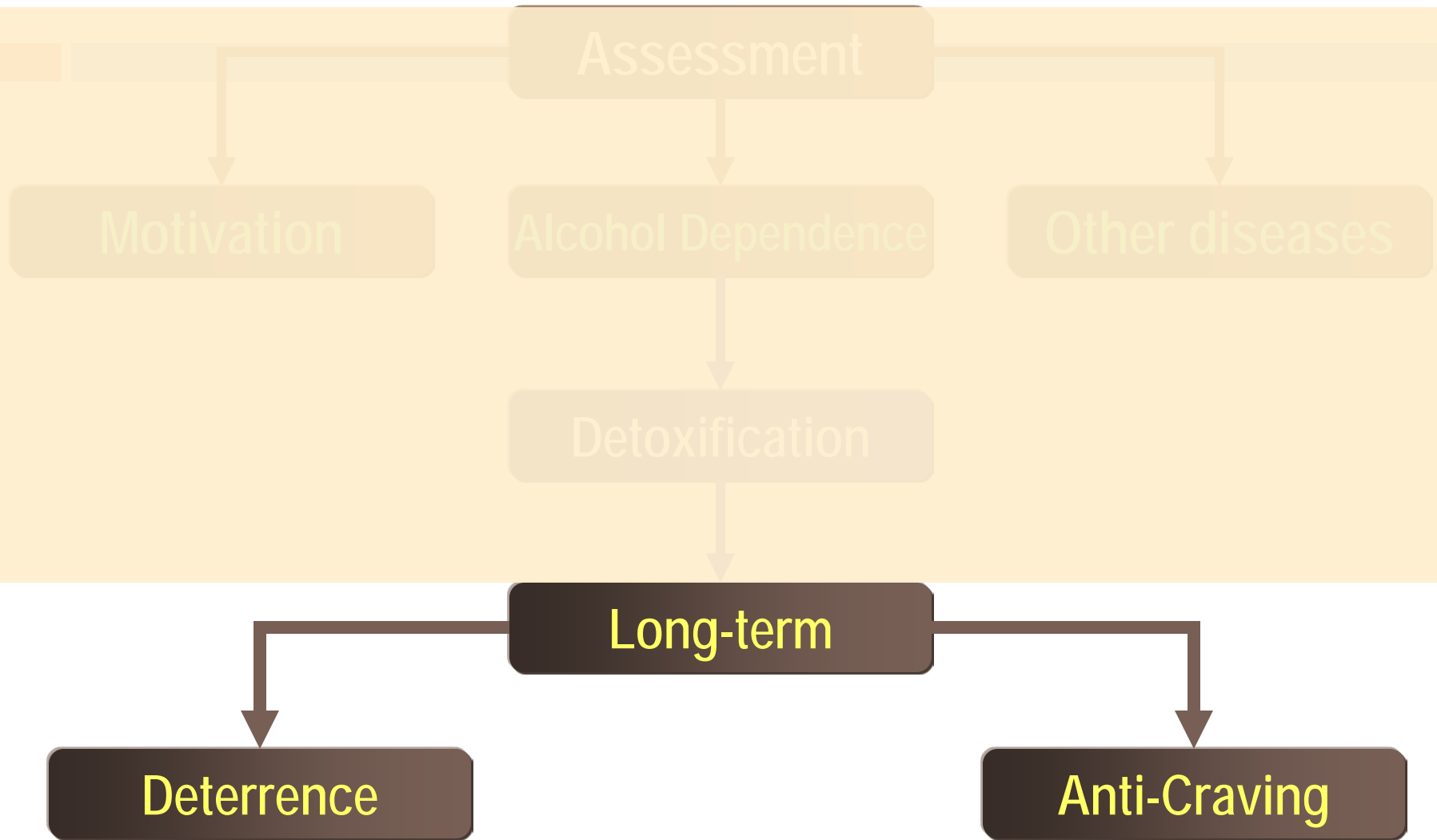


Medical model of treatment is required to treat ADS

Treatment of Alcoholism



Treatment of Alcoholism



Deterrence

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de·ter·rence (dĭ-tŭr'əns, -tŭr'-)

n.

