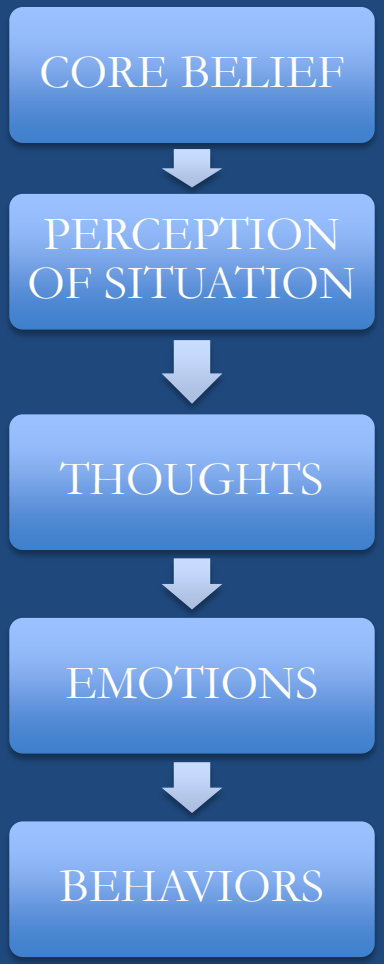
ADDICTION MEDICINE

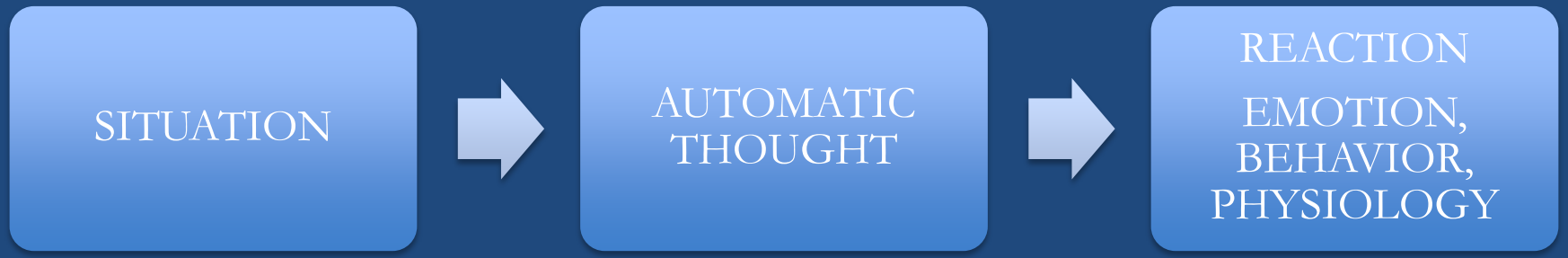
- TOPIC COVERED.

- Basics of behavioral science.
- Alcohol withdrawal management in hospital setting and medication assisted treatment for relapse prevention
- Opioid withdrawal management and Buprenorphine induction
- Resources for after care.
- Law regarding involuntary treatment for substance use in non-compliant, high risk patients.

