

NICOTINE DEPENDENCE SYNDROME



❧ INTRODUCTION

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❧ ETIOLOGY

❧ PATHOPHYSIOLOGY

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INTRODUCTION

- ❧ Cigarette smoking- the most prevalent form of drug dependence in the world
- ❧ Is regarded as the purest pharmacological dependence
- ❧ Smoking is often viewed as a form of self-medication to cope with stress, but there is little evidence that nicotine possesses any anxiolytic or antidepressant properties.
- ❧ Tobacco use is the world's leading cause of death, accounting for 4 million deaths per year

- ✪ 1.1 billion smokers worldwide, 182 million (16.6%) in India
- ✪ Tobacco is addictive in all forms
- ✪ It increases the risk of cancer, cardiovascular disease, stroke, peripheral vascular disease, osteoporosis, chronic obstructive pulmonary disease, diabetes and adverse reproductive outcomes
- ✪ Even second hand smoke adversely affects pregnancy outcomes, causes lung cancer and heart disease

Types of tobacco products

✂ BIDIS

✂ CHEW

✂ CIGARETTES

✂ CIGARS, CIGARILLOS AND LITTLE CIGARS

✂ DISSOLVABLE TOBACCO

✂ E-CIGARETTE

✂ PIPE

✂ SMOKELESS TOBACCO

✂ SNUFF

EPIDEMIOLOGY

- ⌘ Most prevalent SUD in the US with about 20.6% of the adult US population smoking cigarettes
- ⌘ The prevalence is increasing in most developing countries, whereas it is decreasing in most industrialized countries.
- ⌘ Despite an increase in the proportion of smokers quitting, about 20% of the US population continues to smoke, with a lifetime prevalence of nicotine dependence of 24%
- ⌘ Slightly more males than females smoke, although more males than females are successful in stopping smoking.

EPIDEMIOLOGY

⌘ Prevalence of smoking:

⌘ 47 percent in men

⌘ 11 percent in women

⌘ Dependence in 25% population

⌘ Mean age of onset in the United States: 16 years

⌘ Prevalence in psychiatric patients 50 percent, including those with other substance use disorders (80 percent)

INDIAN SCENARIO

- ⌘ Prevalence - 18.4% for tobacco smoking
- ⌘ 21% for tobacco chewing.
- ⌘ Indian women were much less likely to smoke tobacco
- ⌘ Srinivasan and Thara 2002, Reported that the prevalence of smoking was 38% among patients with schizophrenia, 24% among patients with mood disorders, and 23% among those with a non-psychotic disorder.

ETIOLOGY AND PATHOPHYSIOLOGY

⌘ GENETIC FACTORS

- ⌘ Family, adoption and twin studies strongly suggest the role of genetic factors in cigarette smoking.
- ⌘ Comparing twins reared together and apart showed that in men the regular tobacco use has both genetic and rearing-environmental factor accounting for 61% and 20%, respectively (Kendler et al. 2000)
- ⌘ The overall heritability of nicotine dependence is thought to be 60% (True et al. 1999 , Kendler et al.2000).

Cont.

- ⌘ Nicotine is able to achieve the effects –
 - ⌘ by increasing the release of acetylcholine, dopamine, norepinephrine, serotonin, glutamate and gamma amino butyric acid (GABA) in the brain
 - ⌘ and the calcitonin and substance P in the spinal cord (Lloyd and Williams 2000).