- “The prevention from action by fear of the consequences”
- In other words alcohol, when taken with the medication, produces some undesirable consequences.

Deterrents

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- Disulfiram
- Calcium Carbimide
- Metronidazole,
- Nitrofezole

Case vignette...

- Mr. P is a 40 year married male belong to middle socioeconomic status. He lives in small town in Uttar Pradesh. He contacted the de-addiction centre along with wife to get rid of his problem of excessive drinking.
- Mr. P had started drinking about 20 year back but he was started using alcohol in dependent pattern with significant socio-occupational dysfunction from last 10 year.
- There was no history of any chronic medical illness including history suggestive of liver disease like hemetemesis, melana, jaundice.
- On physical examination, he had tremors on outstretched hands, tachycardia (100/min) and hypertension (150/90 mm Hg). Rest of the examination was normal.

Case vignette...

- On mental status examination, Mr. P was slightly restless and appeared anxious. His motivation to give up alcohol appeared fair as he had insight in most of his present problems were because of drinking.
- Mr. P was admitted in ward and baseline Hemogram, LFT & RFT were sent. Investigation were found with in normal range. He was detoxified with benzodiazepine. His detoxification completed and was free from alcohol from last 24 hour & LFT with in normal range. So plan to start disulfiram was made. So pre disulfiram counselling was conducted and explained regarding rationale of giving disulfiram, DER, side effects of disulfiram and precautions to be taken while taking disulfiram.

Case vignette...

- Informed consent taken in front of witness. Disulfiram was started as single tablet containing 250 mg, once a day. His wife was given responsibility of supervision of medication after discharge.
- At the time of discharge, pt was given disulfiram identification card which contain information that he was taking disulfiram, and also contains in brief, the beverages to be avoided with alcohol, the signs and symptoms of disulfiram alcohol reaction, and its treatment.
- Patient was advised to be follow up in the outpatient clinic once in every 15 days for 2 to 3 visits initially; later the frequency may be restricted to once in a month or two.

Disulfiram

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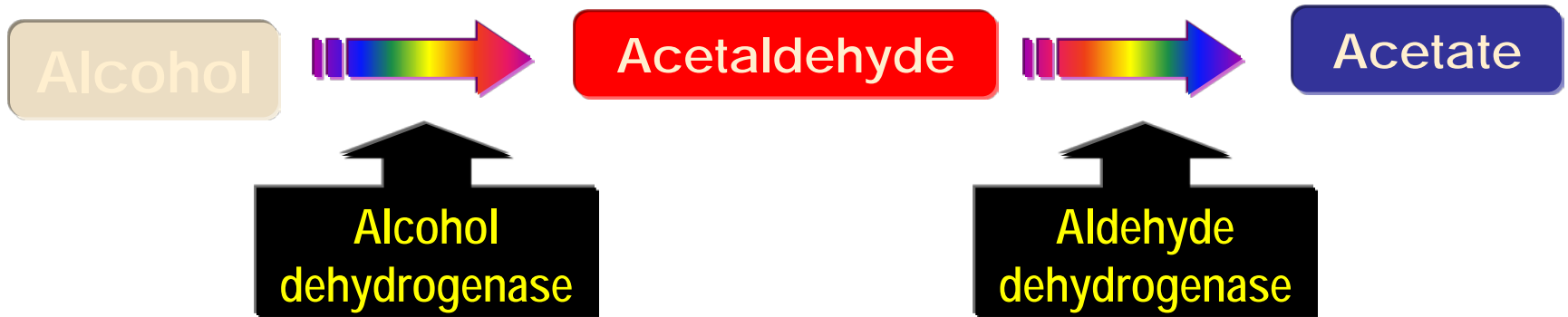
- ❑ One of the oldest and time-tested treatments for alcoholism
- ❑ Sometimes incorrectly referred to as an “aversive agent.”
- ❑ Dose: 250 mg/day (oral) in majority of cases; 500 mg/day in some cases
- ❑ Interferes with Alcohol Metabolism

Rationale for disulfiram use

- Disulfiram is used as an aid in the management of alcohol dependent individuals who want to remain in a state of sobriety, but are unable to maintain an abstinent state
- It acts as a deterrent and helps in delaying the decision to drink if motivation reduces temporarily

