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COMMITTED TO HEALING,
DEVOTED TO CARING

Alcohol Dependence: An update on management

Dr Anil JHUGROO, MRCPsych, CCST in Substance Misuse (London), Consultant Psychiatrist, Apollo Bramwell Hospital

ALCOHOL DEPENDENCE

- **Clinical features**
  - Edwards & Gross criteria
  - ICD 10/ DSM IV
- **Psychiatric complications**
  - Withdrawal state
    - Delirium Tremens
    - Fits
  - Depression
  - Wernicke-Korsakoff's syndrome
  - Othello syndrome
- **Treatment**
  - Psychological
  - Pharmacological
    - » Disulfiram
    - » Acamprosate
    - » Naltrexone

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ALCOHOL DEPENDENCE

- *Increased tolerance*
- *Withdrawal symptoms*
  - *Delirium Tremens*
  - *Fits*
- *Relief drinking*
- *Rapid reinstatement*
  - *Chronic relapsing brain disease*
- *Narrowing of drinking repertoire*
- *Compulsion to drink*
- *Primacy of drinking*

(3 out of above 7 features to diagnose ADS in ICD 10 or DSM IV)

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EPIDEMIOLOGY

- **58% of males** & **28% of females** consume alcohol in Mauritius. (NCD, 2004**)**
- About **3 %** is said to have **alcohol dependence syndrome**
- Mauritians consume > 3,600,000 litres of alcohol/year
  - starting at a younger age.

    (Socrata on National Alcohol Consumption around the world and published 2010)
- Alcohol-related disorders account for > **40%** of **admissions to BSH.**

  (Source**;** Government Information Service, PMO, Mauritius; 2006 figures)

- Alcohol is implicated in
  - 80% of fatal car accidents
  - 75% of homicides
  - 40% of casualty trauma

    (UK figures; Buckley, 1995)

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ALCOHOL CONSUMPTION

The Survey results indicate that 58% of males and 28% of females consume alcohol with 15.0% of male drinkers taking alcohol everyday (Table 20).

Table 20 - Distribution of alcohol consumption by frequency and sex among drinkers.

	Male (%)	Female (%)
Daily	15.0	4.1
4-6 times per week	4.3	1.2
2-3 times per week	18.2	4.4
Once a week or less	19.4	8.9
Occasionally	43.1	81.4
TOTAL	**100.0**	**100.0**

The findings also show that 22.5% of males aged 20-74 years were drinking alcohol more than once a week in 2004. The corresponding figure among females was 5.6%.

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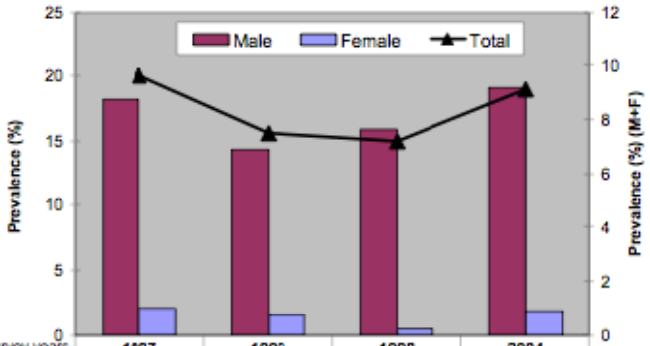
ADMISSION TO BSH, 2008

CAUSE (I.C.D. 10)	MALE		FEMALE		TOTAL	
	No.	%	No.	%	No.	%
Dementia	23	0.7	23	1.8	46	1.0
Epileptic Psychosis NOS	51	1.6	28	2.2	79	1.8
Unspecified mental disorders due to brain damage and dysfunction and to physical disease	2	0.1	2	0.2	4	0.1
Mental and behavioural disorders due to use of alcohol	1,771	57.0	190	14.9	1,961	44.8
Mental and behavioural disorders due to use of opioids/cannabinoids	10	0.3	1	0.1	11	0.3
Mental and behavioural disorders due to multiple drug use and use of other psychoactive substances	39	1.3	1	0.1	40	0.9
Schizophrenia	781	25.1	629	49.4	1,410	32.2
Delusional disorder	1	0.0	1	0.1	2	0.0
Acute psychotic episode	136	4.4	106	8.3	242	5.5
Schizoaffective psychosis NOS	18	0.6	16	1.3	34	0.8
Psychosis unspecified	3	0.1	5	0.4	8	0.2
Hypomania	8	0.3	5	0.4	13	0.3
Bipolar affective disorder	28	0.9	32	2.5	60	1.4
Depressive episode	97	3.1	150	11.8	247	5.6
Persistent mood disorders	1	0.0	4	0.3	5	0.1
Anxiety disorders	2	0.1	2	0.2	4	0.1
Obsessive compulsive disorder	-	0.0	-	0.0	0	0.0
Dissociative (conversion) disorders	1	0.0	6	0.5	7	0.2
Puerperal psychosis NOS	-	0.0	5	0.4	5	0.1
Mental retardation	51	1.6	27	2.1	78	1.8
Conduct disorders	23	0.7	12	0.9	35	0.8
Parkinsonism	2	0.1	1	0.1	3	0.1
Alzheimer	-	0.0	1	0.1	1	0.0
Degenerative disease of nervous system, unspecified	2	0.1	-	0.0	2	0.0
Grand mal seizures, unspecified (with or without petit mal)	16	0.5	14	1.1	30	0.7
Epilepsy, unspecified	26	0.8	7	0.5	33	0.8
Sleep disorders	-	0.0	1	0.1	1	0.0
Other causes	16	0.5	5	0.4	21	0.5
TOTAL	**3,108**	**100.0**	**1,274**	**100.0**	**4,382**	**100.0**

Table 22 - Prevalence of abusive alcohol consumption 1987 - 2004



survey years	1987	1992	1998	2004
Male	13.2	14.4	15.9	19.1
Female	2.1	1.6	0.5	1.9
Total	8.6	7.5	7.2	9.1

NB: *comparability of 2004 figures with previous surveys may be slightly affected because of definition*

Table 7.1. Age-specific prevalence (%) of alcohol consumption according to gender: the Mauritius NCD survey 2009