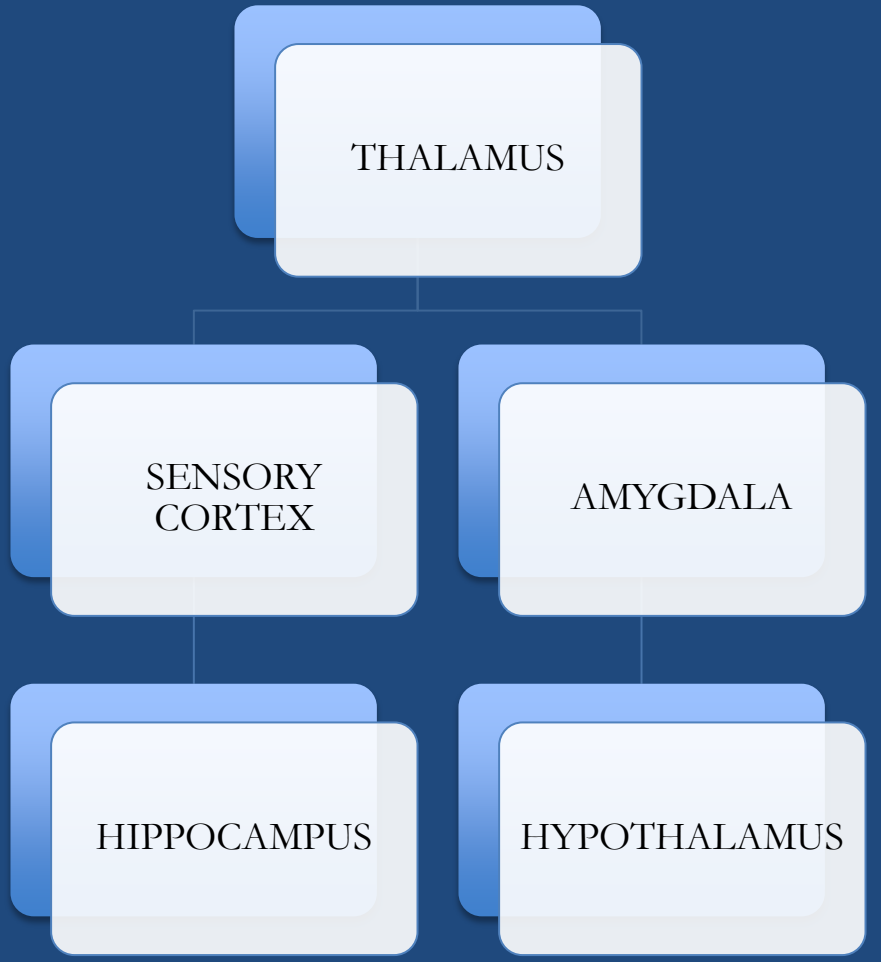
ORIGIN OF EMOTIONS & BEHAVIORS



COGNITIVE MODEL



ANATOMY OF EMOTIONS

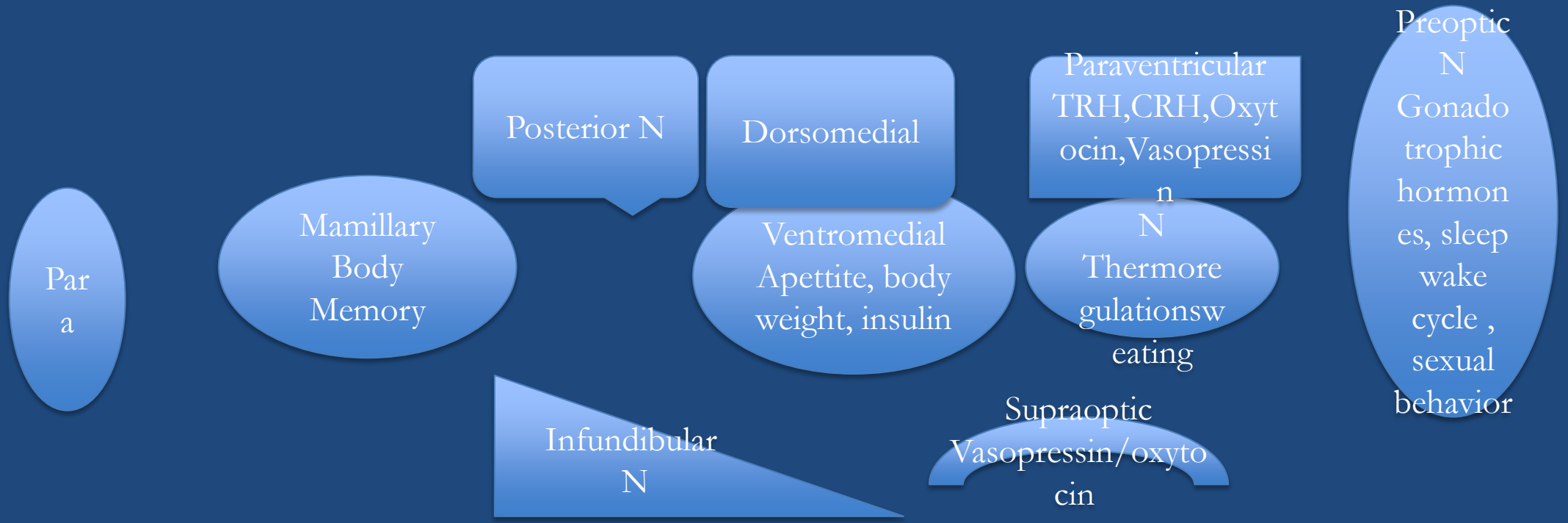


COGNITION

System for comprehending experiences.

System for processing;
information, attention, memory, reasoning, problem solving, computation and language.