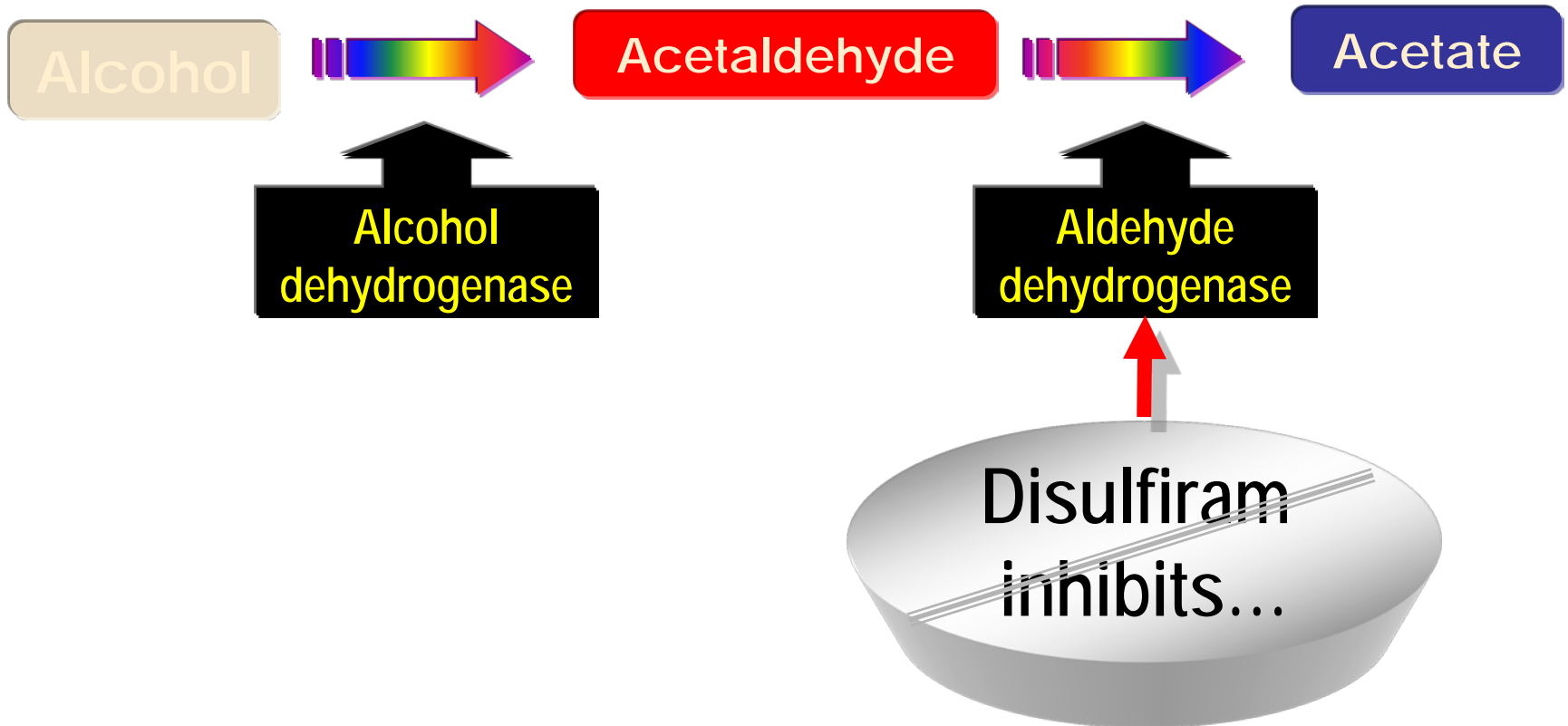
Alcohol Metabolism

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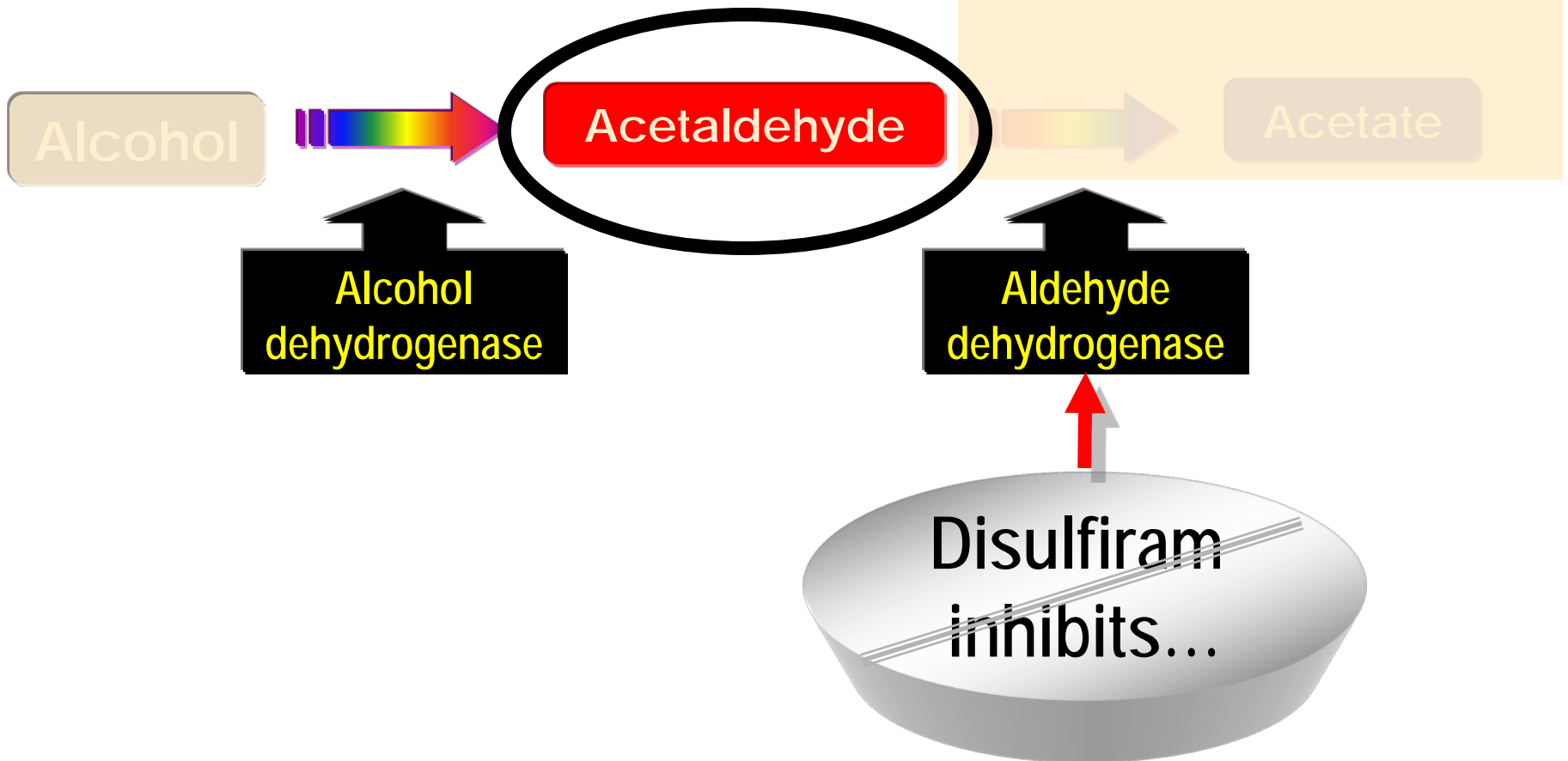
Alcohol Metabolism

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Alcohol Metabolism

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The Disulfiram-Ethanol Reaction (DER)

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- ❑ Flushing, throbbing headache, vertigo, blurred vision,
- ❑ Chest pain, palpitation, tachycardia, hypotension, syncope,
- ❑ Dyspnea, hyperventilation,
- ❑ Nausea, vomiting,
- ❑ Sweating, thirst,
- ❑ marked uneasiness, weakness, and confusion.
- ❑ Severe reactions: may be respiratory depression, cardiovascular collapse, arrhythmias, myocardial infarction, acute congestive heart failure, unconsciousness, convulsions, and death.

