

Nicotine Addiction

Chapter 465 | Part 13: Neurologic Disorders

KEY CLINICAL POINTS

- 1 Nicotine addiction is a chronic disorder characterized by compulsive use of nicotine-containing products to regulate intake and avoid withdrawal.
- 2 Cigarette smoking causes approximately 40% of premature deaths in smokers; risk for cancer increases linearly with quantity (cigarettes per day) and logarithmically with duration.
- 3 Varenicline (3.1) is the most effective pharmacologic intervention for cessation compared to no intervention.
- 4 Cessation reduces risk of second coronary event within 6–12 months; risk of stroke/MI/death from CHD becomes similar to never smokers after 15 years.
- 5 E-cigarettes are as effective as FDA-approved medications for cessation, but dual use negates these benefits.
- 6 Nicotine absorption is influenced by pH; unprotonated (freebase) nicotine is more readily absorbed into the bloodstream.
- 7 Withdrawal symptoms can persist for 4–6 weeks after cessation.
- 8 Cigarette smoking is responsible for 80% of COPD cases.
- 9 Counseling (10 min) and systemwide tracking/assistance are highly effective interventions (RR 1.84 and 5.0, respectively).
- 10 Nicotine salts in e-cigarettes allow for rapid rises in arterial blood concentration due to mildly acidic aerosols reducing airway irritation.

DEFINITION & OVERVIEW

- **Definition:** Nicotine addiction is a chronic disorder characterized by compulsive use of nicotine-containing products to regulate intake and avoid withdrawal.
- **Mechanism of Addiction:**
 - Nicotine binds to nicotinic acetylcholine receptors (nAChRs) in brain networks involved in depression, joy, excitement, and happiness.
 - Prolonged exposure leads to upregulation of these receptors.
 - Intensity/speed of addiction depends on frequency of use and concentration of arterial nicotine reaching the brain.
- **Disease Manifestations:**
 - No benefit for non-addicted individuals; high cost and difficulty to break for others.
 - Any use of nicotine earlier in life predicts greater use of some nicotine product later in life.
 - Diagnosis is based on the patient's loss of control over their next dose.

EPIDEMIOLOGY

- **Trends in Nicotine Product Use:**

- Shift toward non-combusted and non-tobacco-leaf formulations (approx. 40%).
- Current adult cigarette smoking prevalence is approaching 10%.
- Significant decline in high school senior usage: 31% in 2000 → 2.9% in 2023; only 0.7% smoke daily.
- Only 5% of 18- to 24-year-old adults currently smoke.
- Prevalence among those over age 40 (the population most likely to develop disease) declines more slowly.

- **Adolescent and Global Trends:**

- E-cigarette use in high school seniors: 25% in 2019 → 17% in 2023; daily use at 5.8% in 2023.
 - Worldwide tobacco consumption recently declined slightly after decades of growth.
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ETIOLOGY & PATHOPHYSIOLOGY

- **Nicotine Absorption:**

- Influenced by the pH of the delivery medium.
- Unprotonated (freebase) nicotine is more easily absorbed into the bloodstream than protonated forms.
- High concentrations of unprotonated nicotine are irritating to the airway, limiting inhalation.
- Nicotine salts/acidic aerosols:

→ Produce mildly acidic aerosols in the mouth to reduce irritation.

→ Allow for higher doses and rapid rises in arterial blood concentration.

→ Lung environment (alkaline pH $\approx$ 7.4) facilitates conversion of protonated nicotine to unprotonated form for absorption.

- **Withdrawal and Dependence:**

- As time since last use increases, nicotine levels drop and receptors become uncovered, creating a compulsive need for the next dose.
 - Withdrawal symptoms can persist for 4–6 weeks.
 - Genetic susceptibility influences probability of addiction; however, rates of smoking cessation have increased and addiction rates have decreased significantly since the mid-1950s.
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CLINICAL FEATURES

- **General Risk:**

- Approximately 40% of cigarette smokers will die prematurely without cessation.

- **Cancer:**

- Causes cancer of lung, lip, oral cavity, naso/oro/hypopharynx, nasal cavity, paranasal sinuses, larynx, esophagus, stomach, pancreas, liver, colon, rectum, kidney, ureter, bladder, cervix, and acute myeloid leukemia.
- Risk increases linearly with quantity (cigarettes per day) and logarithmically with duration.
- Synergistic risks: Alcohol + smoking (oral/esophagus); Occupational exposure (asbestos/radon) + smoking (lung).

