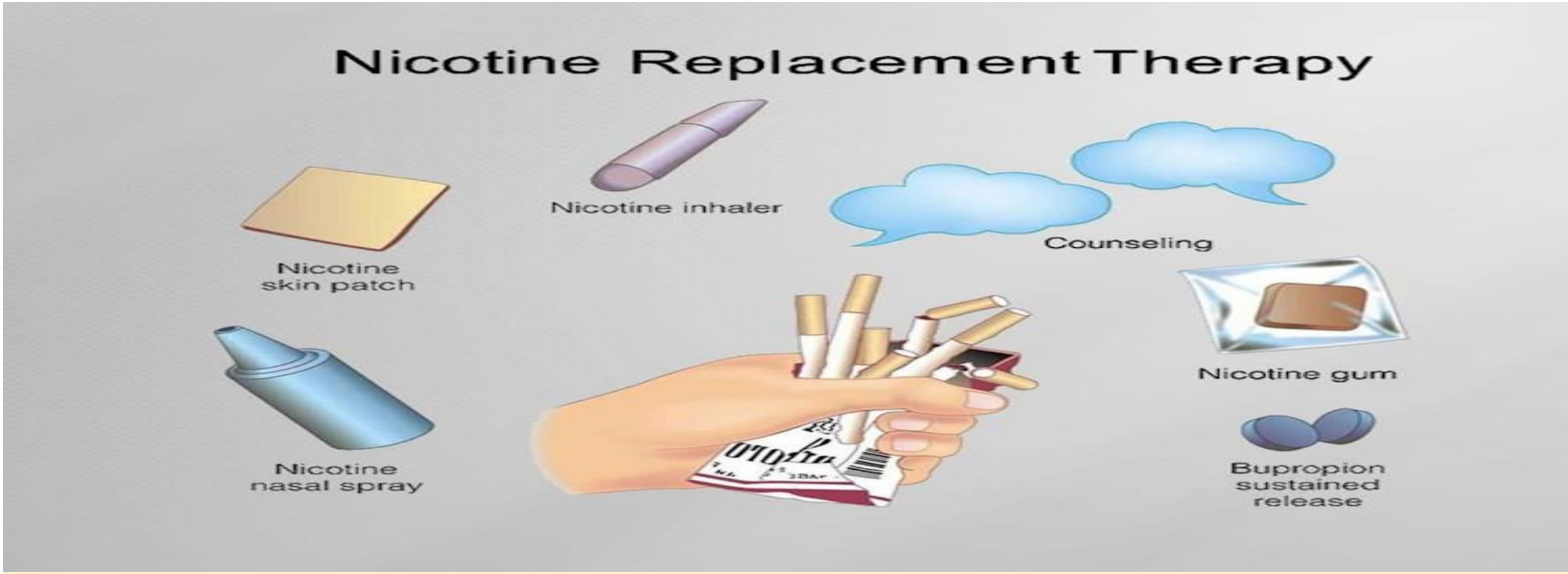

Clinical Pharmacy

Assist Lec. Zainab Abdul Hameed

Lecture 7

CIGARETTE COMPOUND

TAR

ARSENIC

LEAD

FORMALDEHYDE

MERCURY

POLONIUM-210

CARBON MONOXIDE

NICOTINE

CADMIUM

ACETONE

THE RISKS OF SMOKING

BRAIN DAMAGE
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LUNG CANCER
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CANCER
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LARYNX CANCER
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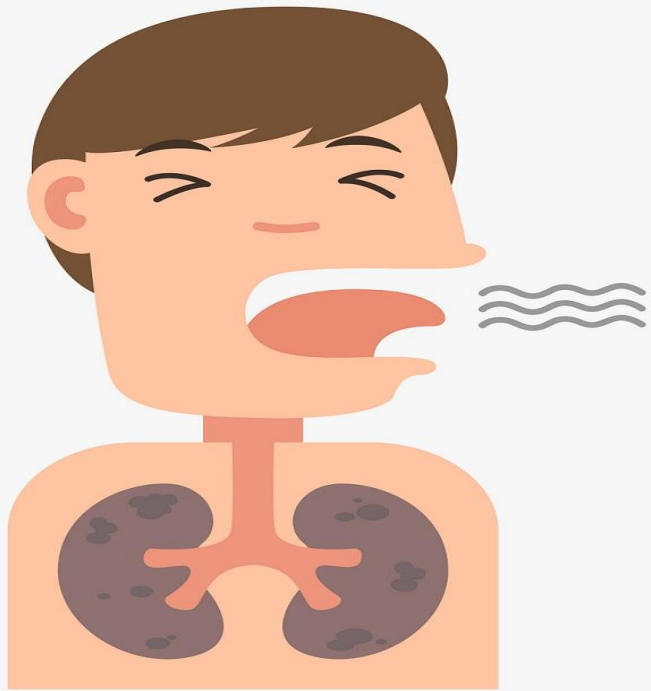