The Disulfiram-Ethanol Reaction (DER)

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- The intensity of the reaction varies
- Generally proportional to the amounts of disulfiram and alcohol ingested
- BAC:-
 - ▣ Mild reactions: 5 to 10 mg/100 mL
 - ▣ Symptoms fully developed: 50 mg/100 mL
 - ▣ Unconsciousness: 125 to 150 mg/100 mL
- The duration of the reaction: 30 to 60 minutes, to several hours in the more severe cases, or as long as there is alcohol in the blood.
- May occur up to 2 weeks after last dose of disulfiram

Disulfiram side effects

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- Mild: headache, drowsiness, restlessness, skin rash, acne, garlic-like aftertaste.
- Significant:
 - ▣ Peripheral Neuropathy
 - ▣ Reversible Liver dysfunction
 - ▣ Psychosis

Disulfiram WARNINGS

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- The patient must be fully informed of the disulfiram-alcohol reaction.
- He must be strongly cautioned against
 - ▣ Surreptitious drinking while taking the drug
 - ▣ Taking alcohol in disguised forms, i.e.
 - Sauces
 - Vinegars
 - Cough mixtures
 - Aftershave lotions
- He should also be warned that reactions may occur with alcohol up to 14 days after ingesting disulfiram.

Disulfiram Contraindications (relative)

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- Patients who are receiving or have recently received alcohol, or alcohol-containing preparations,
- Presence of psychoses, dementia and hypersensitivity to disulfiram, advanced liver disease, severe myocardial disease or coronary occlusion
- Inability to understand implications of therapy
- Pregnancy (1st trimester) is only absolute contraindication

Disulfiram – practical issues

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- ❑ Preferably start in in-patient setting
- ❑ Ensure full patient motivation for COMPLETE ABSTINENCE
- ❑ Involve family / colleague / supervisor
- ❑ Educate patient and others
- ❑ Obtain informed consent
- ❑ Give patient a “Disulfiram-card” to carry
- ❑ ? DER in ward

Disulfiram – practical issues

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- Supervised administration is preferred
- Follow-up: initial – every 2 weeks, later every month, then every 2 months...
- Monitor:
 - ▣ Motivation and abstinence
 - ▣ Supervision and compliance
 - ▣ Side-effects (clinical and laboratory-LFT)

Sample Disulfiram consent form

By accepting disulfiram therapy, I acknowledge the need for assistance in solving a drinking problem. I also understand that, with my full cooperation in this therapy, I am most likely to achieve successful recovery. It has been explained to me and I understand the effects which disulfiram can trigger if I should consume even a small amount of alcohol in any form. These symptoms include flushing, nausea, vomiting, thirst, low blood pressure, and possible convulsions. I understand that this reaction may occur up to 2 weeks after I discontinue disulfiram. It has also been explained to me that the safe use of this drug in pregnancy has not been established. I understand that sexually active women taking disulfiram should be practicing a medically effective, reliable method of birth control. I understand that if I were to become pregnant, it is recommended that I terminate disulfiram therapy.

Patient

Physician

Witness:

Date:

