



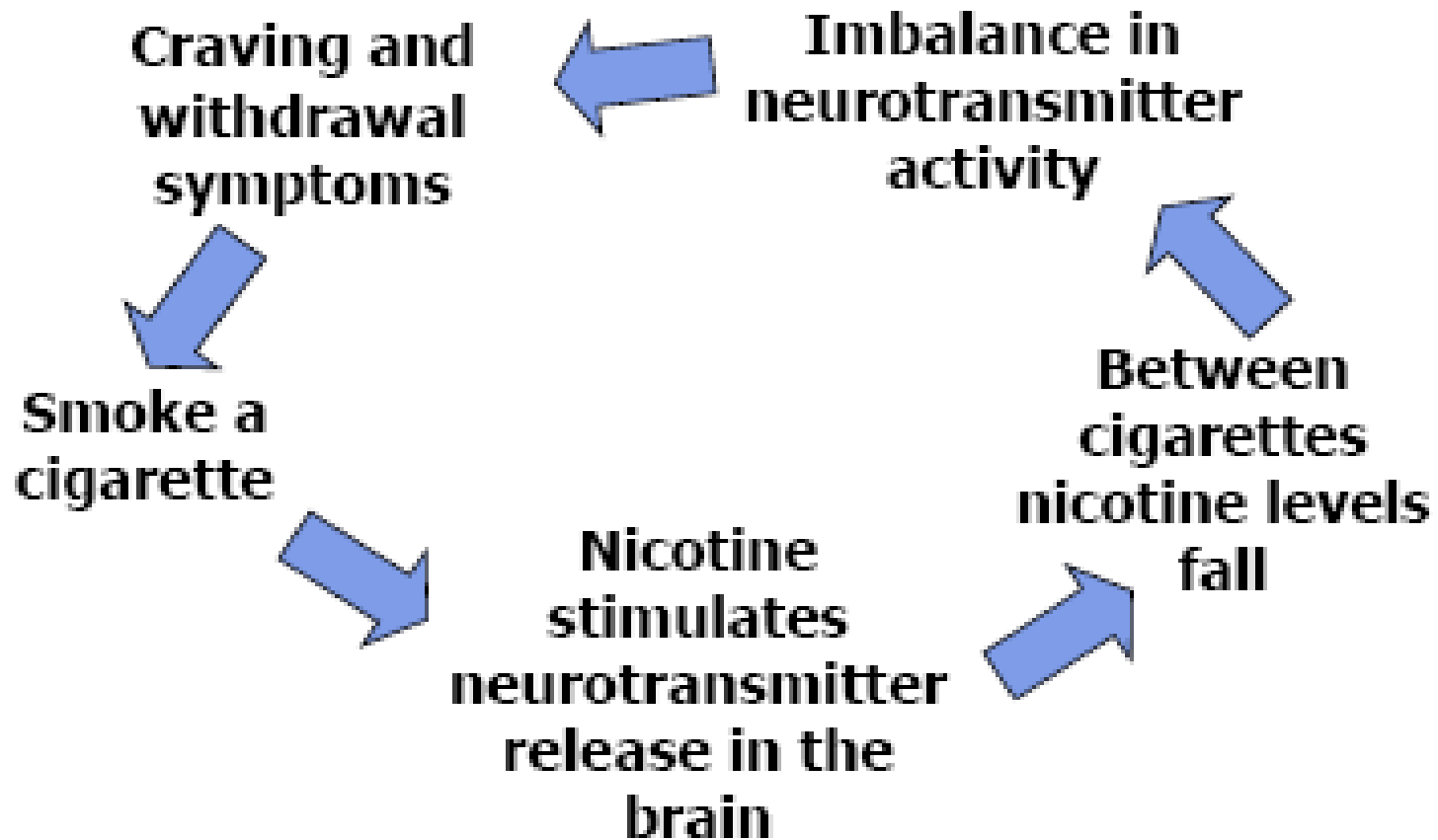
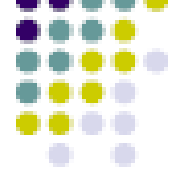
Nicotine replacement therapy