Hypothalamus



ANOTOMY OF EMOTIONS

- LIMBIC SYSTEM INVOLVED IN FEELING
- OF PLEASURE BY REDUCING ACTIVITY IN

- AMYGDALA AND CORTICAL AREAS
- CONCERNED WITH ANXIETY

EMOTIONAL BRAIN

PHYSIOLOGICAL RESPONSES TO STIMULI

DESIGNED TO PUSH US AWAY FROM DANGER AND TOWARD REWARDS

MOST OF THE TIME WE ARE UNAWARE OF EMOTIONS

EMOTIONS ARE GENERATED IN THE LIMBIC SYSTEM

EACH EMOTION IS PRODUCED BY DIFFERENT NETWORK

EMOTIONAL BRAIN

AMYGDALA PROCESS STIMULI & SIGNAL OTHER AREAS
TO PRODUCE EMOTIONAL REACTION.

DIFFERENT NUCLEI GENERATE DIFFERENT RESPONSE TO FEAR .

CENTRAL NUCLEUS: GENERATE FREZZING RESPONSE
BASAL NUCLEUS: GENERATE FLIGHT RESPONSE

EMOTIONAL BRAIN

NUCLEI ARE AFFECTED BY SEX HORMONE .

RESPONSE IS DIFFERENT IN MALE AND FEMALE

AMYGDAL PICK UP EMOTIONAL STTIMULI BEFORE WE BECOME AWARE OF IT

INFORMATION THROUGH CORTICAL AREA PRODUCE CONCIOUS AWARENESS

BEHAVIORAL SCIENCE

WHAT IS A BEHAVIOR:

BIOLOGICAL, EMOTIONAL, SOCIAL, ENVIORNMENTAL OR OTHER CHANGES/ACTIONS OR LACK OF IT.

PURPOSE:

TO RESTABLISH OR MAINTAIN DESIRED STATE (HOMEOSTASIS)