	19-24	25-34	35-44	45-54	55-64	65+	Total*
Men							
Never	27.6	29.0	23.2	26.3	32.2	31.4	28.2
Ex drinker	2.3	3.7	3.7	7.3	6.5	12.6	5.9
Once per week or less	64.9	52.7	53.9	42.4	38.5	36.1	46.8
2-3 days per week	5.2	11.8	12.6	14.0	12.7	10.2	12.2
≥4 days per week	0.0	2.9	6.6	8.0	10.1	9.8	6.9
Women							
Never	63.8	57.5	60.4	66.8	70.3	66.8	64.2
Ex drinker	2.2	2.0	2.1	1.8	1.7	3.3	2.1
Once per week or less	32.3	38.9	35.8	29.2	27.3	27.5	32.1
2-3 days per week	1.7	1.5	1.6	1.9	0.5	0.8	1.4
≥4 days per week	0.0	0.2	0.1	0.3	0.2	1.7	0.3
All persons							
Never	48.3	44.8	43.2	48.0	52.9	52.2	47.7
Ex drinker	2.2	2.7	2.8	4.5	3.9	7.1	3.8
Once per week or less	46.3	45.0	44.2	35.7	32.4	31.0	38.9
2-3 days per week	3.2	6.1	6.7	7.8	6.1	4.7	6.3
≥4 days per week	0.0	1.4	3.1	4.1	4.7	5.0	3.3

Notes: *These estimates are not standardised.

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In 2004, the distribution of alcohol consumption by ethnic group among males are as shown in Table 21.

Table 21 – Alcohol consumption by ethnic group in men (2004)

	Non drinkers %	Casual/Moderate drinkers %	Heavy drinkers %
Hindu	24.7	52.4	22.9
Muslim	94.5	3.5	1.9
Creole	19.7	46.0	34.3
Chinese	37.1	49.5	13.5
Total	**42.0**	**38.9**	**19.1**

Heavy drinkers are those who drink on 2 or more days a week and have at least 3 drinks per day. It also includes those who drink once a week or less but have more than 5 drinks on these days.

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ETIOLOGY

- Ethnic factors
  - Higher in African and Asian
  - Lower in Chinese
  - Different isoenzymes of acetaldehyde dehydrogenase
- Ethanol ➔ Acetaldehyde ➔ Acetate

  oxidation detoxification

  Alcohol dehydrogenase *Aldehyde dehydrogenase*
- Genetic polymorphisms
  - Carcinogen potential of acetaldehyde.
  - May explain higher incidence of cancer e.g buccal, oesophagal in susceptible patients
  - Genetic testing
    - » to identify at-risk population
    - » help clinicians diagnose esophageal cancer earlier
- Twin studies: MZ:DZ = 70%:43% (Prickens et al, 1991)

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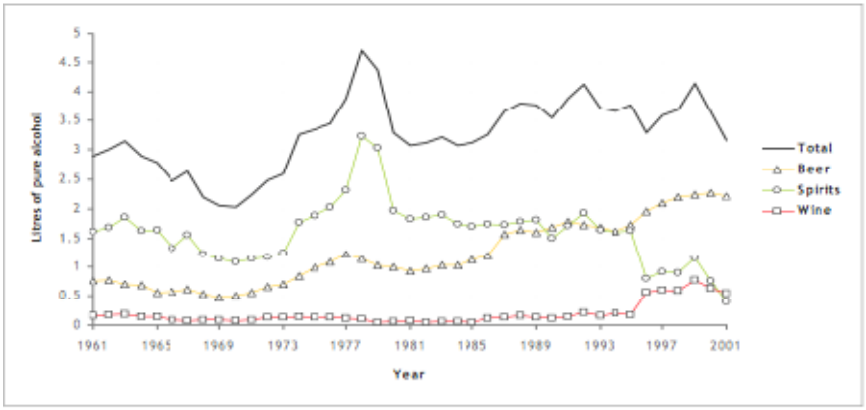
MAURITIUS

Recorded adult per capita consumption (age 15+)



Sources: FAO (Food and Agriculture Organization of the United Nations), World Drink Trends 2003

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ALCOHOL WITHDRAWAL STATE

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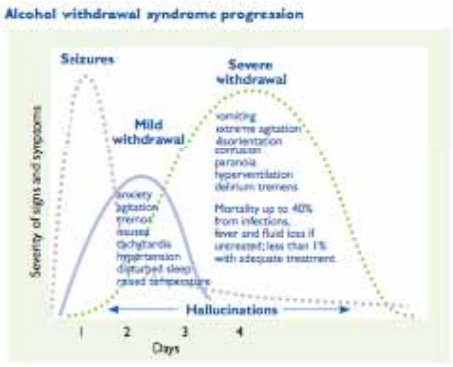
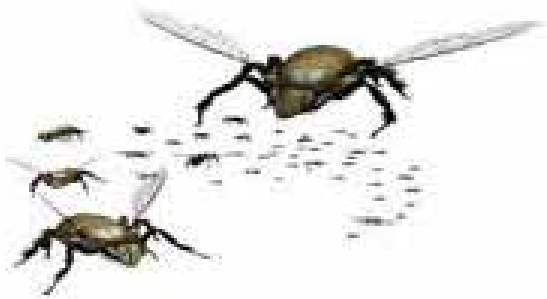
ALCOHOL WITHDRAWAL STATE



VISUAL HALLUCINATIONS WITHDRAWAL STATE



For some time before the onset of a serious skin rash, I had an experience of seeing very strange ceatures appearing in my dreams....

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VISUAL HALLUCINATIONS WITHDRAWAL STATE

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VISUAL HALLUCINATIONS WITHDRAWAL STATE

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DELIRIUM TREMENS

- Alcohol withdrawal delirium or DT
  - an acute organic brain syndrome
    - confusion/disorientation
    - agitation/tremors/visual hallucinations
  - Typically starts 2 to 3 days after stopping drinking
  - Usually lasts for a further 2 to 3 days
- Incidence
  - in untreated patients averages 5%,
  - much lower with treatment of alcohol withdrawal
- Mortality rates
  - Early studies as high as 15%
  - With advances in management: < 1%

BENZODIAZEPINES

- Enhances GABA activity
- **Long-acting benzodiazepines** recommended
  - **Chlordiazepoxide (Librium)**
  - **Diazepam (Valium)**
    - well absorbed orally
    - rapid onset of action (within one hour)
    - long-acting: important in preventing symptom recurrence between doses.
    - important in seizure prophylaxis
- **Short-acting benzodiazepines**
  - **Lorazepam (Ativan)**
    - concern about prolonged sedation
    - in the elderly, recent head injury, liver failure or respiratory failure
    - rapid onset after oral administration (within 2 hours)
    - short to medium duration of action (half life of 10-20 hrs)
    - Has a simpler hepatic metabolism

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Benzodiazepines detox regimes

NB: This is only a guide. The best method is prn dosing combined with tapering the dose as response varies from patient to patient.