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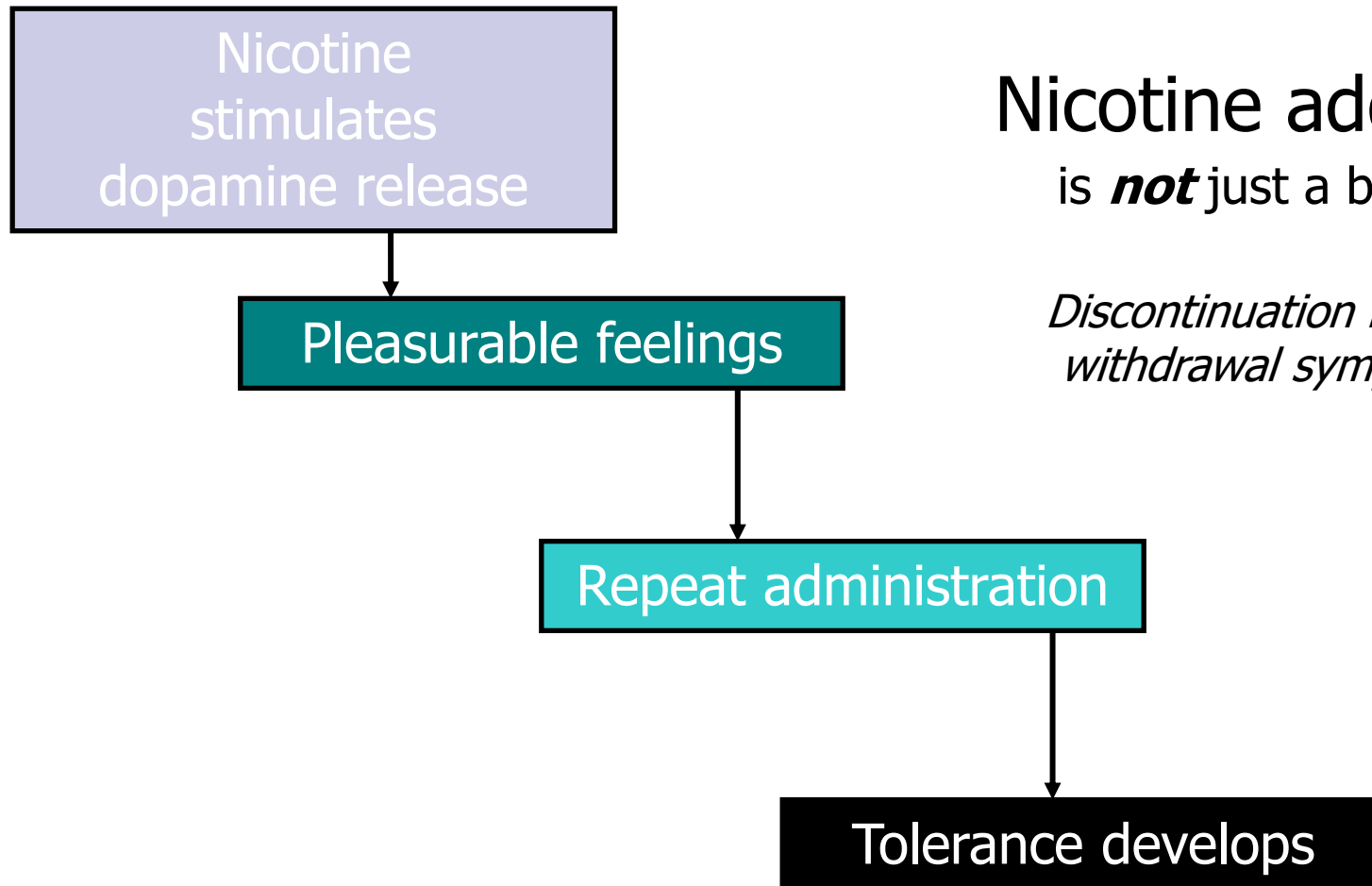
Addiction to nicotine

- An understanding of how nicotine produces addiction and influences smoking behavior provides a necessary basis for smoking cessation therapies.
- Chronic nicotine exposure results in neuroadaptation, that is, the development of tolerance.
- Neuroadaptation is associated with an increased number of brain nicotinic cholinergic receptors.
- Chronic exposure to nicotine also results in changes in gene expression and neural plasticity; which is defined as “ability of the brain to reorganize neural pathways based on new experiences”

Nicotine Addiction



BIOLOGY of NICOTINE ADDICTION: ROLE of DOPAMINE



Nicotine addiction
is ***not*** just a bad habit.