BONE AND MUSCLE
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SEXUAL DYSFUNCTION
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HEART DISEASE
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GI DISEASE
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DEATH
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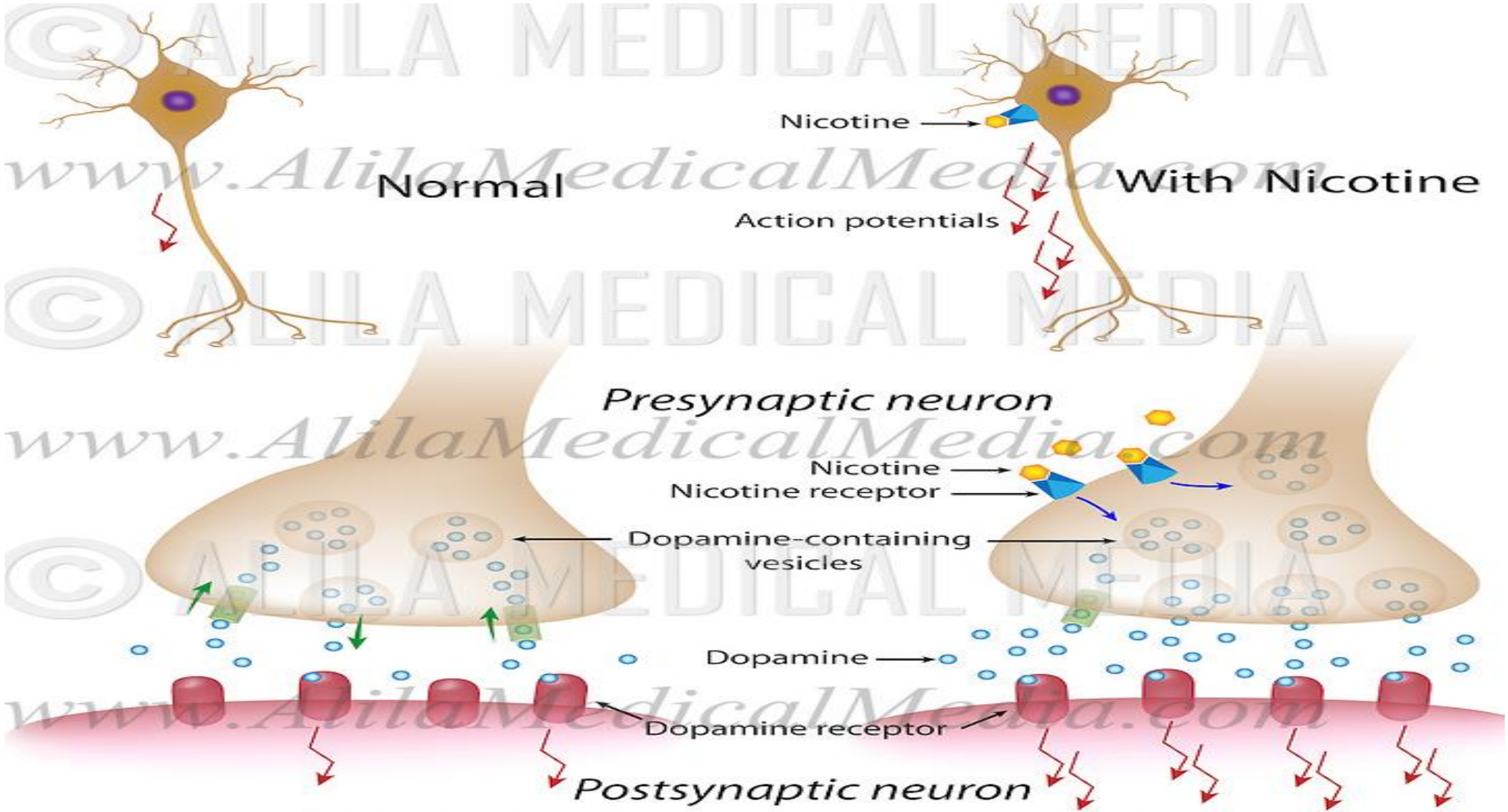
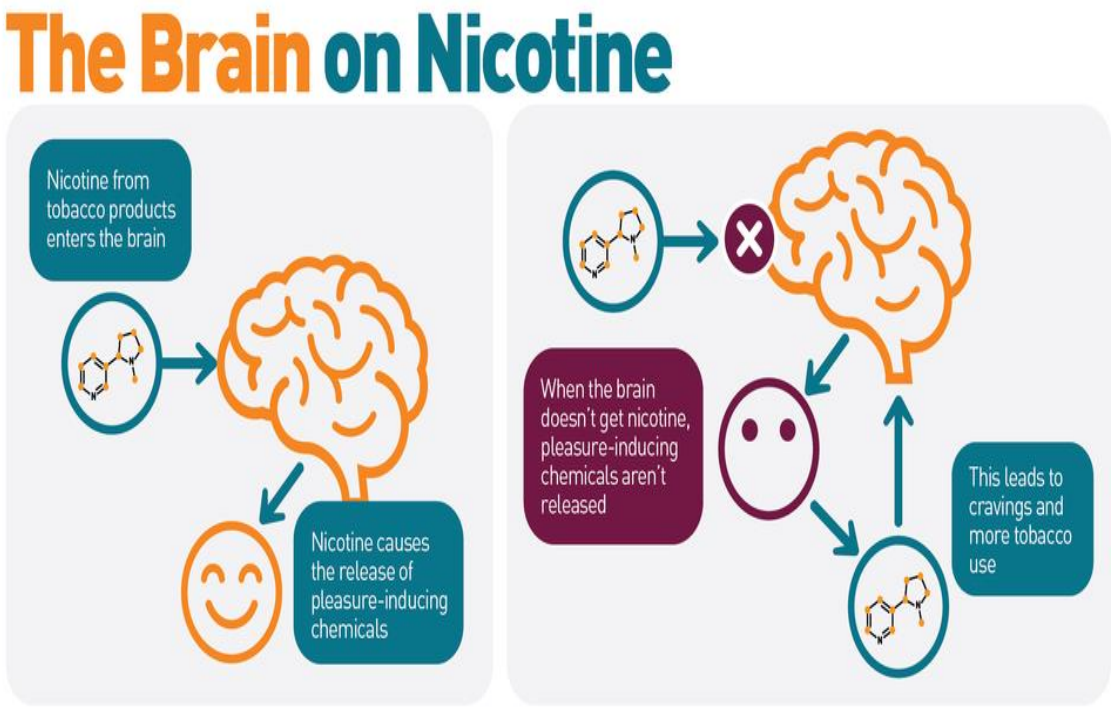
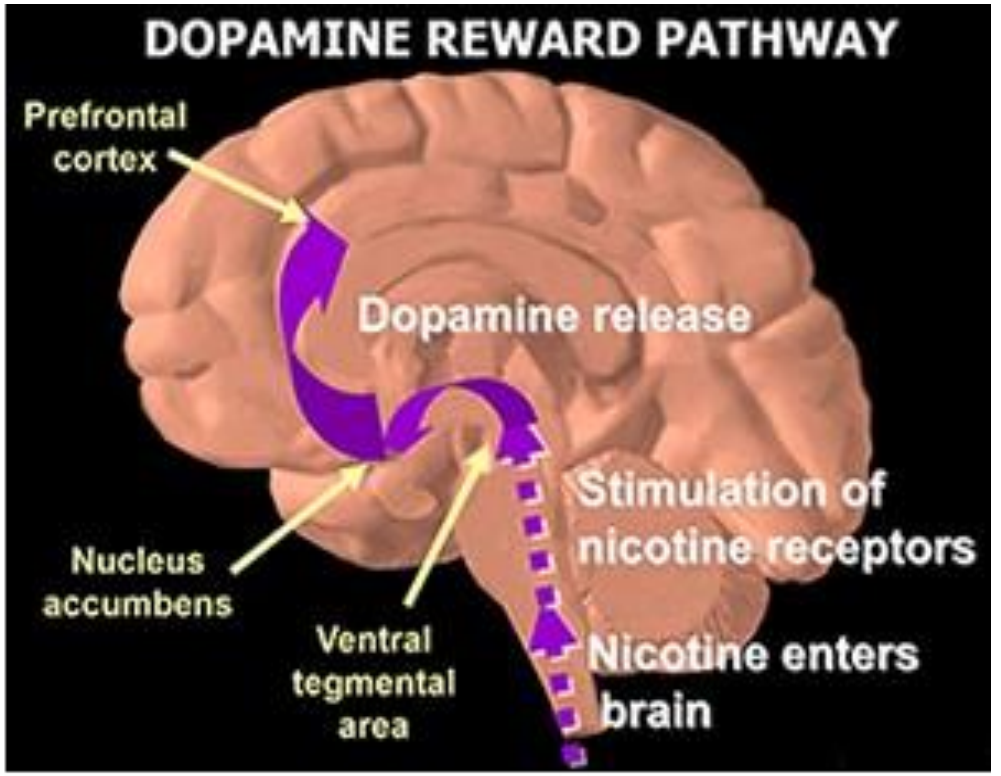