	Chlordiazepoxide (Librium)	Diazepam (Valium)	Lorazepam (Ativan)
Day 1	15mg qds	10mg qds	1 mg qds
Day 2	10mg qds	10mg tds	1 mg tds
Day 3	10 mg tds	10mg bd	1 mg bd
Day 4	10mg bd	5 mg tds	0.5 mg tds
Day 5	5mg bd	5 mg bd	0.5 mg bd
Day 6	5mg od	5 mg od	0.5 mg od
Day 7	Discharge	Discharge	Discharge

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ALCOHOL WITHDRAWAL SEIZURES

- **Generalised tonic-clonic seizures**
  - Occurs within 6-48 hrs after last drink
  - Occurs in 2-9% of alcohol dependent people
- **Carbamazepine** (600-1200 mg/day)
  - effectively minimises alcohol withdrawal symptoms and prevents alcohol withdrawal seizures.
  - as an alternative to benzodiazepines.
- **Phenytoin** and **valproate**
  - are **not effective** in preventing alcohol withdrawal seizures and are not recommended.
- **Newer anticonvulsant** agents (such as gabapentin)
  - are **not recommended** due to limited clinical evidence.
- Adding anticonvulsants to benzodiazepines to manage alcohol withdrawal?
  - no benefit

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PSYCHIATRIC COMPLICATIONS

- **Depression**
  - Anxiety
- **Psychosis**
  - Othello syndrome
- **Memory**
  - Alcohol dementia
  - Wernicke's-Korsakoff's syndrome

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ALCOHOL & DEPRESSION

- Powerful depressant of CNS
- In up to 80% of cases, depression resolves 4 weeks after stopping alcohol.

  Nakamura et al, 1994
- The frequency of alcohol intake was significantly related to the onset of depression.
- We also found a significant relation between **younger age** and **depression onset**.
- Body mass index and physical illness, including diabetes mellitus, had no significant association with depression onset.

  Ogasawara et al, 2010

ALCOHOL-INDUCED PSYCHOSIS

- Withdrawal state
- Alcoholic hallucinosis
- Alcoholic paranoia
  - Delusions of jealousy
  - Delusions of infidelity
  - Morbid jealousy
  - Othello syndrome
  - Domestic violence
  - Looks for evidence
    - Check whereabouts
    - Check mobile phone
    - Check clothes
  - Tragic consequences

ALCOHOL DEMENTIA

Magnetic Resonance Imaging of the Brain

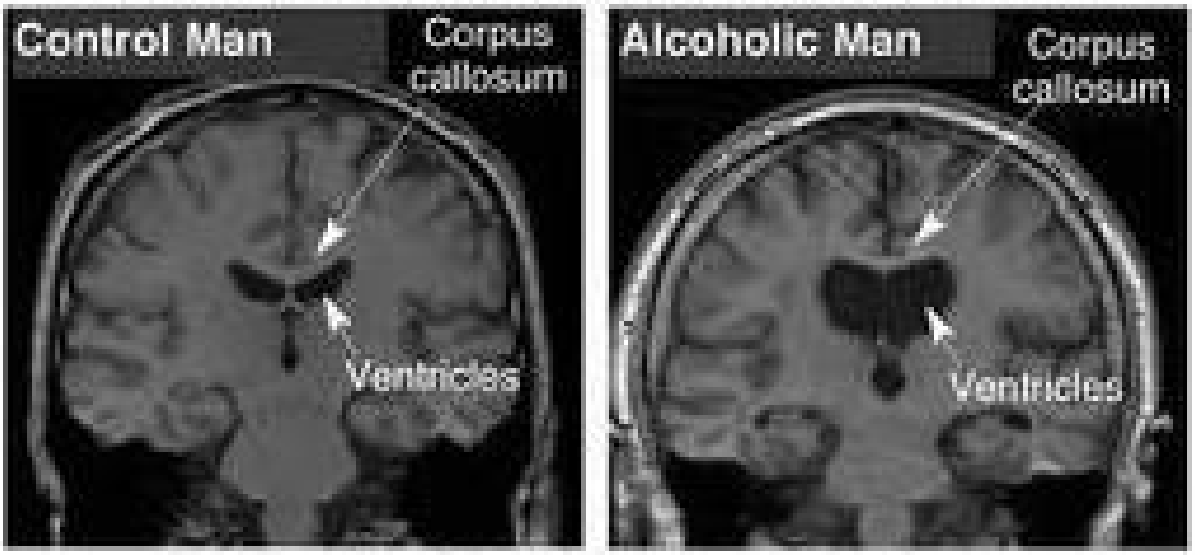

Image courtesy of the National Institute on Drug Abuse

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WERNICKE- KORSAKOFF'S SYNDROME

- **Wernicke's encephalopathy (acute)**
  - Caused by Thiamine deficiency in alcoholics
  - Sudden onset of Triad
    - **Confusion**
    - Cerebellar **ataxia** (atrophy of the cerebellar cortex, pons & mamillary bodies)
    - Abnormal eye movements with **ophthalmoplegia** (paralysis of ocular muscles)
    - Nystagmus and peripheral neuropathy
  - Pathology
    - petechial haemorrhages from small vessels in mamillary bodies; assoc necrosis, atrophy and gliosis.
  - Vitamin treatment (high risk group: malnutrition, heavy intake, severe withdrawal, PN)
    - 2 pairs pabrinex ampoules (= 500 mg thiamine) tds by iv infusion for 3 days
    - followed by 1 pair pabrinex ampoule (= 250 mg thiamine) daily for 3-5 days
  - Vitamin prophylaxis (low risk group: well nourished, low intake, mild withdrawal)
    - Oral thiamine 100 mg tds + Vit B complex strong 2 tabs tds
  - iv glucose➔ rapid absorption of thiamine in tissues and precipitate Wernicke's enc.
- **Korsakoff's syndrome (chronic)**
  - Amnesia: anterograde (severe) & retrograde
  - Confabulation (telescoping of memory)
  - Cognitive deficits