- **Table 465-1 (Relative Risks):**

→ Lung cancer risk increases significantly with age (e.g., Males 35–44: 14.33 → 65–74: 28.29; Females 35–44: 13.30 → 65–74: 23.65).

→ COPD risk is high across all ages (e.g., Females 65–74: 38.89; Males 65–74: 29.69).

- **Table 465-3 (Other Cancers):**

→ Larynx (M 14.6, F 13); Lip/Oral/Pharynx (M 10.9, F 5.1); Esophagus (M 6.8, F 7.8); Bladder (M 3.3, F 2.2); Kidney (M 2.7, F 1.3); Pancreas (M 2.3, F 2.3); Stomach (M 2, F 1.4); Liver (M 1.7, F 1.7); Colorectal (M 1.2, F 1.2); Cervix (F 1.6); AML (M 1.4, F 1.4).

- **Cardiovascular Disease:**

- 90% of peripheral vascular disease in non-diabetics attributed to smoking.
- 50% of aortic aneurysms; 24% of coronary artery disease; 11% of stroke.
- Synergistic interaction with hypertension or elevated serum lipids.
- Rapid benefit from cessation for new coronary events due to reduced platelet aggregation and vascular occlusion.

- **Respiratory Disease:**

- Smoking is responsible for 80% of COPD.
- Small airway changes (inflammatory) occur within 1–2 years; these reverse after 1–2 years of abstinence.
- Large airway changes (mucous hyperplasia) cause chronic cough in 80% of smokers >60 years old.

- **Pregnancy and Other Conditions:**

- Pregnancy: Risk of premature rupture of membranes, abruptio placentae, placenta previa, SIDS, and developmental lag.
- Others: Delays healing of peptic ulcers; risk of periodontal disease, diabetes, RA, osteoporosis, cataracts, and macular degeneration.

- **Environmental Tobacco Smoke (ETS):**

- Increases lung cancer/CAD in non-smokers.
- Increases respiratory infections, chronic otitis media, and asthma in children.

DIFFERENTIAL DIAGNOSIS

- **Other Forms of Tobacco Use:**

- Oral tobacco (moist snuff/chewing): leads to gum disease; risk for oral and pancreatic cancer.
- Nicotine salts: Deliver higher amounts of nicotine due to acidic formulation, leading to more rapid blood concentration.

- **Vaping and E-cigarettes:**

- Used for recreation, sustaining addiction, or attempting to quit.
- Dual use: Simultaneous use of e-cigarettes and combusted cigarettes (negates benefits).

- **Assessment Criteria:**

- Frequency of use; timing (e.g., within 30 min of waking as a marker of intensity).
- History of failed attempts; craving after abstinence.

DIAGNOSTIC APPROACH

1. Clinical Assessment:

- Identify all tobacco and nicotine products used.
- Determine frequency of use (number of uses per day, spacing).
- Assess timing (e.g., usage within 30 min of waking as a marker of intensity).

2. Behavioral Evaluation:

- Evaluate history of attempts to quit → identify patterns of compulsive need for next dose.

3. Risk Assessment:

- Identify specific comorbidities (lung cancer, COPD, cardiovascular risk factors).
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MANAGEMENT & TREATMENT

1. Physician Actions:

- Ask: Systematically identify all tobacco and nicotine use at every visit.
- Advise: Strongly urge all smokers to quit.
- Identify: Determine which smokers are willing to quit.
- Assist: Provide assistance in quitting.
- Follow-up: Arrange follow-up contact.

2. Pharmacologic Interventions (Table 465-2/465-5):

- **Varenicline:** Most effective pharmacologic intervention (RR 3.1).
- **Bupropion:** Effective pharmacologic intervention (RR 2.0).
- **Nicotine Replacement Therapy (NRT):**
 - Nicotine gum (RR 1.5)
 - Nicotine patch (RR 1.9)
 - Nicotine nasal inhaler (RR 2.3)
 - Nicotine oral inhaler (RR 2.1)
 - Nicotine lozenge (2 mg: RR 2.0; 4 mg: RR 2.8).