- **Nicotine** is a ganglionic cholinergic-receptor agonist with dose-dependent pharmacologic effects, including:

- ✓Stimulation and depression in the central and peripheral nervous systems.
- ✓Respiratory stimulation.
- ✓Skeletal muscle relaxation.
- ✓Catecholamine release by the adrenal medulla.
- ✓Peripheral vasoconstriction and increased blood pressure, heart rate, cardiac output, and oxygen consumption.

- ✓Low doses produce increased alertness and improved cognitive functioning.
- ✓Higher doses stimulate the “reward” center in the brain.





NICOTINE WITHDRAWAL

- • Abrupt cessation of nicotine results in withdrawal symptoms usually within **24 hours**, including anxiety, cravings, difficulty concentrating, frustration, irritability, hostility, insomnia, and restlessness.

SMOKING CESSATION AND NICOTINE REPLACEMENT THERAPY

- Community pharmacies have an important role to play in local education and treat large numbers of people who use tobacco.

- They may be able to meet the needs of disadvantaged groups and those who have difficulty accessing other community services.

- They sell a range of nicotine replacement therapy (NRT) products alongside behavioural support, and supply of ***varenicline*** or ***bupropion*** via patient group directions.

- Smokers who use NRT are about **twice** as likely to stop long-term smoking and up to **six times** more likely to succeed when NRT and behavioural support are combined.

- **NRT** should not be used at the same time as *bupropion* or *varenicline*.

- Some patients do appear to benefit from using a combination of NRT products (e.g. both a patch and a mouth spray).

- It is important to recognise that many attempts to stop smoking fail, but that this should not dissuade people from further attempts.

- It is estimated that over a **third** of smokers attempt to quit each year and that with support 19% of these people will have quit 1 year after taking steps to do so.

Smoking cessation: tips for customers about quitting

- ✓• Set a quit date, prepare for it and stick to it.
- ✓•Get support and advice from friends, family and health professionals.
- ✓• Make a list of reasons to quit.
- ✓• Consider NRT for the first few weeks.
- ✓• Avoid situations where you will find it difficult not to smoke.
- ✓• Change your routine to distract yourself from times and places you associate with smoking.

- ✓ Stop completely if you can, rather than cut down.
- ✓ Get rid of all cigarettes, lighters and ashtrays before your quit date.
- ✓ Ask people not to smoke around you and tell everyone you are quitting.
- ✓ Keep busy, especially when cravings start; exercise can act as a distraction.
- ✓ Reward yourself for not smoking.
- ✓ Calculate how much money you will save and plan how you will now spend it.

Nicotine replacement therapy: formulation options

- A range of NRT products are available and vary in the ease and frequency of use, the speed of nicotine release and the nicotine dose.