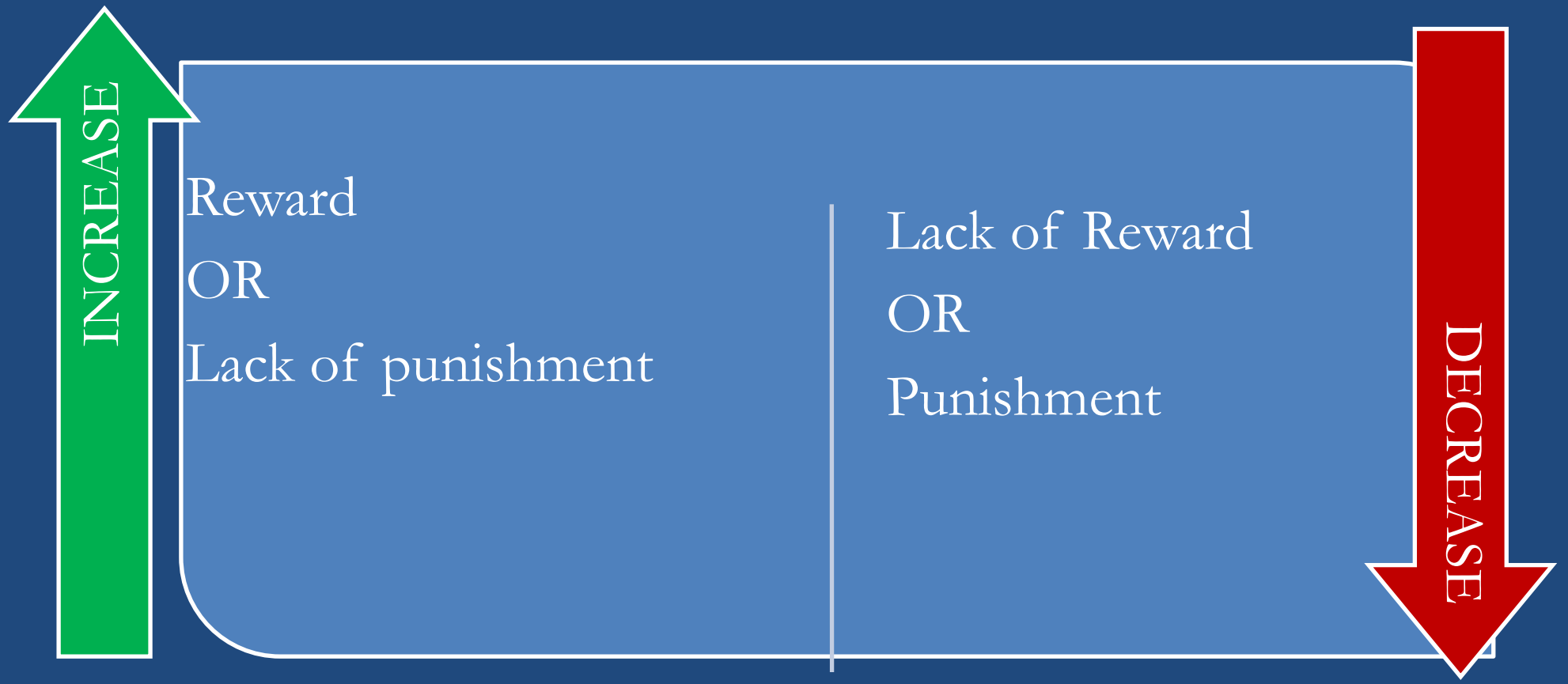
TO DECREASE SUFFERING

BEHAVIOR WILL CEASE TO EXIST IF IT DOES NOT SERVE THE PUPOSE

IDENTIFY BEHAVIOR

Sleeping	Fever
Drinking	Coughing
Eating	Sneezing

REGULATORS OF BEHAVIOR



BEHAVIORAL SCIENCE

Increase in behavior	Decrease in behavior
Reward	Lack of reward
Decrease in suffering	Suffering

BEHAVIORAL ANALYSIS
THRESHOLD

POINT **WHERE BEHAVIOR WILL LIKELY OCCUR** **OR** **WILL CEASE TO EXIST**	**VARIABLES EFFECTING THRESHOLD**
SEIZURE THRESHOLD	SLEEP DEPRIVATION

NORMAL VERSUS ABNORMAL BEHAVIOR

- CONTEXT (TIME AND SPACE) DETERMINE IF BEHAVIOR IS NORMAL OR ABNORMAL

LACK OF IT WHEN NEEDED	**PRESENT WHEN SHOULD NOT BE**
TOO MUCH	TOO LITTLE
WRONG PLACE	WRONG TIME

BEHAVIORS

Name	Purpose	Frequency	Threshold	Variables	Reward /Lack of suffering	Lack of reward/suffering
Sleep	Multiple physiological activities take place during sleep	Circadian	>16-20 hours of being awake	Multiple	Not feeling tired	Psychomotor retardation
Eating	Fuel	2-6 times per day when awake	3-6 hours	Multiple	Satiety/lack of hunger	Hunger
Fever	Multiple		>37.2 c			
Sweating	Maintain body temperature		Increase in Body temp		Homeostasis	Disorder
Substance use	Relieve suffering	variable	Craving Intoxication	Availability Affordability Poor impulse control	Euphoria or relief from withdrawal	No pleasure Negative consequences

Normal Versus Abnormal

	Quality	**Qunatity**	**Pattern**	
Sleep	Refreshing	6-10 hours	Regular pattern	
Sleep	Refreshing	6-10 hours	Regular pattern	
	Not refreshing	<5, >12	Unpredictable	
ABNORMAL				
SLEEP	INSOMNIA	HYPERSLOMOLENCE	NARCOLEPSY	WRONG TIME
EATING	ANOREXIA	BINGE EATING	UNHEALTHY DIET	WRONG TIME

BEHAVIORAL ANALYSIS

Specify behavior	Alcohol use, opioid use, anorexia nervosa,	Intervention
Purpose of behavior	If behavior does not serve the purpose, it will not continue	Look for alternate
Quantify	Frequency	Increase, decrease, eliminate
Qualify	Satisfactory versus not satisfactory	
Pattern	Pattern help to predict	Change
Predict	Situation or time in which behavior is likely to occur.	
Prevent	If you can not predict, will be hard to prevent.	Change threshold
Replacement behaviors	One maladaptive behavior might get replace with another maladaptive behavior.	Choose replacement behaviors
Change	Pattern, quantity, quality,	

Common Addictive Disorder

Substance use	**Pyromania**	**Gaming**	Gambling
Binge eating	Kleptomania	Internet addiction	

Treatment

Purpose of the treatment	Communication with the patient
Decrease mortality and morbidity	Thoughts- Relapse: Failure to maintain sobriety indicate period of sobriety and failure of treatment.
Decrease suffering of the patient	Patient should be given credit for sobriety.
Should we hold patient responsible for the illness.	Failure should be shared.
At some point use of substance is to decrease suffering.	