3. Behavioral Interventions:

- Counseling by physician or other medical personnel (10 min) (RR 1.84).
- Intensive group smoking cessation programs (at least 4–7 sessions of 20- to 30-min duration lasting at least 2 and preferably 8 weeks) (RR 1.3).
- Intensive individual counseling (RR 1.7).
- Systemwide cessation tracking and assistance (RR 5.0).
- Telephone counseling (RR 1.6).
- Exclusive E-cigarette use (RR 3.0).

4. E-cigarettes:

- Effective as a tool for cessation unless dual use occurs.
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PROGNOSIS & COMPLICATIONS

- **Risk Reduction Timelines:**
 - Coronary event risk reduction within 6–12 months.
 - Risk of stroke/MI/death from coronary heart disease becomes similar to never smokers after 15 years.
- **Long-term Impact:**
 - Small airway changes reverse in 1–2 years.
 - Large airway changes (mucous hyperplasia) do not reverse.

SPECIAL CONSIDERATIONS

- **Pregnancy:**
 - Vaping/oral use of nicotine is a concern unless used as a strategy to abstain from cigarette smoking.
- **Pediatrics:**
 - Environmental tobacco smoke increases respiratory infections, chronic otitis media, and asthma in children.

KEY PEARLS & CLINICAL TRAPS

- **High-Yield Pharmacology:** Varenicline is the most effective single pharmacologic intervention (RR 3.1).
- **Clinical Trigger:** A clinician's recommendation at the time of acute illness is a powerful trigger for cessation.
- **Nicotine Salts:** These allow for rapid blood concentration and higher doses due to acidic formulation in the mouth reducing irritation.
- **Lung Cancer Risk:** Increases linearly with quantity (cigarettes per day) and logarithmically with duration; risk from older non-filtered cigarettes is not reduced by modern designs.
- **Lower Tar/Nicotine Cigarettes:** Do not reduce disease risk because smokers compensate for lower nicotine delivery by changing puffing patterns or increasing the number of cigarettes smoked.

REFERENCE TABLES

TABLE 465-1

Relative Risks for Current Smokers of Cigarettes AGE Males Lung cancer Coronary heart disease Cerebrovascular disease...

AGE	35–44	45–64	65–74	≥75
Males				
Lung cancer	14.33	19.03	28.29	22.51
Coronary heart disease	3.88	2.99	2.76	1.98
Cerebrovascular disease	2.17	1.48	1.23	1.12
Other vascular diseases			7.25	4.93
Chronic obstructive pulmonary disease (COPD)			29.69	23.01
All causes	2.55	2.97	3.02	2.40
Females				
13.30	18.95	23.65		
1.28	2.08	2.06		
4.98	3.25	3.29		

AGE	35–44	45–64	65–74	≥75
2.27	1.70	1.24		
		6.81		
		38.89		
1.79	2.63	2.87		
Relative Risks for Selected Other Cancers				
Other cancers	Male		Female	
Larynx	14.6		13	
Lip, oral cavity, pharynx	10.9		5.1	
Esophagus	6.8		7.8	
Bladder	3.3		2.2	
Kidney	2.7		1.3	
Pancreas	2.3		2.3	
Stomach	2		1.4	
Liver	1.7		1.7	
Colorectal	1.2		1.2	
Cervix			1.6	
Acute myeloid leukemia	1.4		1.4	

TABLE 465-2

Clinical Practice Guidelines Physician Actions Ask: Systematically identify all tobacco and nicotine use at every visit...

- Physician Actions
- Ask: Systematically identify all tobacco and nicotine use at every visit
- Advise: Strongly urge all smokers to quit
- Identify smokers willing to quit
- Assist the patient in quitting
- Arrange follow-up contact
- Effective Pharmacologic Interventionsa
- First-line therapies
- Nicotine gum (1.5)
- Nicotine patch (1.9)
- Nicotine nasal inhaler (2.3)
- Nicotine oral inhaler (2.1)
- Nicotine lozenge (2 mg: 2.0, 4 mg: 2.8)
- Bupropion (2.0)

- Varenicline (3.1)
- Other Effective Interventionsa
- Physician or other medical personnel counseling (10 min) (1.84)
- Intensive group smoking cessation programs (at least 4–7 sessions of 20- to 30-min duration lasting at least 2 and preferably 8 weeks) (1.3)
- Intensive individual counseling (1.7)
- Systemwide cessation tracking and assistance (5)
- Telephone counseling (1.6) Exclusive E-cigarette use (3.0)