- All products appear to increase the chances of success if used correctly. Enabling choice to fit with the person's preference and lifestyle is important.
- Smokers should be **advised** not to smoke while using NRT products.

- The main adverse effects are similar to overconsumption of cigarettes and include nausea, dizziness, flu-like symptoms, palpitations, dyspepsia, insomnia and vivid dreams.

Nicotine product formulations that can be provided for smoking cessation:

Patches

- • Discreet – easy to wear and forget about.
- • Continuous nicotine release – suitable for regular smokers.
- • 16-hour patch (removed at night) – reduces insomnia.
- • 24-hour patch – good for early morning cravings.
- • Three strengths – allows a step-down reduction programme.
- • Can cause skin irritation.

Chewing gum

- • Flexible regimen – controls cravings as they occur.
- • Various flavours – allows customer preference.
- • Various strengths – allows step-down reduction programme.
- • Chewed slowly – to release nicotine and then ‘park’ gum between cheek and gum.

Nasal spray

- • Fast acting – helpful for highly dependent smokers.
- • Usually advised to use twice an hour for 16 h.
- • Local side effects (sore throat and rhinitis) – usually pass after first few days.
- • Follow product instructions.

Oral spray

- • Used when urge to smoke appears.
- • Fast acting.
- • Follow instructions on maximum use.

Sublingual tablet

- • Discreet – placed under tongue and dissolves over 20 min.
- • Dose variation – one or two (2-mg) tablets may be used per hour.
- •Sublingual – sucking or chewing the tablet will reduce its effectiveness.

Lozenge

- • Various strengths – allows step-down reduction programme.
- • Highest strength (4 mg) – good for smokers who start within 30 min of waking.
- • Sucked until taste is strong – lozenge then ‘parked’ between cheek and gum.

Licenced indications for OTC nicotine replacement therapy

- ✓NRT can be recommended for adults and children aged 12 years or over, for pregnant women and for those who are breastfeeding.

- ✓The duration of treatment with NRT is usually 8–12 weeks (depending on which form of NRT is used and which dose is initiated), followed by a gradual reduction in dose.

- ✓Higher-doses NRT may be more effective in people who are more highly dependent on cigarettes, and more dependent smokers may need to use NRT for longer.

Drug	Dosing	Duration	Comments/Monitoring Parameters
Nicotine replacement therapies (NRTs)			
Nicotine patch	Based on cigarettes smoked per day: >10 cigs/day: Step 1: 21 mg/day: Weeks 1–6 Step 2: 14 mg/day: Weeks 7–8 Step 3: 7 mg/day: Weeks 9–10 <10 cigs/day: Step 2: 14 mg/day: 6 weeks Step 3: 7 mg/day: 2 weeks	10 weeks	Tapering dosing is considered optional after 6 weeks on a dose Patch can be worn for up to 24 hours per day If patient has sleep disturbances, remove patch at night and place one patch in morning (~16 hours per day) If waking up with cravings, patch should be worn for 24 hours Recommended to place patch on determined quit day Place a new patch on each day, hold patch on for 10 seconds to help adherence Rotate patches to avoid skin irritation
Nicotine gum	1st cigarette <30 minutes after waking: 4 mg 1st cigarette >30 minutes after waking: 2 mg Weeks 1–6: 1 piece of gum every 1–2 hours prn Weeks 7–9: 1 piece every 2–4 hours prn Weeks 10–12: 1 piece every 4–8 hours prn Then stop Do not exceed 24 pieces/day	12 weeks	Continuous use can lead to adverse effects (pyrosis, nausea, hiccups) 4 mg strength has shown to be more efficacious in heavy smokers over 6-week time period If patient uses with a cigarette, there is no major risk Counseling on proper use of gum: Repeat process until peppery sensation does not reoccur Use alternate sides of mouth when using chew and park method Park between cheek and gum after a peppery sensation becomes apparent Do not eat or drink 15 minutes before or during use of gum Chew each piece slowly
Lozenge available as Nicorette lozenge or Nicorette mini lozenge	1st cigarette <30 minutes after waking: 4 mg 1st cigarette >30 minutes after waking: 2 mg Weeks 1–6: 1 lozenge by mouth every 1–2 hours prn Weeks 7–9: 1 lozenge by mouth every 2–4 hours prn Weeks 10–12: 1 lozenge by mouth every 4–8 hours prn Then stop Do not exceed 20 lozenges/day	12 weeks	Counseling points: Do not eat or drink anything 15 minutes prior to or during lozenge use Allow the lozenge to dissolve slowly, approximately 20–30 minutes Nicotine release could create a tingling or warm sensation Do not chew or swallow the lozenge Periodically rotate the lozenge to different areas of the mouth
Nicotine oral inhaler + cartridge plus mouthpiece (Nicotrol®)	24–64 mg (6–16 cartridges) per day 1. Stop smoking completely before use 2. Use device by frequent continuous puffing (20 minutes) and use as needed (dosing is very individualized) based on nicotine needed 3. Recommended duration of treatment is 3 months 4. Gradual daily dose taper over 6–12 weeks	3–6 months	Patients should stop smoking prior to starting this product Most successful patients in trials; use ranged from 6 to 16 cartridges per day, 20 minutes continuous puffing Recommended duration of treatment: 3 months with subsequent weaning with gradual reduction over 6–12 weeks Treatment longer than 6 months has not been studied Precautions: patients with asthma, chronic pulmonary disease, history of recent myocardial infarction, serious arrhythmias, or worsening angina Pregnancy Category D
Nicotine metered nasal spray (Nicotrol NS®)	One spray (0.5 mg nicotine/spray) into each nostril one to two times each hour when craving cigarette Max. dose: 10 sprays per hour (max. of 80 sprays per day)	3 months	Two sprays is considered 1 dose Treatment duration is 3 months; safety beyond 6 months has not been studied Counseling: Breathe normally while administering spray, do not sniff or inhale deeply while administering spray For best results, use at least 16 sprays per day which has been found as the minimum effective dose