*Discontinuation leads to
withdrawal symptoms.*

DOPAMINE REWARD PATHWAY

Prefrontal cortex

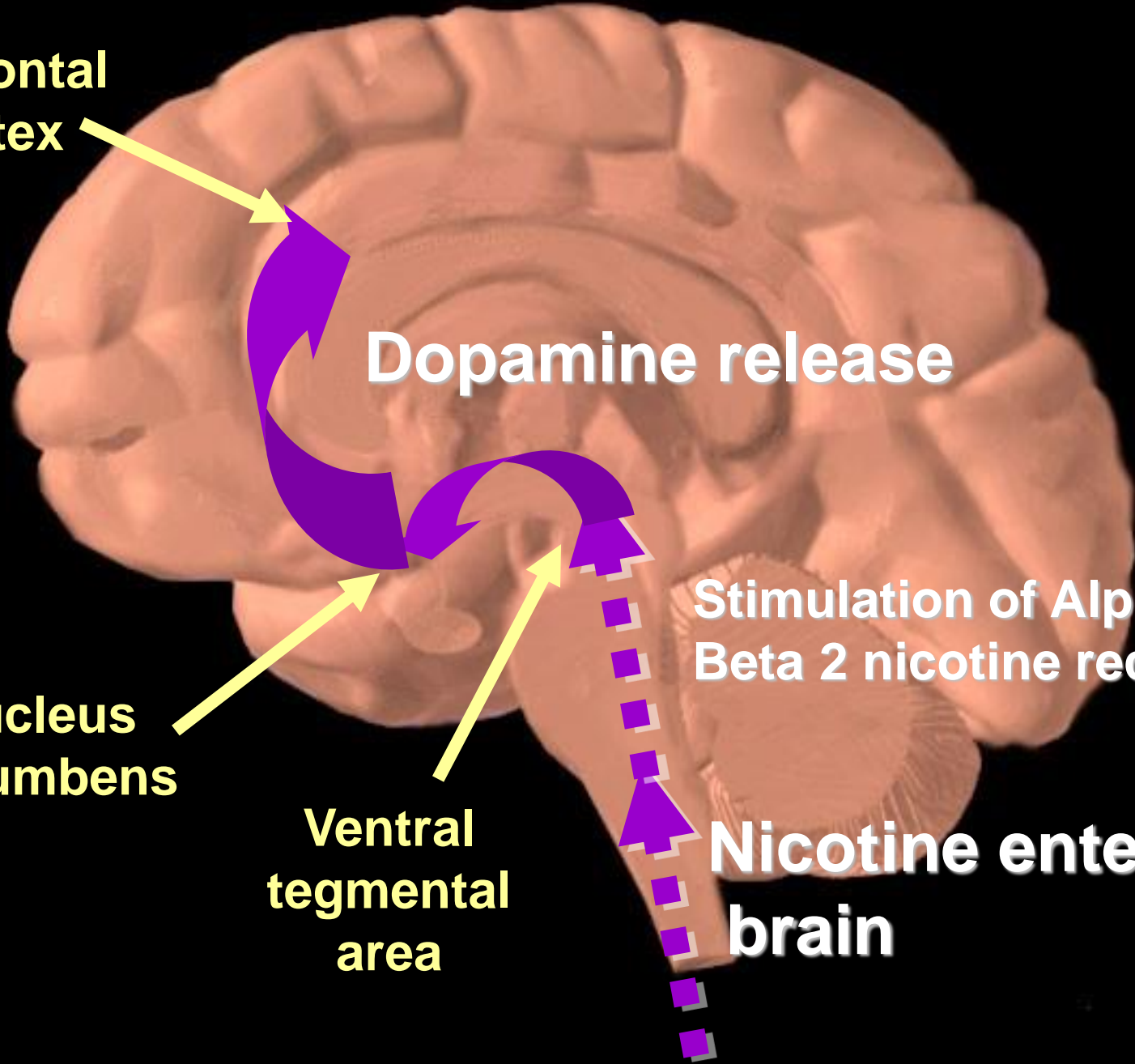
Dopamine release

Nucleus accumbens

Ventral tegmental area

Stimulation of Alpha 4
Beta 2 nicotine receptors

Nicotine enters
brain



Dopamine

- **Dopamine induces feelings of euphoria and pleasure and is responsible for activating the dopamine reward pathway**
- The dopamine reward pathway, as depicted in this simplified diagram, is a network of nervous tissue in the middle of the brain that elicits feelings of pleasure in response to certain stimuli.



Addiction to nicotine

- **Addiction to tobacco is multifactorial:**
- It includes a desire for the direct pharmacologic actions of nicotine, relief of withdrawal symptoms, and learned associations.
- Smokers usually provide different reasons for smoking that could include pleasure, arousal, enhanced vigilance, improved performance, relief of anxiety or depression, reduced hunger, and control of body weight



Addiction to nicotine

- The absence of nicotine due to smoking cessation results in subnormal release of dopamine and other neurotransmitters.
- Nicotine withdrawal results in the state of deficient dopamine responses to novel stimuli in general and a state of malaise and inability to experience pleasure.
- This leads to development of nicotine withdrawal symptoms.

NICOTINE PHARMACODYNAMICS: WITHDRAWAL EFFECTS

- Depression
- Insomnia
- Irritability/frustration/anger
- Anxiety
- Difficulty concentrating
- Restlessness
- Increased appetite/weight gain
- Decreased heart rate
- Cravings*

Most symptoms
peak 24–48 hr
after quitting and
subside within
2–4 weeks.

Timeline of health benefits after stopping smoking

Time line (After ...)	Health Benefit
72 hours	Breathing becomes easier. Bronchial tubes begin to relax and energy levels increase.
1 month	Skin appearance improves, owing to improved skin perfusion.
3-9 months	Cough, wheezing, and breathing problems improve and lung function increases by up to 10%.
1 year	Risk of a heart attack falls to about half that of a smoker.