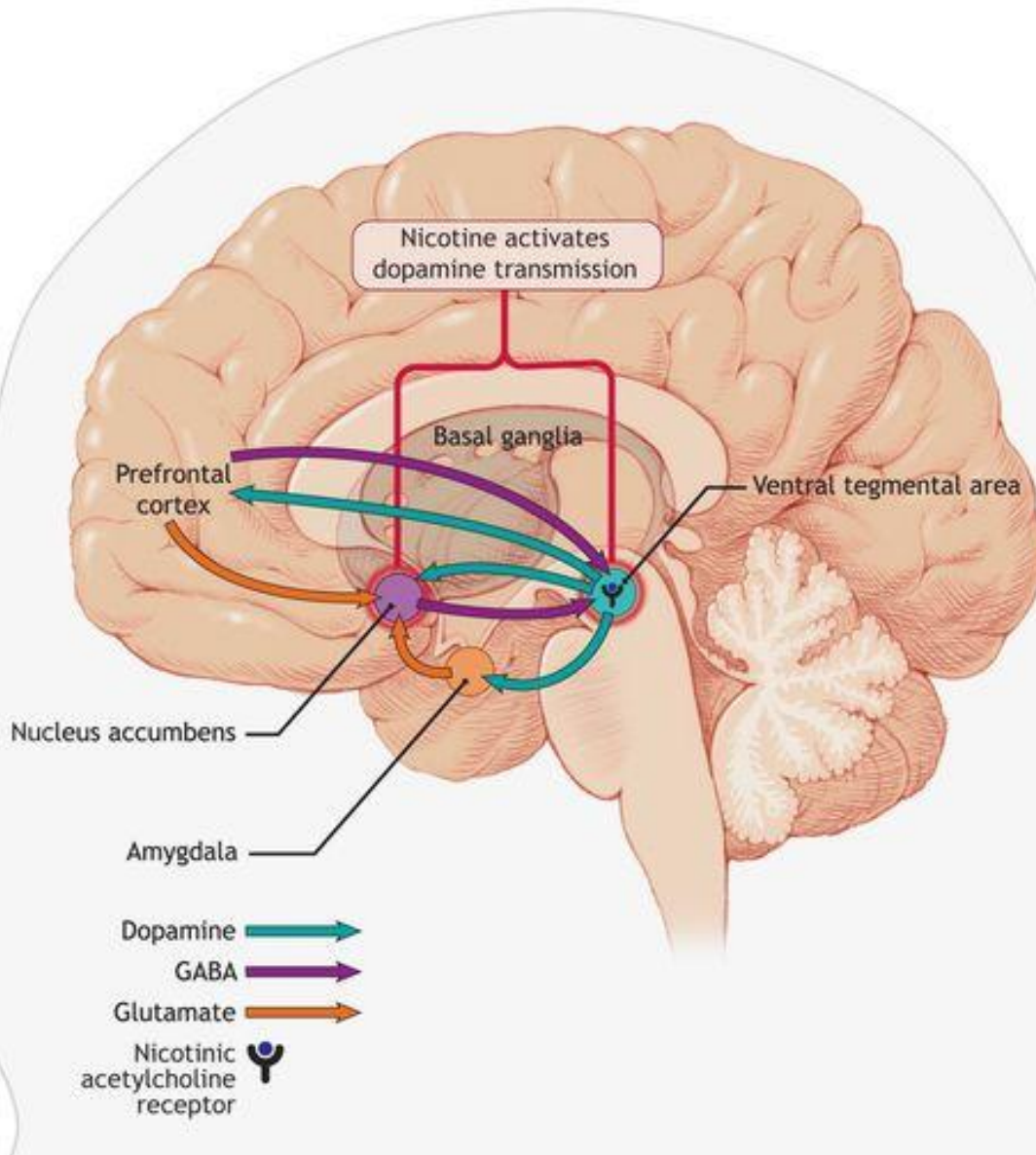
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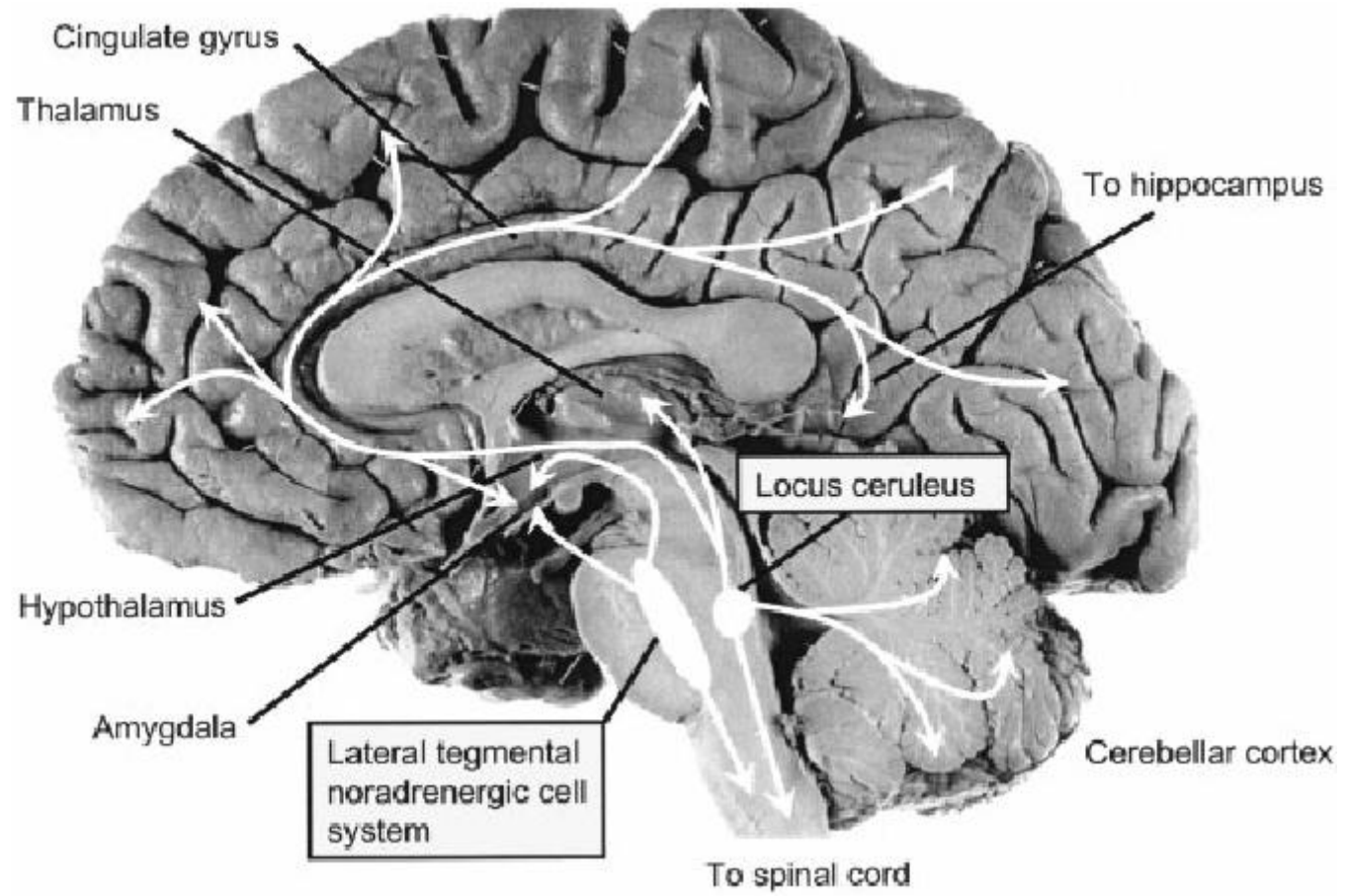
- ✧ It acts in two primary areas of the brain—
 - ✧ The mesolimbic dopaminergic system (the brain reward pathway), which is related to the euphoriant effects of the drug,
 - ✧ The locus coeruleus, which mediates stress reactions and vigilance and relates to the higher mental and cognitive functions.