Self-analysis when treating patient

Situation	Automatic thoughts	Perception	Emotions	Behavior/Action
Pt with h/o opioid addiction, multiple overdose, admitted for overdose	Patient is responsible for action/consequence	Negative perception	Lack of empathy	Standard care.
	Wish we had better and effective treatment for this illness	Patient is seen as a victim of serious illness and ineffective treatment	Empathy/Compassion	Standard care + Thinking of interventions which can be more effective
Pt with history of hypertension admitted for stroke	----	----	---	---

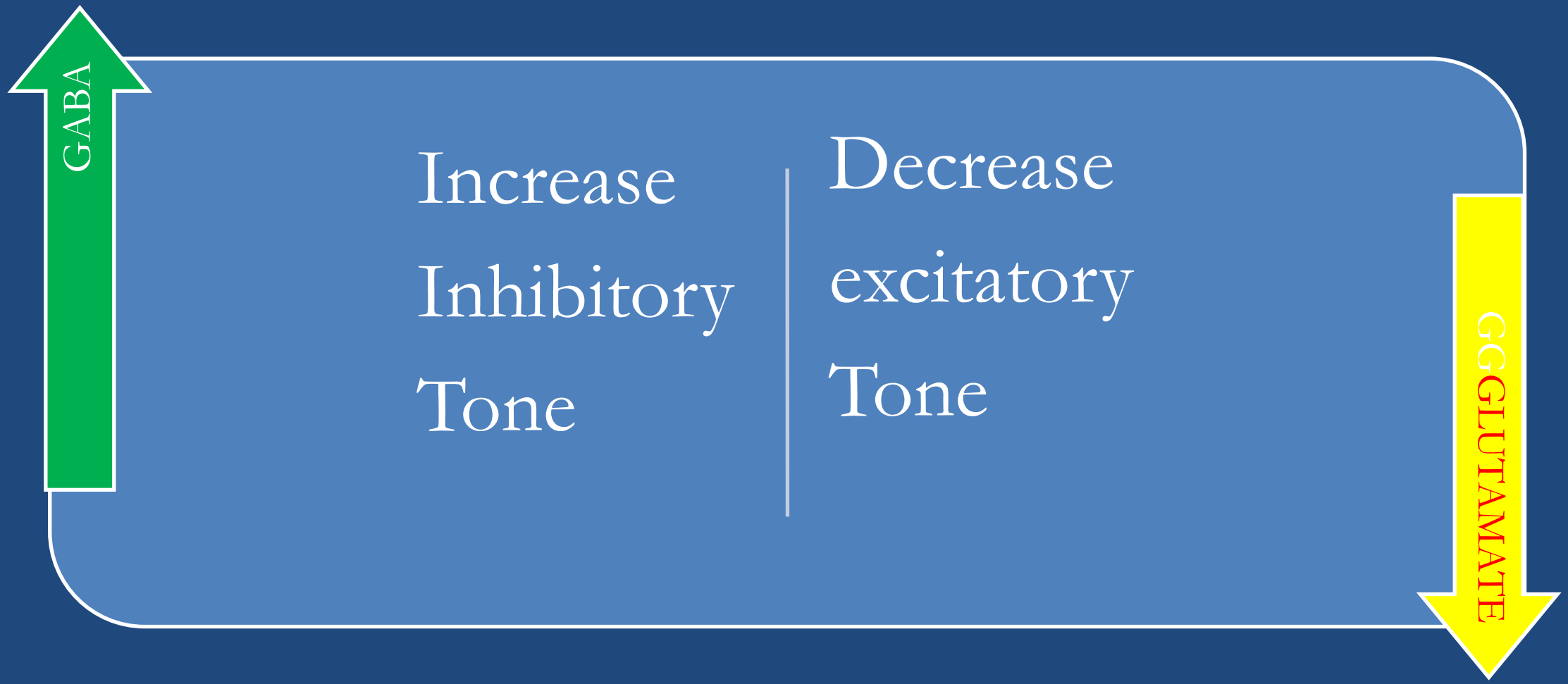
Therapeutic communication

When to say	**Right time, right place. Patient is in receptive state**
How to say	Nonverbal and verbal communication is visible component (behavior) of our emotions and very important factor which will influence patient perception.
What to say	Words should illicit hope and motivation.
	Relapse can be described as a failure of patient to maintain sobriety or success of the patient to maintain sobriety for a period of time. Both description are same; but will illicit different perception, emotions and behaviors.