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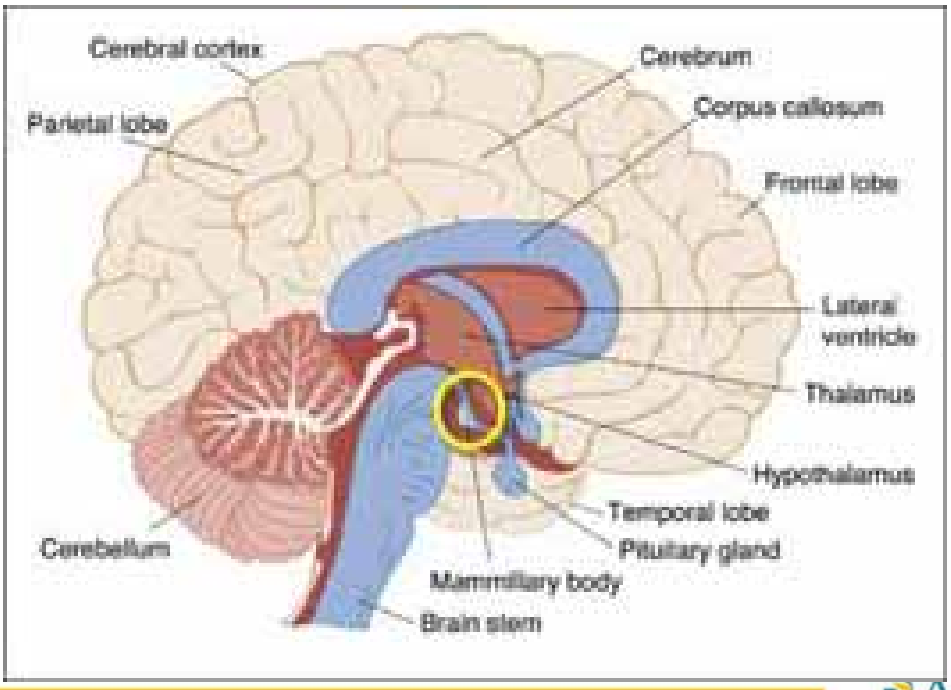

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MAMMILLARY BODY HAEMORRHAGES

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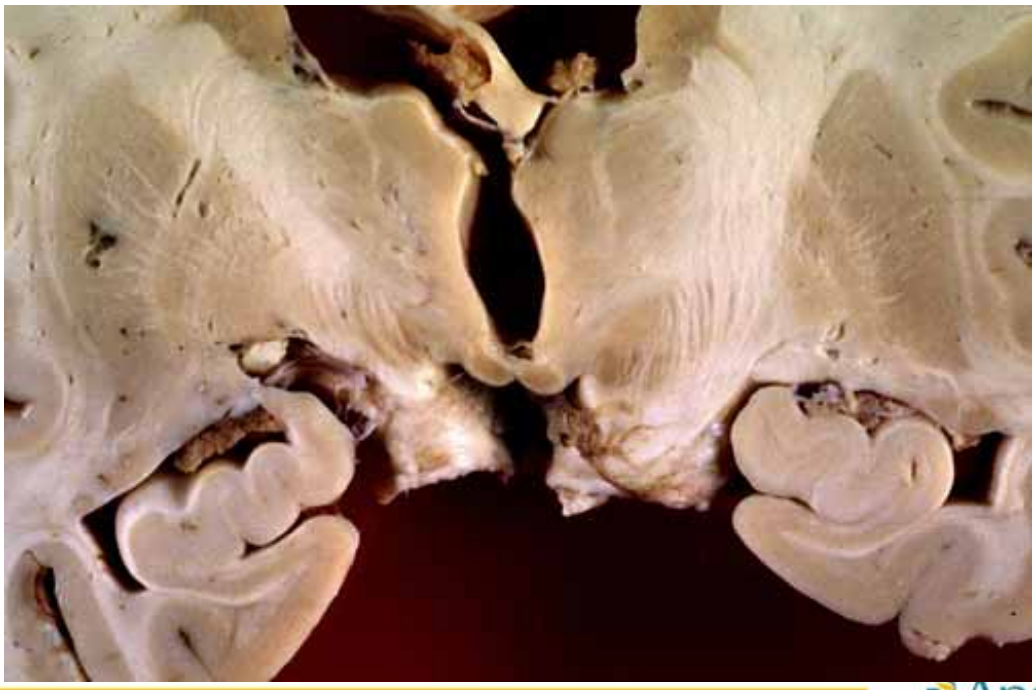
MAMMILLARY BODY ATROPHY



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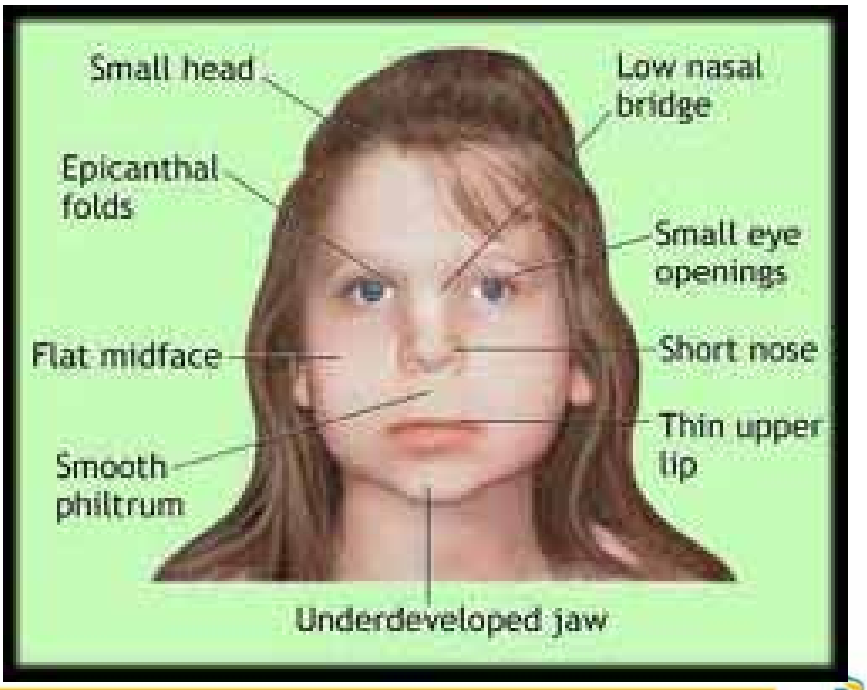
FETAL ALCOHOL SYNDROME