(*Continued*)

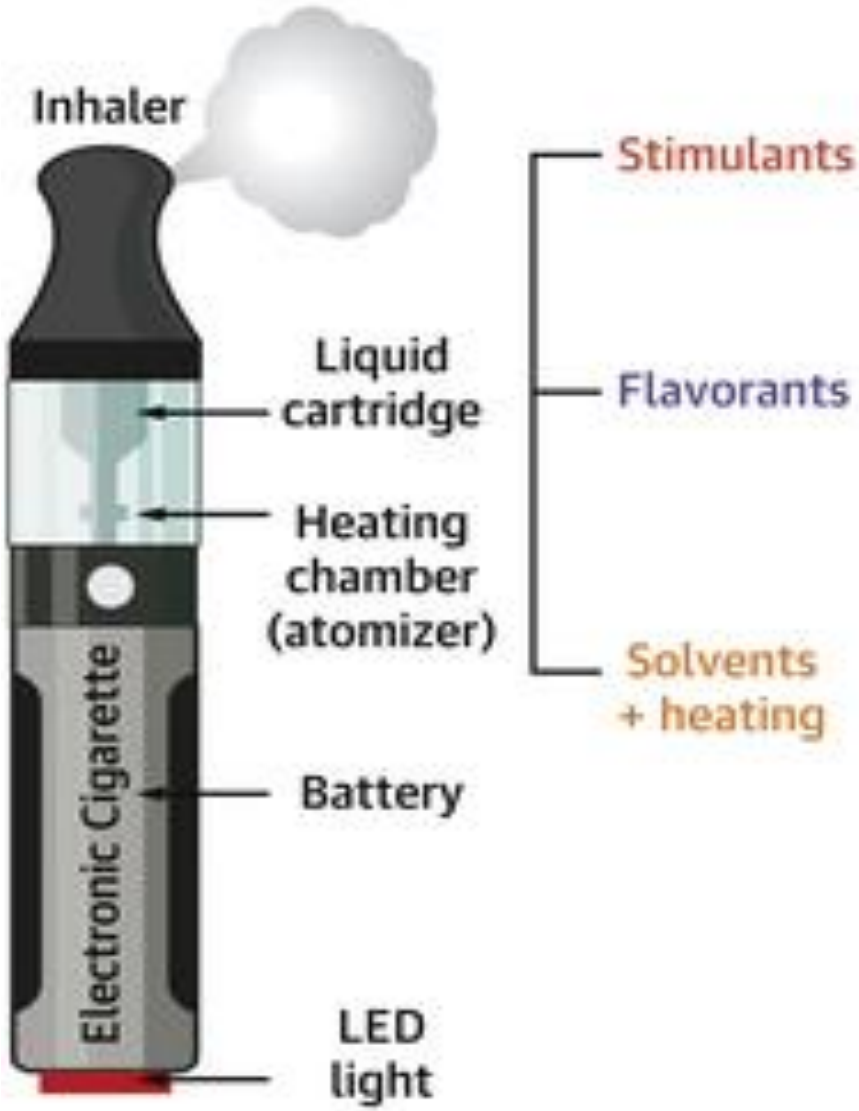
Positive messages for prospective and new non-smokers