Alcohol

- CNS depressant
- Enhance inhibitory tone (increase in GABA activity)
- Decrease excitatory tone (decrease in Glutamate activity)

Alcohol


GABA
Increase
Inhibitory
Tone
Decrease
excitatory
Tone
GGLUTAMATE

Alcohol

Increase inhibitory tone 	**Decrease excitatory tone** 	
CNS DEPRESSION	CNS DEPRESSION	

GABA

GABA-A

GABA-B

Withdrawal Symptoms

	Onset time	Symptoms
Alcohol hallucinosis	12-24 hour of last use	Mainly visual
Withdrawal Seizures	12-48 hours after last use.	Generalized tonic – clonic
Delirium Tremens	48-96 hours	Disorientation, hyperthermia, hypertension, tachycardia, agitation, diaphoresis

Withdrawal Symptoms

Symptoms	Onset time	Management
Anxiety	4-6 hours	Hydroxyzine, clonidine, benzodiazepine
Insomnia	4-6 hours	Hydroxyzine (25-75) Melatonin, Trazodone (50 to 150) Mirtazapine (7.5 to 30 mg), Seroquel (25-100mg) Zolpidem
Tremors	4-6 hours	Propranolol 10-20 mg TID, avoid using Clonidine and Propranolol simultaneously
Palpitation	4-6 hours	Propranolol
Headache	4-6 hours	NSAID
Diaphoresis	4-6 hours	

Electrolyte Disturbance

Hypovolemia	**Decrease po intake**	
Hypokalemia	Change in distribution across cell membrane, aldosterone concentration, potassium loss	
Hypomagnesemia	Increase risk of seizures, dysrhythmias, inhibit response to thiamine.	
Hypophosphatemia	Increase risk of cardiac failure &rhabdomyolysis	
Metabolic acidosis	Alcoholic ketoacidosis, thiamine deficiency,infection,hypoperfusion	

Risk factor for DT

Age greater than 65	Multiple signs and symptoms of AW	Elevated blood alcohol concentration
Comorbid medical or surgical conditions	Multiple prior episodes of alcohol withdrawal	Seizures during the current withdrawal period
Dependence on GABA agonist.	History of AW delirium or seizure or DT	Marked autonomic hyperactivity
Long duration alcohol consumption	Longer period since the last drink	History of TBI

Management

- Prophylaxis treatment
- Start early.
- Monitor closely (CIWA)
- Treat comorbid conditions aggressively

Phenobarbital
Half life 50-140 hours, Protein bound 20-45%.

Day-1 Loading dose 12mg/kg		**for 70 kg 840 mg**	
1St dose	40% of LD	4.8mg/kg	336 mg
2nd dose. 3 hours after 1st dose	30% of LD	3.6 mg/kg	252 mg
3rd dose. 3 hours after 2nd dose	30% of LD	3.6 mg/kg	252 mg
Day 2		64.8 mg Q12 hours	
Day 3		64.8 mg Q12 hours	
Day 4		32.4 mg Q12 hours	
Enzyme induced	CYP 1A2, B6,	C9, C10,C19,	CYP3A4

LORAZEPAM

Lorazepam	1mg dosing	2mg dosing (high risk)
00-24 Hour Day-1	1mg Q6	2mg Q6
24-48 Hour Day 2	1mg Q8 h	2mg Q8
48-72 Hour Day 3	0.5mg Q8	1mgQ8
72-96 Hour Day 4	0.25 mg Q8	0.5mg Q8
96-120 Hour Day 5	0.25 BID	0.5mg BID

CHLORDIAZEPOXIDE

Day 1	**50 mg Q6**
Day 2	50 mg Q8 h
Day 3	50 mg Q12 h
Day 4	50 mg QHS

GABAPENTIN TAPER

Day 1	**300 mg Q6 Hour**
Day 2	300mg Q8 Hour
Day 3	300 mg Q12 Hour
Day 4	300 mg QHS

Gabapentin

	Helps with anxiety and pain
Avoid	Standard contraindications, lower dose in patient with impaired renal functions
Dose	100mg TID may increase up to 600 mg TID
Side effects	Weight loss, cognitive impairment (Dopamax) paresthesia, GI symptoms, kidney stones
Monitor	LFT 2-4 weeks after initiation; thereafter, Q6 months

Naltrexone

Tablet	**50 mg once daily, may go up to 100 mg daily**
Long acting injectable VIVITROL	380 mg Q4Week
Avoid	Patient on opioid , acute hepatitis or hepatic failure, pregnant, breast feeding
Acamprosate	
Avoid	Severe renal dysfunction, creatinine clearance <30 Pregnancy, breastfeeding
Dose	666 TID. 33TID for patient with BW<60 KG , Creatinine Clearance 30-50

Acamprosate

Acamprosate	
Avoid	Severe renal dysfunction, creatinine clearance <30 Pregnancy, breastfeeding
Dose	666 TID. 333 TID for patient with BW<60 KG , Creatinine Clearance 30-50
Side effects	Diarrhea, anxiety, insomnia, depression
Monitor	