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PSYCHOLOGICAL THERAPIES

- **Before detox**
  - Psychoeducation
  - Visualisation techniques
  - Motivation enhancement therapy
- **After detox**
  - Cognitive Behaviour therapy
    - » Cue exposure
    - » Managing cravings
  - Group therapy
    - » Alcoholic Anonymous

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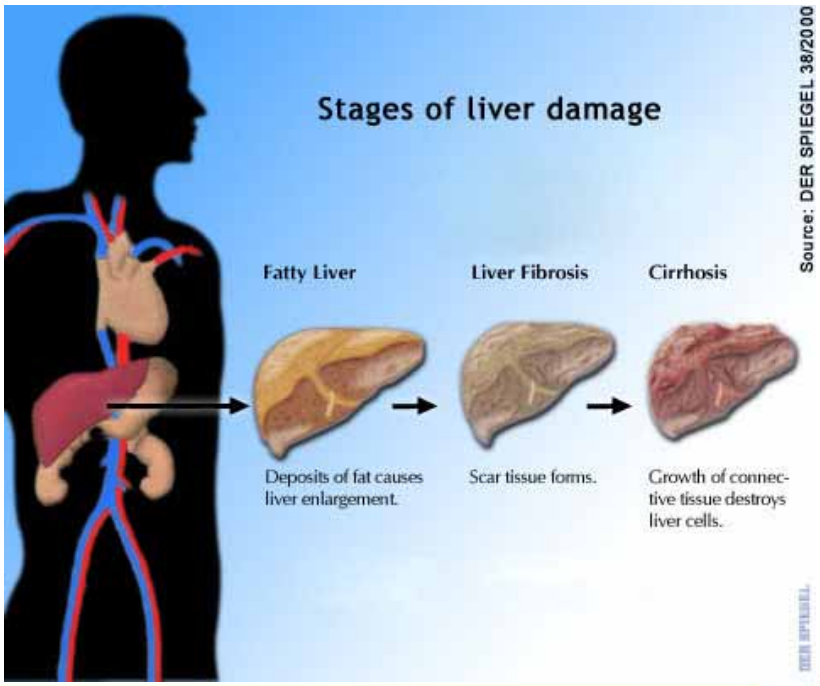
PSYCHOEDUCATION



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VISUALISATION TECHNIQUES

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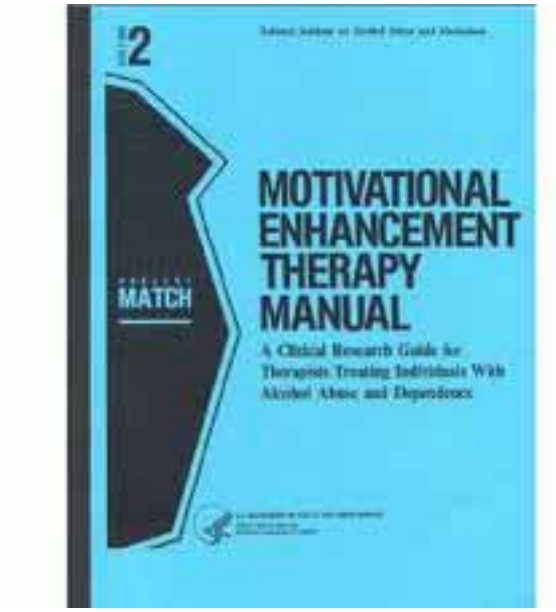
MOTIVATIONAL INTERVIEWING



- It is a style of counselling that focuses on helping the patient explore and resolve ambivalence about change
- Turn denial into acceptance
- The patient's own reasons for change are elicited and used to motivate movement towards action and behaviour change.
- It is directive in that it guides the person towards resolution of ambivalence and towards change.

MANAGING CRAVINGS

- **Cravings**
  - urges to drink alcohol.
  - normal part of any addiction and withdrawal.
  - vary in intensity with time, and are only severe for short periods (e.g, < 1 hr).
  - often triggered by opportunities to drink, physical or psychological discomfort.

- The **3-D method** has been successful for many people:
  - **Delay** the decision as to whether you will drink for one hour. You may or may not drink, but that is something to be decided later (when the severity of the craving has reduced).
  - **Distract** yourself with an activity during this hour that will take your mind off whether you will drink or not.
  - **Desist**: After the hour, say to yourself: 'Why I don't want to drink' and 'What have I got to lose? By this stage the craving should have settled down – although probably not gone away.

CUE EXPOSURE

- Derives from learning theory.
- It assumes that people, places or events that regularly precede drinking become associated with the pleasant effects of alcohol,
- Therefore alcohol consumption becomes a conditioned response to these cues.
- The goal of cue exposure is to decrease the likelihood of a relapse to drinking by
  - either decreasing the strength of the association between alcohol related cues and the urge to drink
  - or increasing the use and effectiveness of coping skills when confronted with alcohol related cues in daily life.