- ✓ Giving up smoking reduces the risk of developing smoking-related illness.
- ✓ 8 hours after quitting, nicotine and carbon monoxide levels in the blood are reduced by half and oxygen levels return to normal.
- ✓ After 24 h, carbon monoxide is eliminated.
- ✓ After 48 h, nicotine is eliminated.
- ✓ After 3 days, breathing becomes easier.
- ✓ After 2–12 weeks, circulation is improved and smokers' coughs start to get better.

- ✓• After 6 months, lung efficiency will have **improved by 5–10%.**
- ✓• After 5 years, the risk of having a heart attack is **half** of that of a smoker.
- ✓• After 10 years, the risk of heart attack is **the same** as that of a non-smoker.
- ✓• After 10–15 years, the risk of developing lung cancer is only slightly greater than that of a non-smoker.
- ✓• Research has shown that people who stop smoking before the age of 35 years survive about as well as lifelong non-smokers.

E-cigarettes containing nicotine (vapes, e-cigs)

- An EC is a device for inhaling nicotine in a vapour (hence vaping). They heat a liquid that contains nicotine and propylene glycol or vegetable glycerine (sometimes both) with a flavouring.
- The long-term safety of electronic cigarettes is **unknown**, particularly if used recreationally, as this results in nicotine addiction and the 'flavours' or vapourised compounds inhaled may be potentially **harmful**.
- Certain ingredients were banned, including colourings, caffeine and taurine, and there are new labelling requirements and warnings.
- E-liquids are restricted to a maximum nicotine strength of **20 mg/ml** and EC tanks to a maximum of **2 ml** of liquid.