The mesolimbic pathway can be seen here as the blue projections from the VTA to the nucleus accumbens.

mesolimbic pathway regulates incentive salience, motivation, reinforcement learning, and fear, among other cognitive processes

This pathway plays a central role in the neurobiology of addiction in particular, a drug addiction is defined as the compulsive use of a drug that is rewarding (i.e., activate *this pathway*)





PSYCHOLOGICAL FACTORS

- ❧ Involves the perceived benefits/reasons a person smokes, such as a perception that they are able to improve mood and sense of well-being, to satisfy craving, and to provide stimulation and relaxation (Goldstein et al. 1991).
- ❧ For women these beliefs are also in the context of sociocultural attitudes that reinforce the belief that smoking helps to manage and control mood (anger, stress, depression), control weight gain, and increase an adolescent's sense of being independent and trendy.

SOCIAL AND ENVIRONMENTAL FACTORS

- ⌘ Cues that become associated with the behavior of smoking cigarettes, such as the association with drinking coffee or alcohol, talking on the telephone, taking a work break, or smoking at parties or social functions.
- ⌘ Adolescents and college age young adults,
 - ⌘ peer smoking and peer-group identification

COMORBIDITY

- ⌘ 55- 90% patients with psychiatric disorder vs. 20.6% general population
- ⌘ 70-90% - schizophrenia
- ⌘ 46% - GAD
- ⌘ 43.5% - alcohol abuse or dependence
- ⌘ 49% - drug abuse or dependence
- ⌘ 36.6% - major depression

ICD-10 Dependence syndrome

⌘ A cluster of physiological, behavioural, and cognitive phenomena in which the use of a substance or a class of substances takes on a much higher priority for a given individual than other behaviours that once had greater value

⌘ *Diagnostic guidelines*

⌘ A definite diagnosis of dependence should usually be made only if three or more of the following have been present together at some time during the previous year:

⌘ (a) a strong **desire** or sense of compulsion to take the substance;

⌘ (b) difficulties in **controlling** substance-taking behaviour in terms of its onset, termination, or levels of use;

Cont.

- ⌘ (c) a physiological **withdrawal** state: the characteristic withdrawal syndrome for the substance; or use of the same substance with the intention of relieving or avoiding withdrawal symptoms;
- ⌘ (d) evidence of **tolerance**, such that increased doses of the psychoactive substance are required in order to achieve effects originally produced by lower doses
- ⌘ (e) progressive **neglect of alternative pleasures** or interests because of psychoactive substance use, increased amount of time necessary to obtain or take the substance or to recover from its effects;
- ⌘ (f) **persisting** with substance use despite clear evidence of overtly harmful consequences

DSM-5 Diagnostic Criteria

- ⌘ A problematic pattern of tobacco use leading to clinically significant impairment or distress,
- ⌘ as manifested by at least two of the following, occurring within a 12-month period:
 - ⌘ 1. Tobacco is often taken in larger amounts or over a longer period than was intended.
 - ⌘ 2. There is a persistent desire or unsuccessful efforts to cut down or control tobacco use.
 - ⌘ 3. A great deal of time is spent in activities necessary to obtain or use tobacco.
 - ⌘ 4. Craving, or a strong desire or urge to use tobacco.
 - ⌘ 5. Recurrent tobacco use resulting in a failure to fulfil major role obligations at work,
school, or home (e.g., interference with work).

- ⌘ 6. Continued tobacco use despite having persistent or recurrent social or interpersonal problems caused or exacerbated by the effects of tobacco (e.g., arguments with others about tobacco use).
- ⌘ 7. important social, occupational, or recreational activities are given up or reduced because of tobacco use.
- ⌘ 8. Recurrent tobacco use in situations in which it is physically hazardous (e.g., smoking in bed).
- ⌘ 9. Tobacco use is continued despite knowledge of having a persistent or recurrent physical or psychological problem that is likely to have been caused or exacerbated by tobacco.
- ⌘ 10. Tolerance

11. Withdrawal

Differential Diagnosis

- ❧ Many of the symptoms of nicotine withdrawal can mimic, exacerbate, or mask the symptoms of psychiatric disorders or the adverse effects of psychiatric medications;
- ❧ for example, akathisia, anxiety, depression, irritability, insomnia, and weight gain.
- ❧ Cessation of smoking appears to be able to reinitiate depression, alcoholism, and, perhaps, other psychiatric disorders in a small subgroup of smokers.

TREATMENT

First-line pharmacological therapies

Nicotine Replacement Therapies

- ⌘ Nicotine gum
- ⌘ Nicotine inhaler
- ⌘ Nicotine lozenge
- ⌘ Nicotine nasal spray
- ⌘ Nicotine patch
- ⌘ Nicotine patch plus lozenge or gum or inhaler

⌘ Varenicline

⌘ Bupropion plus nicotine medication

⌘ Second-line pharmacological therapies

⌘ Calonidine

⌘ Nortriptyline

⌘ **Psychosocial therapies**

⌘ Behavior therapy

⌘ Social support

NICOTINE REPLACEMENT THERAPY

- ☞ Most widely used medication option
- ☞ Available over-the-counter or by prescription
- ☞ **Principle** -nicotine is the dependence producing constituent of cigarette smoking, and that smoking cessation and abstinence can be achieved by replacing nicotine without the harmful impurities in cigarette smoke.