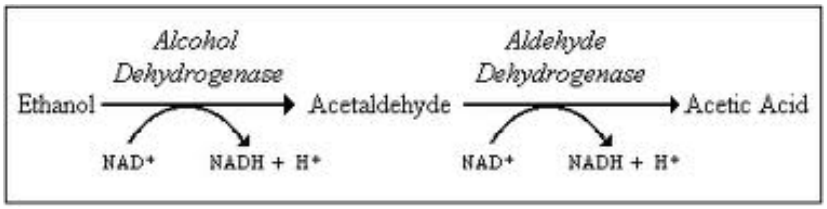
GROUP THERAPY

- **Instillation of Hope** - faith that the treatment mode can and will be effective.
- **Universality** - demonstration that we are not alone in our misery or our "problems".
- **Imparting of information** – learning about the disease process itself.
- **Altruism** - opportunity to help somebody else; the feeling of usefulness.
- **Corrective recapitulation of primary family group** - experiencing transference relationships growing out of primary family experiences providing the opportunity to relearn and clarify distortions.
- **Development of socializing techniques** - social learning or development of interpersonal skills.
- **Imitative behavior** - taking on the manner of group members who function more adequately.
- **Catharsis** - opportunity for expression of strong affect.
- **Existential factors** - recognition of the basic features of existence through sharing with others (e.g. ultimate aloneness, ultimate death, ultimate responsibility for our own actions).
- **Direct Advice** - receiving and giving suggestions for strategies for handling problems.
- **Interpersonal learning** - receiving feedback from others and experimenting with new ways of relating.

PHARMACOLOGICAL TREATMENT

- Disulfiram
- Acamprosate
- Naltrexone

DISULFIRAM



- Disulfiram inhibits aldehyde dehydrogenase
  - ↑Acetaldehyde → Histamine release
  - Vasodilatation, Hypotension, Flushing, Palpitations,..
  - Nausea & vomiting
  - Headache
- Dose: loading dose 800 mg; then 100-200 mg/day; may req higher doses if limited alc-disulf reaction
  - People have died from high doses
- Contraindications
  - Psychosis
    - blocks *dopamine β hydroxylase* causing ↑ DA (↓NA) levels in brain
    - DA → NA
  - Epilepsy
    - Disulfiram → CS_2 which interacts with pyridoxal-5-PO_4
    - Glutamate → GABA↓ (enz: GAD; coenz: Pyridoxine)
      GAD
    - Lower seizure threshold
  - Severe liver or cardiac disease (CS_2 is cardiotoxic and hepatotoxic)

GLUTAMATE V/S GABA

- Brain physiology rests upon 2 systems
  - Excitatory v/s Inhibitory
  - Glutamate v/s GABA
- Alcohol
  - enhances GABA receptors activity.
  - inhibits Glutamate (NMDA) receptors activity.
- Chronic alcohol consumption
  - leads to the overproduction (upregulation) of Glutamate (NMDA) receptors .
- Suddenly stopping alcohol (alcohol withdrawal)
  - causes these excessive numbers of glutamate receptors to be more active than normal
  - induces a surge in release of glutamate
  - results in symptoms of delirium tremens
  - can cause excitotoxic neuronal death
    - ↑ Ca influx to cell → hyperexcitability and cell death.
- **Acamprosate** (calcium acetylhomotaurinate)
  - reduces this glutamate surge
  - glutamate receptor blocker (partial agonist/antagonist)
    - Blocks calcium influx to cells
    - Neuroprotective; protects neurons from damage and death from excitotoxicity.
  - GABA enhancer (agonist).
    - taurine derivative; mimics GABA
  - restores the chemical balance in the brain that would otherwise be disrupted by alcoholism.
  - Also ↑ NA & 5HT activity

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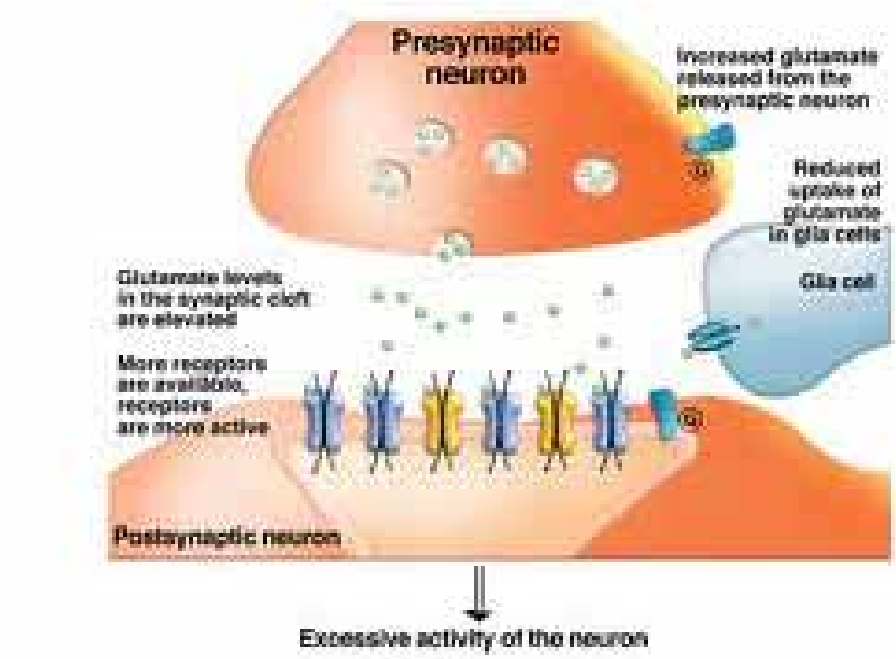
ALCOHOL WITHDRAWAL