10 years	Risk of lung cancer falls to about half that of a smoker.
15 years	Risk of heart attack falls to the same level as someone who has never smoked.

Source: <http://www.ash.org.uk/stopping-smoking/quitting-smoking>



Management of smoking cessation

Behavioural therapy

and

Nicotine replacement therapy

Or nicotine receptors antagonists

Nicotine replacement therapy (NRT)

- Provides smoker with nicotine without using tobacco, thereby relieving nicotine withdrawal symptoms.
- NRT products differ in the route of delivering nicotine to the circulation.
- Nicotine is absorbed transdermally with the nicotine skin patch, through the nasal mucosa by the nasal spray, or through the oral mucosa with the nicotine chewing gum, nicotine lozenge, or nicotine inhaler.
- Nicotine patches are more tolerated than nasal spray and provides the most continuous delivery of nicotine of nicotine replacement therapies.



Nicotine replacement therapy (NRT)

- Principle:

Many of the difficulties in smoking cessation stems from problems posed by nicotine withdrawal.



Nicotine Replacement Therapy (NRT)

- Reliably attenuates severity of withdrawal, making it easier for would-be ex-smokers to cope with abstinence while unlearning the deeply ingrained habit elements of smoking

Selected Medication Options: Monotherapy and Combination Therapy

Medication	Number of arms	Estimated odds ratio (95% C.I.)	Estimated abstinence rate (95% C.I.)
Nicotine Patch	32	1.9 (1.7 - 2.2)	23.4% (21.3 - 25.8)
Bupropion SR	26	2.0 (1.8 - 2.2)	24.2% (22.2 - 26.4)
Varenicline	5	3.1 (2.5 - 3.8)	33.2% (28.9 - 37.8)
Patch (>14 wks) + NRT (gum or spray)	3	3.6 (2.5 - 5.2)	36.5% (28.6 - 45.3)
Patch + Bupropion SR	3	2.5 (1.9 - 3.4)	28.9% (23.5 - 35.1)



NRT - Therapeutic Effect

- The primary therapeutic effect of NRT is to reduce the severity of symptoms associated with smoking cessation.
- NRT provides steady levels of nicotine and may reduce the pleasurable effects of tobacco desired by smokers.
- NRT makes it easier to cope in difficult situations.