Nicotine Gum



Nicotine Patches



Microtabs



☞ The substituted nicotine initially prevents significant withdrawal symptoms that may lead to relapse during the early period of smoking cessation.

☞ The substituted nicotine is then gradually tapered and discontinued.

☞ Replacement produces a lower overall plasma level of nicotine than that experienced with smoking.

Lozenges



Inhalators



Nasal Sprays



NICOTINE GUM



- ✧ Approved in 1984, was the first NRT approved
- ✧ It slowly releases nicotine from an ion exchange resin when chewed. The nicotine released is absorbed through the buccal mucous membranes.
- ✧
- ✧ The NRT gum is available in doses of 2 and 4 mg, and the recommended dosing is in the range of 9–16 pieces/day.

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- ⌘ Nicotine gum is more effective when
 - ⌘ used in conjunction with psychosocial intervention
 - ⌘ used for longer than 3 months
- ⌘ Tapering may be necessary after 4–6 months of use
- ⌘ Not effectively utilized in patients with
 - ⌘ Temporomandibular joint problems,
 - ⌘ Dental problems,
 - ⌘ Dentures.

Cont.

☞ **Instructions**

☞ Is not like bubble gum

☞ Is crunched a few times and “parked” between the gum and cheek.

☞ Should not be used soon after drinking acidic substances such as coffee, soda, or orange juice

☞ **Adverse effects**

☞ include local irritation in the mouth, tongue, and throat, mouth ulcers, hiccups, jaw ache, gastrointestinal symptoms ,anorexia, and palpitations

Nicotine lozenge

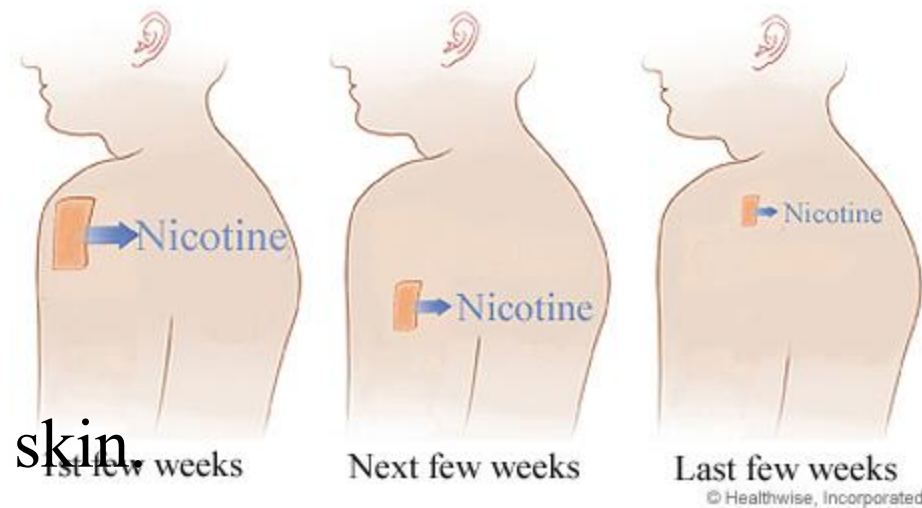
✧ FDA approved in 2002

✧ Nicotine lozenge, an OTC product, is available in 4 mg (for those who smoke within 30 minutes of arising) and 2 mg (for those who do not smoke until more than 30 minutes after arising) forms. The lozenge is held under the tongue and delivers levels of nicotine similar to gum. Because it does not require chewing, it may be more acceptable than gum.

Nicotine patch

Nicotine patch size/strength is reduced over time
Location is changed to avoid skin irritation

- ✧ Transdermal delivery system provides continual sustained release of nicotine, which is absorbed through the skin.
- ✧ Eliminates repeated nicotine use
- ✧ Compliance rates are higher
- ✧ once-daily dosing
- ✧ its administration is simple and discreet.