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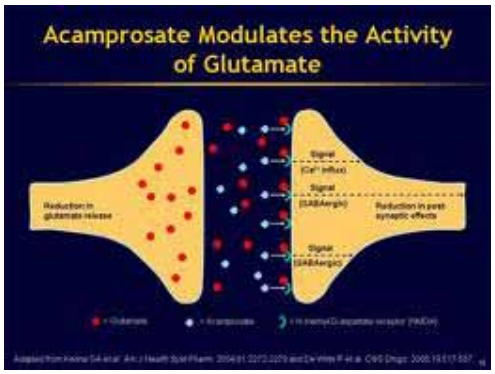
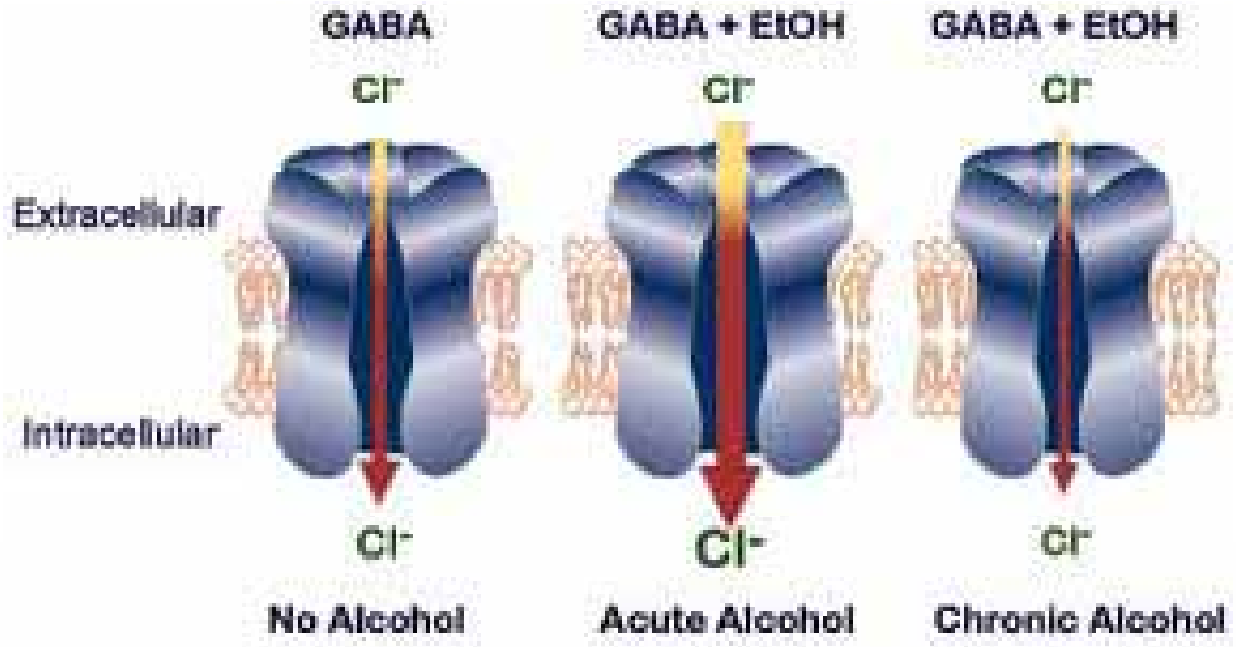
GLUTAMATE RECEPTOR BLOCKADE BY ACAMPROSATE



Acute v/s chronic alcohol on GABA receptors



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ACAMPROSATE

- **Start early during detox**
  - Prevents kindling leading to withdrawal seizures/neuroprotective
- **Dose** (1 tab = 333 mg)
  - <60 kg: 4 tabs/day
  - >60 kg: 2 tabs tds
- **Duration of treatment**
  - 6-12 months
  - Abstinence focussed tx but continue if lapse
- **Contra indications**
  - Pregnancy, breast feeding
  - Renal insufficiency (creatinine > 120)
- **Side effects**
  - Mild diarrhoea, nausea, vomiting, abd pain
  - Occasional pruritis, maculopapular rash, rarely bullous rash
  - Occasional depression, reduced libido

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NALTREXONE

- Block opiate receptors in brain.
  - Blocks endogenous opioid pathway stimulated by alcohol
  - Therefore no “good feeling” experience from alcohol
  - Cravings eventually die away.
- Dose
  - Starting dose: 25 mg daily
  - Treatment dose : 50 mg daily
- Side effects
  - Nausea, headache, dysphoria
  - Hepatotoxicity (check LFTs 3/12)
  - Requirement for analgesia
- Naltrexone depot & implants
  - Promising results
  - NNT as high as 2.
- In alcohol dependence,
  - reduces relapse rate
  - reduces craving
- Contraindicated in *acute hepatitis* or *liver failure*.

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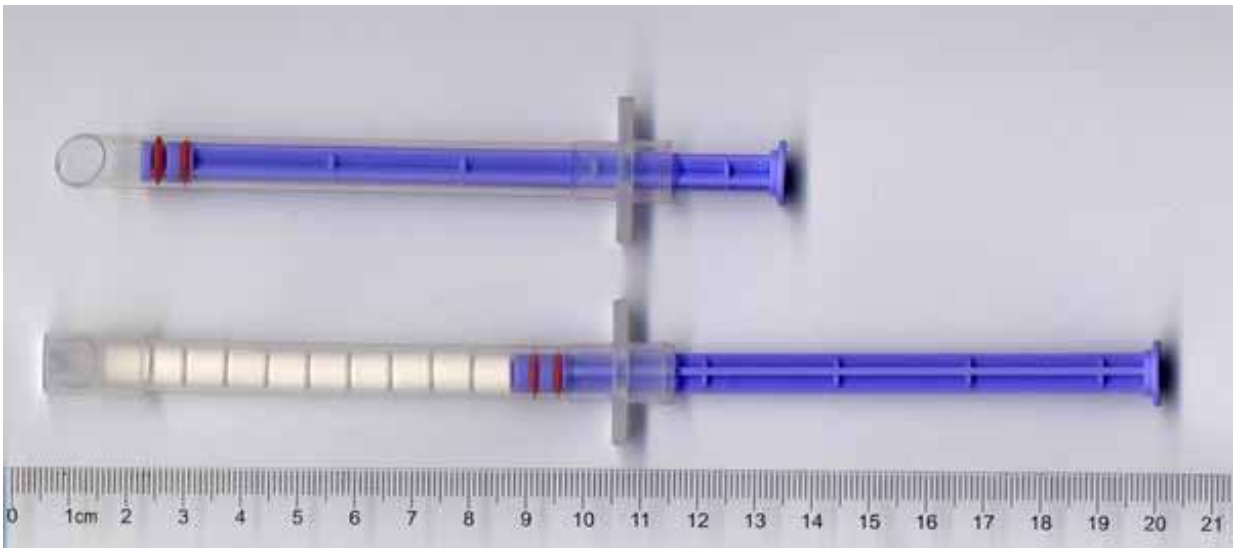
Implant pellets in syringe