Nicotine patches

- Transdermal patch (waterproof)
- Nicotine Replacement Therapy (NRT)
- To overcome withdrawal symptoms
- 24-hour patch to deliver constant nicotine levels
- 12 week weaning program that reduces and eliminates body's dependence for nicotine
- Clinically-proven to be better than willpower alone
- **2-4 times the success rate of placebo patches**

Hajek P, West R, Foulds J, Nilsson F, Burrows S, Meadow A. Randomized comparative trial of nicotine polacrilex, a transdermal patch, nasal spray, and an inhaler. *Arch Intern Med.* 1999;159:2033-2038.

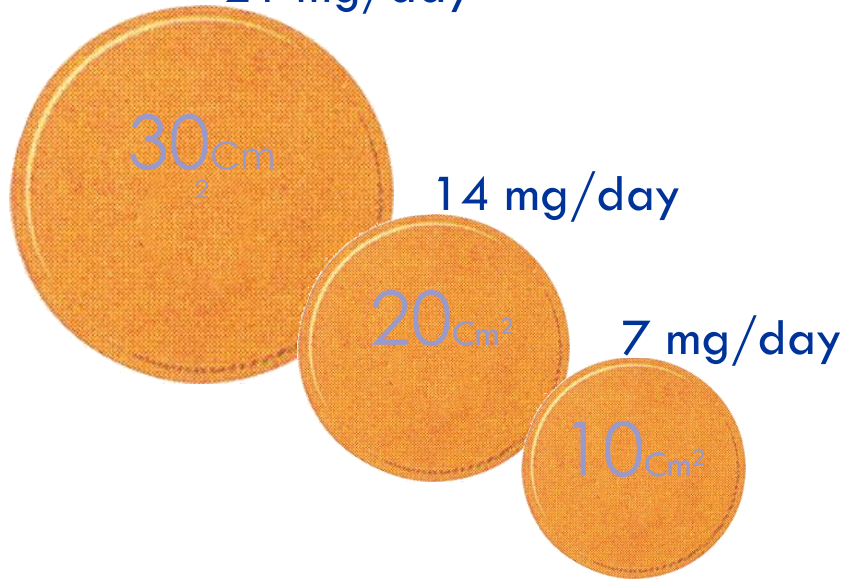
Nicotine patches

21 or 24mg/24hrs, 14mg/24hrs, 7mg/24hrs

21 or 24mg/16hrs, 14mg/16hrs, 7mg/16hrs

15mg/24hrs, 10mg/24hrs, 5mg/24hrs

21 mg/day



Precautions

- ❑ women who are pregnant or breast feeding
- ❑ smokers with cardiovascular conditions

Doctors should weigh risks/vs benefits when prescribing NRT to pregnant women or smokers with cardiovascular conditions.

- ❑ smokers using other nicotine replacement products
- ❑ children
- ❑ non-smokers
- ❑ smokers of fewer than 10 cigarettes a day

Nicotine patches– Application

- Apply to non-hairy, clean, dry skin
- Rotate between sites (this helps to reduce the risk of skin irritation)
- Choose a flat surface
- Avoid joints or skin folds
- Replace the same time everyday



**DO NOT SMOKE WHILE
USING THE PATCH**

Why a 24-hour patch ?

- ▶ Many of the dependent smokers
 - Either smoke just before to go to bed,
 - Or wake up at night for smoking
 - Or wake up early in the morning to have a cigarette

Night smoking is a criteria for strong addiction to nicotine

Aubin, H. J. Comparison of the effects of a 24-hour nicotine patch and a 16-hour nicotine patch on smoking urges and sleep. *Nicotine.Tob.Res.* 8.2 (2006): 193-201.