Cont.

⌘ Dose of NRT patch is 21 or 15 mg patch

⌘ **Advantage**

⌘ It can be used despite dental or temporomandibular joint problems.

Disadvantage

⌘ Does not allow for self-titrated dosing, craving, and nicotine withdrawal symptoms

⌘ 25% -local skin irritation or erythema

⌘ sleep problems

⌘ nicotine toxicity

Nicotine nasal spray

- ⌘ Rapidly absorbed
- ⌘ produces a higher nicotine blood level than does transdermal nicotine or gum.
- ⌘ A single dose of the spray delivers 0.5 mg to each nostril and it can be used one to three times/hr.
- ⌘ Onset of action of the spray is the most rapid of all nicotine replacements

Cont.

- ⌘ An initial concern about the nasal spray had been the potential for abuse because it has the most rapid absorption rate of the NRTs.
- ⌘ It replicates repeated administration of nicotine in smoking, resulting in reinforcing peaks in the plasma level of the drug.
- ⌘ **Side effects**
 - ⌘ include local airway irritation
 - ⌘ Systemic effects include nausea, headache, dizziness, tachycardia, and sweating

Nicotine inhaler

- ✂ Provides nicotine through a cartridge that must be “puffed.”
- ✂ It mimics the upper airway stimulation experienced with smoking
- ✂ Absorption is primarily through the oropharyngeal mucosa.
- ✂ **Side effects** include local irritation, cough, headache, nausea, dyspepsia, the need for multiple dosing

E - cigarette

- First invented in the 1960's,
 - E-cigarette first entered the market in China in 2004
 - Currently over 250 brands available
- 3 Main Components of the E-Cigarette:
 - Battery
 - Atomizer
 - Inhaler
- Battery-powered heating devices, often resembling cigarettes, cigars or pipes
- Designed to deliver nicotine to users in the form of a vapor (instead of smoke)
- The vapor comes from heating liquid nicotine

⌘ Fluids* may contain:

- ✓ Nicotine (in varying concentrations 0-100 ml/mg)
- ✓ Humectants: propylene glycol (or vegetable glycerin) for vapor production
- ✓ Flavorings (tobacco, menthol, coffee, vanilla, fruit, cotton candy, etc.)

E - cigarette



When heated, the cartridge that contains the liquid nicotine converts the contents into a vapor that the user inhales.

Bupropion

In 1996 bupropion was approved by the U.S. Food and Drug Administration (FDA) approval in the treatment of depression, bupropion is also approved for smoking cessation and is the only antidepressant to receive FDA approval for the preventive treatment of seasonal affective disorder (SAD)

⌘ Non-nicotine pill

⌘ FDA-approved medication

⌘ Heterocyclic, atypical antidepressant

⌘ Blocks the reuptake of both dopamine and norepinephrine

- ⌘ Smoking cessation rates appear to improve further when bupropion is combined with the nicotine patch (Nides 1997).
- ⌘ **Adverse events** included dry mouth, insomnia, nausea and skin rash
- ⌘ **C/I** -in patients with a history of seizure disorders.
- ⌘ Dosages of 450 mg per day

- ⌘ In one pivotal trial, only 27 percent of patients experienced nicotine cravings 1 month after smoking cessation on bupropion 300 mg per day versus 56 percent of those on placebo.
- ⌘ About 30 percent of patients on bupropion are able to quit after 1 to 3 months versus about 15 percent of placebo-treated patients. After 1 year of treatment, patients who remain on bupropion are about 1.5 times as likely to remain abstinent as placebo-treated patients.

Varenicline

- ✧ Is an $\alpha 4 \beta 2$ nicotinic acetylcholine receptor partial agonist.
- ✧ Relieves craving and withdrawal
- ✧ Mediate the rewarding properties of nicotine through the release of dopamine in the mesolimbic system, and in particular nucleus accumbens.
- ✧ Varenicline's maximum plasma concentration is reached after 3–4 hr. and following repeated oral doses the steady-state occurs within 4 days.