Management of DER

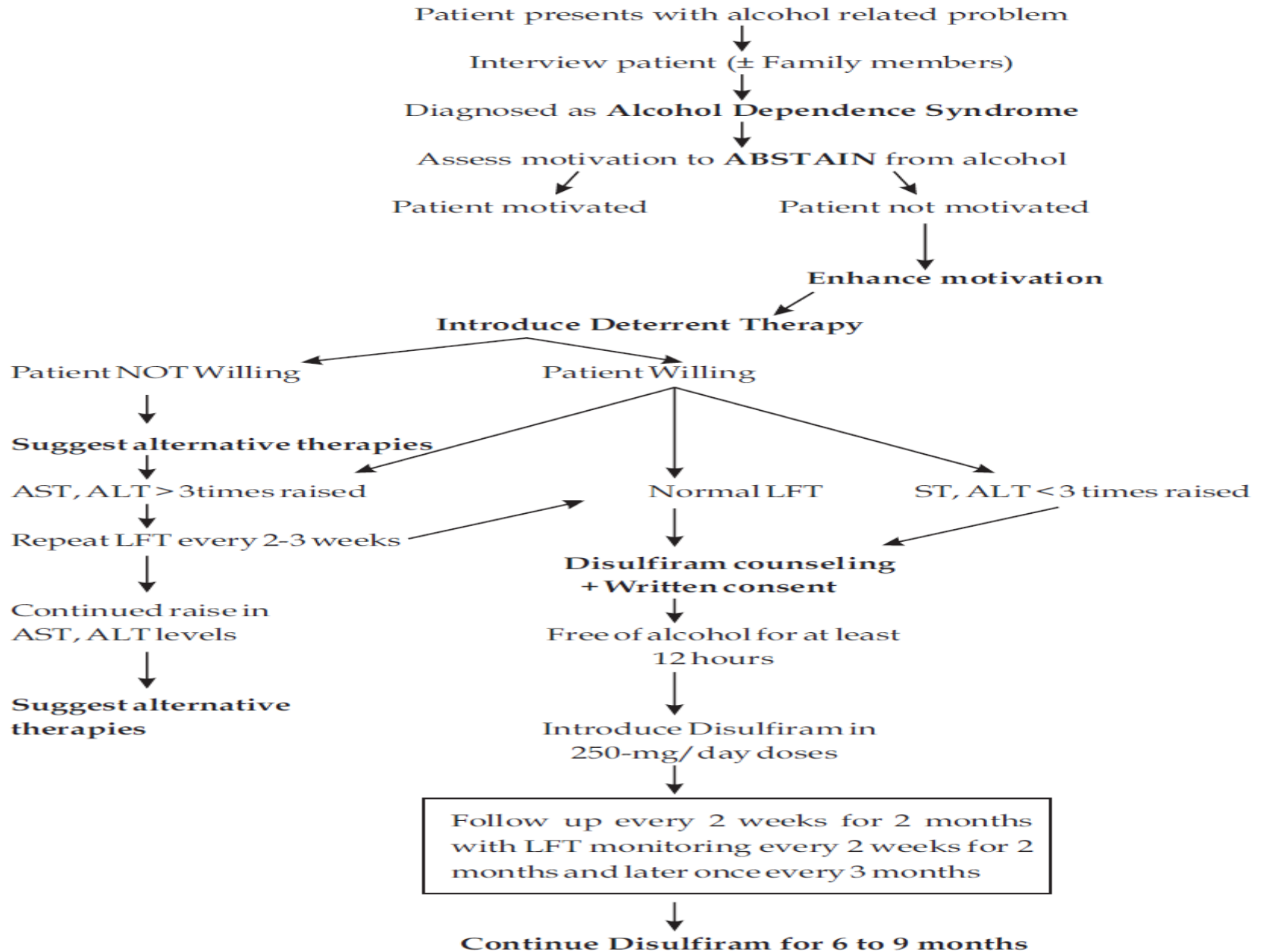
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- DER warrants in patient treatment
- Priority: Control of fall in blood pressure
- Mild DER: Assurance, observation and oral fluids
- Moderate or severe DER: intravenous fluids and dopamine infusion

Duration of disulfiram therapy

- Usually disulfiram therapy should be continued for a period of 6 to 9 months
 - ▣ Patient feels confident to abstain from alcohol without the need for treatment for the same,
 - ▣ Risk for relapse has been reduced and patient is rehabilitated.
- However, in some patients, the therapy would have to continue for a longer period of time

Algorithm for Disulfiram Therapy



Frequently Asked Questions

- 1. Can Disulfiram be given surreptitiously to patient?**
- 2. Do deaths occur with Disulfiram?**
- 3. Do I need to stop Disulfiram during fever, diarrhea, etc?**
- 4. I am having weakness after starting Disulfiram. Should I stop it?**

Frequently Asked Questions

- 5. I was addicted to whiskey before starting Disulfiram. Is it safe now to consume beer on Disulfiram?**
- 6. Can Disulfiram be administered to a person who is intoxicated with alcohol?**



Thank You