Nicotine Lozenges

- Nicotine Lozenges are new products that have similar efficacy to nicotine gum but it is easier to use and does not require special technique for optimal use.
- It also delivers more nicotine than equivalent dose of the gum.
- Unlike nicotine gum, smokers with dentures or poor dentition can use Lozenges.



High level of smoking addiction

Combination of behavioural therapy with
nicotine patches and nicotine lozenges
(used for cravings)

Or

Combination of varenicline with behavioural
therapy




For patients with ischaemic heart disease with moderate or high level of addiction:

The best approach is to start with
behavioural therapy

If failed, you can start with nicotine patches

Varenicline (Champix, Chantix)

- a partial agonist at the alpha4beta2 subunit of the nicotinic acetylcholine receptor.
- This drug binds to nicotinic receptors leading to reduction of withdrawal symptoms and decrease rate of cigarettes' nicotine binding to these receptors.



Varenicline (Champix, Chantix)

- This medication has shown a good abstinence rate when compared to nicotine patches, but the difference is small when compared to combined nicotine patches with gum or lozenges.

Varenicline (Champix, Chantix)

- Week 1: Starting dose: 0.5mg once daily for three days, then 0.5mg twice daily for four days.

Smokers have to decide on quit day during this week.

- Then
1mg twice daily for 8-12 weeks.

Contraindications

- Varenicline has not been studied in children and should not be taken by young people who are under 18 years of age.
- Breast feeding. Varenicline may pass into breast milk.

Either use an alternative therapy or follow other ways of feeding the baby may be appropriate if she is currently taking the drug.



Precautions for varenicline use

- kidney problems or on dialysis. It may be appropriate for prescribe a lower dose.
- Pregnancy. The effects of Varenicline on the foetus are not known and it would be better if the lady quits smoking before getting pregnant.



Precautions for varenicline use

- Depression or any psychiatric illnesses in the past.

Varenicline: Side effects

- Vomiting and nausea
- Headaches
- Sleep disturbances and atypical dreams
- Gas (wind)
- Changes in the way food tastes
(Dysgeusia)
- Constipation
- Suicidal thoughts

Bupropion (Zyban)

- Available as an antidepressant in the United States since 1989, is believed to act by enhancing central nervous system noradrenergic and dopaminergic release.
- A sustained-release formulation of the drug is licensed as an aid to smoking cessation (Zyban); it is identical to the antidepressant Wellbutrin SR and is available as a generic drug.

Bupropion (Zyban)

- **Safety** — The most common side effects of [bupropion](#) are insomnia, agitation, dry mouth, and headache.
- A more serious side effect is seizure, which can occur because bupropion reduces the seizure threshold.
- In clinical trials, the risk of seizure was 0.1 percent, and **the drug is contraindicated in patients with a seizure disorder or predisposition to seizure.**



The Fagerstorm Scoring:

1. How soon after you wake up do you smoke your first cigarette?
 - Within 5 minutes (3 points)
 - 5 to 30 minutes (2 points)
 - 31 to 60 minutes (1 point)
 - After 60 minutes (0 points)
2. Do you find it difficult not to smoke in places where you shouldn't, such as in church or school, in a movie, at the library, on a bus, in court or in a hospital?
 - Yes (1 point)
 - No (0 points)
3. Which cigarette would you most hate to give up; which cigarette do you treasure the most?
 - The first one in the morning (1 point)
 - Any other one (0 points)
4. 4. How many cigarettes do you smoke each day?
 - 10 or fewer (0 points)
 - 11 to 20 (1 point)
 - 21 to 30 (2 points)
 - 31 or more (3 points)
5. 5. Do you smoke more during the first few hours after waking up than during the rest of the day?
 - Yes (1 point)
 - No (0 points)
6. 6. Do you still smoke if you are so sick that you are in bed most of the day or if you have a cold or the flu and have trouble breathing?
 - Yes (1 point)
 - No (0 points)

Scoring: 7–10 points = highly dependent; 4–6 points = moderately dependent; less than 4 points = minimally dependent.