Cont.

- ⌘ Should be started 1 week before the set date for patients to stop smoking.
- ⌘ The approved course of treatment is 12 weeks.
- ⌘ The recommended dose of 1 mg twice daily should be arrived at after a 1-week titration.
- ⌘ The **adverse reactions** include nausea, vomiting, constipation, headache, insomnia and abnormal dreams.
- ⌘ Major adverse event is nausea, which occurs in about 30 percent of patients, but causes discontinuation of medication in only about 3 percent. Varenicline has been associated with psychiatric problems, but whether it caused these problems is unclear.

Tricyclic antidepressants

- ✧ May help reduce nicotine withdrawal, craving, and relapse, including doxepin, imipramine and nortriptyline.
- ✧ Adverse effects include increased appetite, weight gain, dry mouth, blurred vision, constipation, urinary hesitancy, and sedation.

Nortriptyline

- ✧ It appears to be effective for smoking cessation; however, owing to its more significant side effects than nicotine replacement or bupropion, it is typically used only when other medications have failed.
- ✧ Selective serotonin reuptake inhibitors (SSRIs) do not appear to be effective for the treatment of nicotine dependence. Whether other antidepressants (e.g., MAOIs) are effective is unclear.

Non-FDA Approved Medications

⌘ **Clonidine**

⌘ oral (0.1 mg) and transdermal forms (0.1–1.3 mg)

⌘ antihypertensive drug with central sympatholytic activity (locus ceruleus), is a presynaptic alpha-2-receptor agonist

⌘ **Adverse effects** include sedation, dry mouth, and hypotension.

Buspirone

✧ It has been shown to act on two types of receptors: Serotonin (5-HT) and dopamine (D). It has high affinity for the 5-HT_{1A} serotonin receptor, acting as an agonist or partial agonist, and moderate affinity for the D₂ dopamine receptor, acting as both an agonist and antagonist.

Cont.

- ⌘ Nonsedative, nonaddictive, nonbenzodiazepine antianxiety agent
- ⌘ Decrease craving, anxiety, and fatigue during withdrawal from nicotine

Psychosocial Treatments

- ⌘ The core psychotherapies in substance abuse
 - motivational enhancement therapy
 - cognitive–behavioral therapy

- ⌘ Psychosocial interventions, particularly Behavioral Therapy, have been shown to increase abstinence rates significantly (Ferry et al. 1992).

⌘ **Motivation Enhancement Therapy**

- ⌘ Helpful for the smoker who continues to be ambivalent about quitting.
- ⌘ Aim to enhance the smoker's commitment and motivation to quit smoking.
- ⌘ The therapist maintains
 - ⌘ a patient-centered approach
 - ⌘ empathic and optimistic.
 - ⌘ adopts a focused but non-confrontational style

- ❧ Without an external motivator, a confrontational approach is likely to provoke resistance and treatment dropout.
- ❧ Poorly motivated patient -increase awareness of the impact of tobacco and the possibility of change.
- ❧ An important initial component of MET is to provide personalized feedback on how tobacco may be affecting their lives and others.

CONCLUSION

- ❧ Tobacco use is common throughout the world with there being about 1.25 billion smokers of which 1 billion are male.
- ❧ Tobacco-caused diseases are the second most common cause of death in the world, including 5 million in 2005 and an estimate of 10 million in 2020
- ❧ Tobacco use and nicotine dependence has serious health consequences for the user, family members, and others who breathe environmental tobacco smoke or are exposed during pregnancy.
- ❧ Tobacco use and nicotine dependence increases morbidity and mortality.

- ❧ A large proportion of individuals with nicotine dependence has comorbid psychiatric disorder
- ❧ APA guidelines recommend that all smokers to be offered medication to aid in smoking cessation
- ❧ Combining medication and behavior therapy increases quit rates over either therapy alone though medications are effective in the absence of psychosocial therapy.

⌘ Kaplan & Sadock's comprehensive textbook of psychiatry, 9th edition

⌘ Internet references

⌘ <https://www.drugabuse.gov/publications/research-reports/tobacco/tobacco-use-comorbidity>

THANK YOU