Disulfiram

Avoid	Myocardial disease, psychosis Pregnancy, breastfeeding
Dose	250 mg daily (125-500 mg)
Side effects	Bitter taste, neuropathy
Monitor	LFT 2-4 weeks after initiation; thereafter, Q6 months

Topiramate

Avoid	Myocardial disease, psychosis Pregnancy, breastfeeding					
Dose (MAX 300mg)	**Week 1**	**Week 2**	**Week 3**	**Week 4**	**Week 5**	**Week 6**
	25 mg	50 mg	75 mg	100 mg	150 mg	200 mg
Side effects	Weight loss, cognitive impairment (Dopamax) paresthesia, GI symptoms, kidney stones					
Monitor	LFT 2-4 weeks after initiation; thereafter, Q6 months					

Opioid

Endogenous Opioid Peptide	Precursor		
Endorphins			
met-enkephalins			
leu-enkephalin			
Dynrophoins			

Common Opioid Analgesics

Name	Approximate Equivalent Dose (mg)	Name	Approximate Equivalent Dose (mg)
Morphine	10 mg	Codeine	30-60
Methadone	10 mg	Hydrocodone	5-10
Hydromorphone	1.5 mg	Oxycodone	4.5
Oxymorphone	1.5 mg		
Buprenorphine	0.3 mg		
		Meperidine	60-100 mg

Opioid

Endogenous Opioid Peptide	Precursor		
Endorphins	POMC Prepro-opiomelanocortin		
met-enkephalins	Preproenkaphalin A		
leu-enkephalin			
Dynrophoin	Preprodynrphin A		

Opioid Receptors

Receptor	Endogenous opioid Peptide Affinity			
Mu	Endorphins>Enkephalin>Dynorphin	Supraspinal & spinal analgesia Modulation of hormone & neurotransmitter release	Slow GI transit	Sedation, Respiratory depression
Delta	Enkephalin>Endorphin>Dynorphin	Supraspinal & spinal analgesia Modulation of hormone & neurotransmitter release		
Kappa	Dynorphin> Endorphin>Enkephalin	Supraspinal & spinal analgesia	Slow GI transit	Psychomimetic effects
ORL1	Orphanin opioid-receptor like subtype	Endogenous ligand		
		Nociceptin/orphanin/FQ		

Clinical Opioid Withdrawal Scale

Mild	Moderate	Moderately sever	Sever
5-12	13-24	25-36	>36

	0	1	2	3	4	5
Pulse	<80	81-100	101-120		>120	
Sweating	No subjective report	Observable moistness.	Beads of sweat on brow or face		Sweat streaming off face	
Restlessness	No	Subjective report without visible movements.		Frequent shifting	Unable to sit still	
Pupil size	Normal size for room temperature	Possibly larger	Moderately dilated			Very dilated (rim of iris is visible)
Anxiety	Not present	Patient report anxiety/irritability	Visibly anxious/irritable		Extremely anxious and irritable	
Bone/joint aches	Not present	Mild diffuse discomfort	Pt report diffuse aching of joints/muscles		Rubbing joints/muscles and unable to sit still because of discomfort	
Runny nose/ tearing	Not present	Nasal stiffness or moist eyes	Nose running or tearing		Nose constantly running or tears streaming down cheeks	

Buprenorphine

Buprenorphine (Subutex)	**Partial opioid agonist. Displaces other opioid agonists from mu receptors and precipitate withdrawal in patient using opioid.**
Naloxone	Combined with Buprenorphine to discourage from dissolving film/tab for IV use. Minimal bioavailability/efficacy with sublingual/po use. IV use will precipitate withdrawal
Buprenorphine + Naloxone (suboxone)	4:1 available dose 2-0.5, 4:1, 8::2, 12:3
Induction	When patient is in state of mild withdrawal (sweating, yawning, piloerection, tremors, irritability, shivering, runny nose) Short acting opioid, heroin: 4-12 hours Methadone: 12 to 36 hours
Monitor	

Buprenorphine Dosing in Hospitalized Patient

Buprenorphine (Subutex)	**Patient must be in mild withdrawal before talking first dose. COW >12** Symptoms; sweating, yawning, piloerection, tremors, irritability, shivering, runny nose) Short acting opioid, heroin: 4-12 hours Methadone: 12 to 36 hours
Day 1	4mg SL, if withdrawal symptoms persist after 1 hour, give additional 4mg. If patient continue to have withdrawal symptoms give 4 to 8mg every Q6 hour upto 32 mg per 24-hour period.
Day 2	Total dose of Day 1. Once daily dose if <16 mg 8 mg daily in AM 12 mg daily in AM 16 mg daily in AM Two divided doses if > 16 mg . Evening dose before 5 pm to avoid insomnia. 12 mg BID 16mg BID