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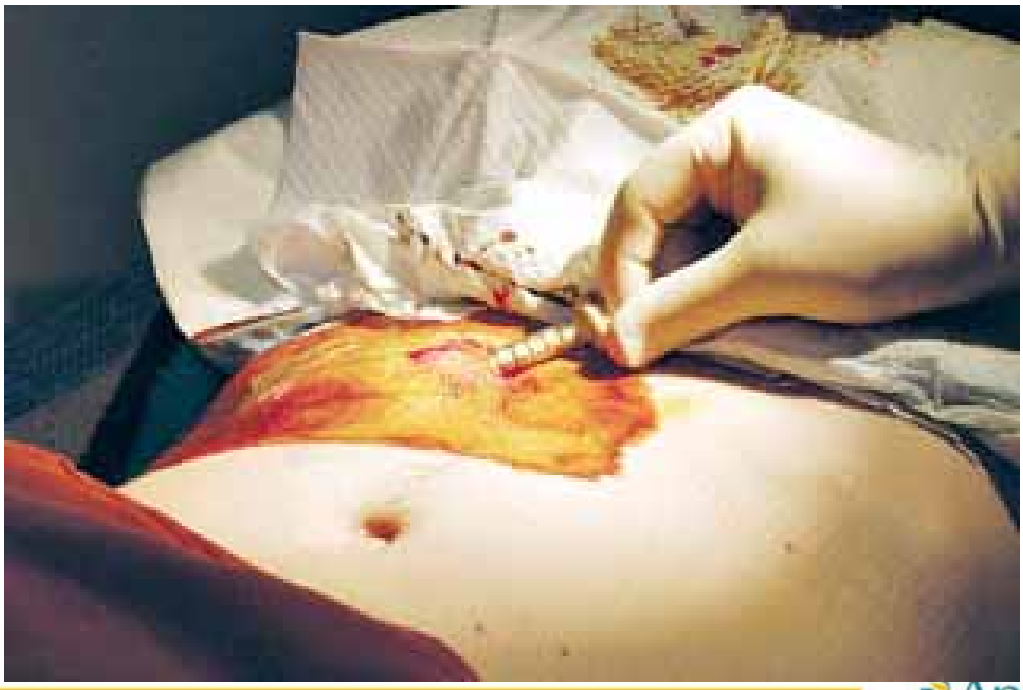
Implant insertion in abdomen



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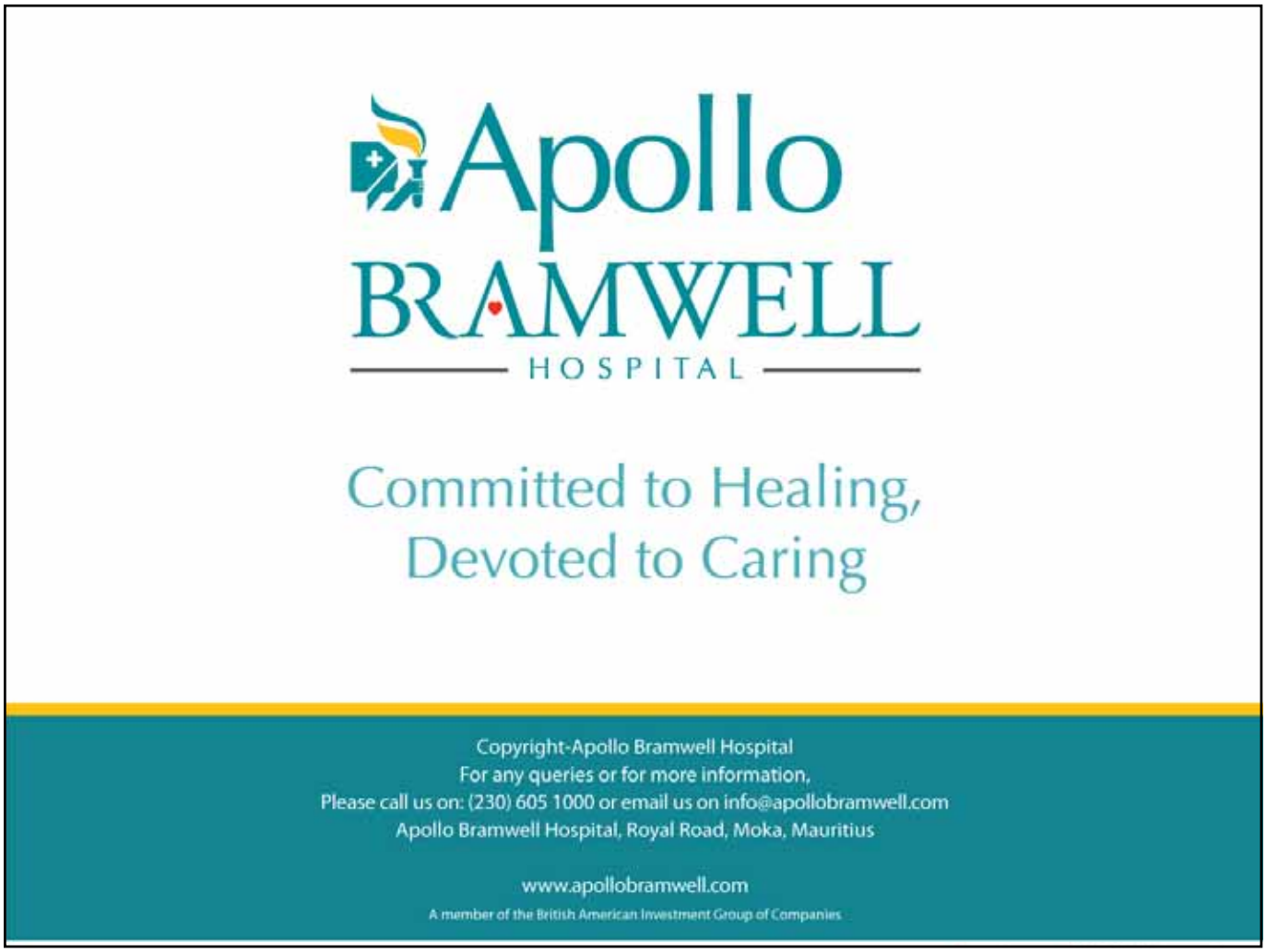
BioPsychoSocial Rx of ALCOHOL DEPENDENCE

- Chronic relapsing brain disease
  - Neuroplasticity
  - Non judgemental approach
- Needs treatment
  - Medical
  - Behavioural
  - Social
- Needs follow up
  - Relapse prevention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