Buprenorphine Induction **Traditional dosing**

Day 1	**4mg.** **Max: 8 mg if additional dose required for**	**May give additional 4 mg if patient is still experiencing withdrawal symptoms. Patient will experience improvement in symptoms in 5-60 minutes. COW<5**
Day 2	8 mg Maximum 16 mg	May give 4 mg every 2 hours if needed based on COW score up to total dose of 16 mg
Day 3	16 mg	

Buprenorphine Induction **Micro dosing**

Micro dosing	**Dose**	**Total daily dose**	
Day-1 (0-24 Hours)	0.5mg SL Q3 Hours	4mg	
Day-2 (24-48 Hours)	1mg SL Q3 Hours	8mg	
Day-3 (48-72 Hours)	4mg Q8 Hours	16 mg	
Day-4 (72-94 Hours)	8mg BID	16 mg	

Buprenorphine Induction with opioid agonist PRN or scheduled

Micro dosing	Dose	Total daily dose	Methadone	Hydromorphone	
Day-1 (0-24 Hours)	0.5mg SL Q3 Hour	4mg	5mg Q3 Hour, additional PRN	2mg PO Q3 Hour, Additional PRN	
Day-2 (24-48 Hours)	1mg SL Q3 Hour	8mg	5mg Q3 Hour	2mg PO Q3 Hour	
Day-3 (48-72 Hours)	4mg Q8 Hour	12 mg			
Day-4 (72-94 Hours)	8 mg BID	16 mg			

Transitioning from SL Buprenorphine TO SUBQ

Buprenorphine SL	ER SUBQ injection weekly	ER SUBQ injection monthly
8-10	16 mg	64 mg
12-16	24 mg	96
18-24	32 mg	128 mg

Methadone

Full mu – opioid agonist	**Does not induce withdrawal symptoms. Risk of overdose and cardiac arrhythmia. Prolongation of Qtc. Use cautions if Qtc >450. Do not use if Qtc >500.**
Legal issues.	Use of Methadone to treat Opioid withdrawal is legally restricted to federally designated Opioid Treatment Program (OTP). In other settings it has different rules.
Dosing	When patient is in state of mild withdrawal

Alpha-2 Adrenergic Agonist

Alpha-2 agonist. Clonidine, Lofexidine, Tizandine	**Decrease autonomic symptoms by decreasing locus cerulus hyperactivity including sweating, abdominal cramps, nausea, anxiety, irritability.** **Side effects; hypotension, rebound hypertension, sedation, sedation.** **Tricyclic antidepressant desensitize alpha-2 adeno receptors; ideally should be stopped 3 weeks prior to use of alpha-2 agonist.**
Clonidine Dosing	0.1mg (BW<90KG) 0.2 mg (BW>90KG) tablet TID or weekly transdermal patch. Patch does not provide sufficient blood level for 72 hours. BP>90/60, HR >60 Taper down gradually after 5 day by one tablet (0.1 or 0.2) per day to prevent rebound hypotension.

HISTAMINE

Subtype	Distribution	Mechanism (PR)	Partial selective agonist	Partial selective agonist
H1	Smooth muscle, endothelium, brain	IP3, DAG	Histaprodifen	Mepyramine
H2	Gastric mucosa, cardiac muscle	IP3, DAG cAMP	Amthamine	Ranitidine, tiotidine
H3	Presynaptic Brain, Neuron, myenteric plexus		R-α Methylhistamine imetit, immepip	Thioperamide, iodophenopropit
H4	Eosinophil, neutrophils,CD4 T cells	cAMP	Clobenpropit, imetit, clozapine	Thioperamide

HISTAMINE

Subtype	Distribution	Mechanism (PR)		
H1	Smooth muscle, endothelium, brain			
H2		cAMP		
H3	Presynaptic Brain, Neuron, myenteric plexus	cAMP		
H4		cAMP		

ANTIHISTAMINE

Subtype	Distribution	Mechanism (PR)		
H1	Smooth muscle, endothelium, brain	IP3, DAG		
H2				
H3				
H4				

Benzodiazepine **Barbiturates**	**Risk of withdrawal seizures**	**Treat like alcohol withdrawal**		
Amphetamine	High risk of cardiac problems, seizures, hallucination	Symptomatic		