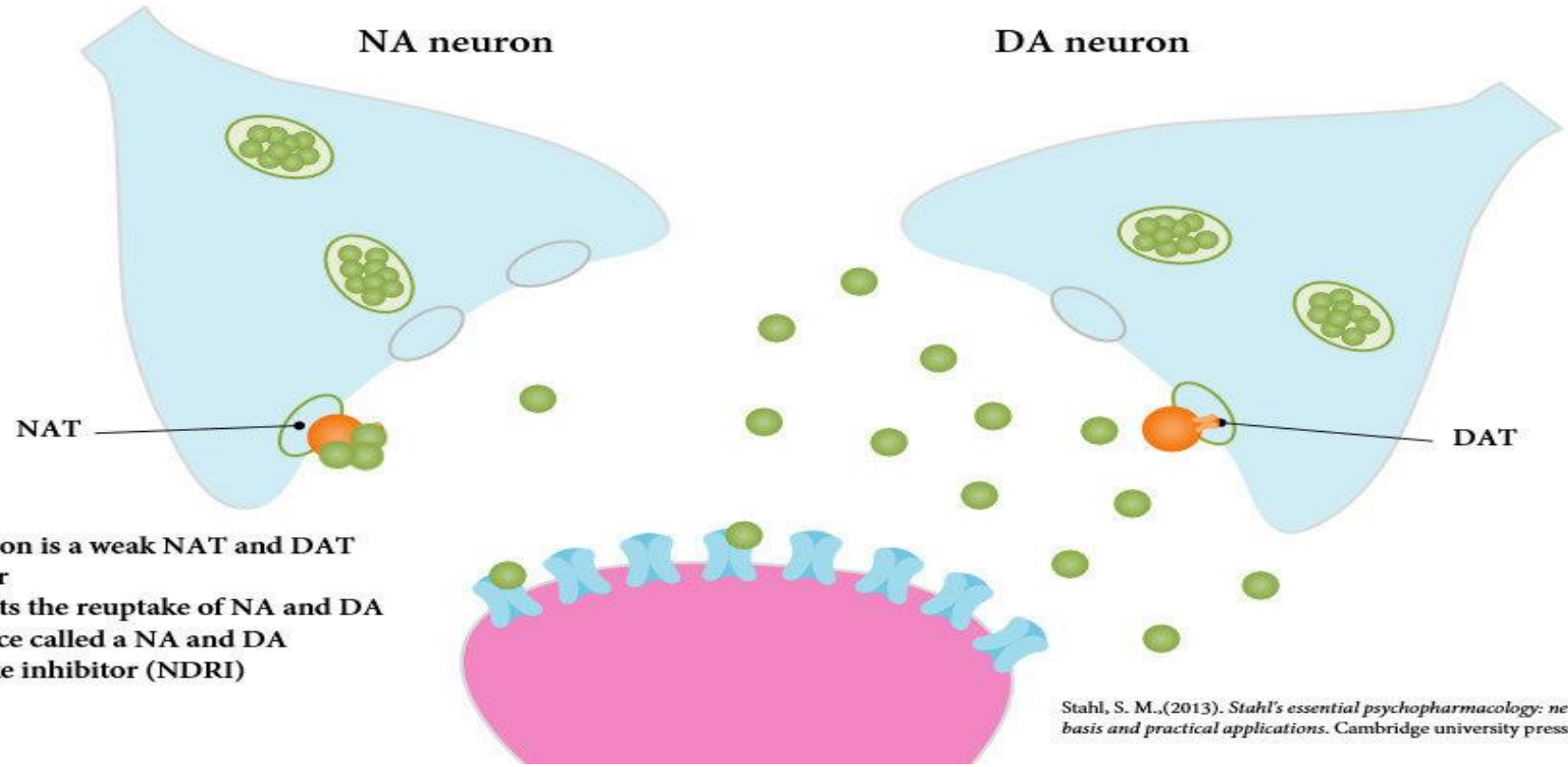


Constituents	Potential Cardiovascular Effects
Stimulants Marijuana Nicotine	**Sympathetic activation** ↑Heart rate ↑Blood pressure **Vascular injury** Endothelial dysfunction Oxidative stress Inflammation **Thrombogenicity** Oxidative stress Platelet activation **Arrhythmia** Abnormal calcium handling **Cardiac dysfunction** Direct cellular toxicity **Hypertension** **Other major organ effects** Carcinogenesis Lung injury
Flavorants Menthol Mango Cinnamon Butter (diacetyl) ...	
Solvents + heating Propylene glycol Glycerin Aldehydes (e.g., acrolein) Heavy metals Volatile organic compounds Particulate matters Other toxins	

Bupropion and Varenicline

- • Bupropion sustained release (SR) inhibits neuronal reuptake, and potentiates the effects of norepinephrine and dopamine. Its use is contraindicated in patients with current or past seizure disorder, current or prior diagnosis of bulimia or anorexia nervosa, and use of a monoamine oxidase inhibitor within the last 14 days.
- ✓✓Side effects of bupropion may include neuropsychiatric symptoms including depression, anxiety, agitation, hostility, suicidal thoughts/behavior, and attempted suicide.

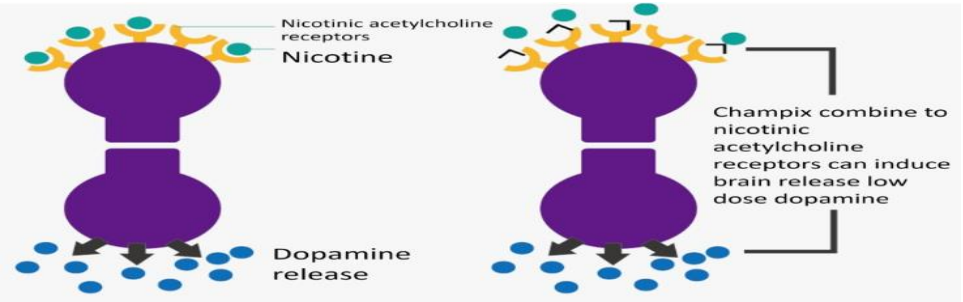
MOLECULAR ACTION OF BUPROPION



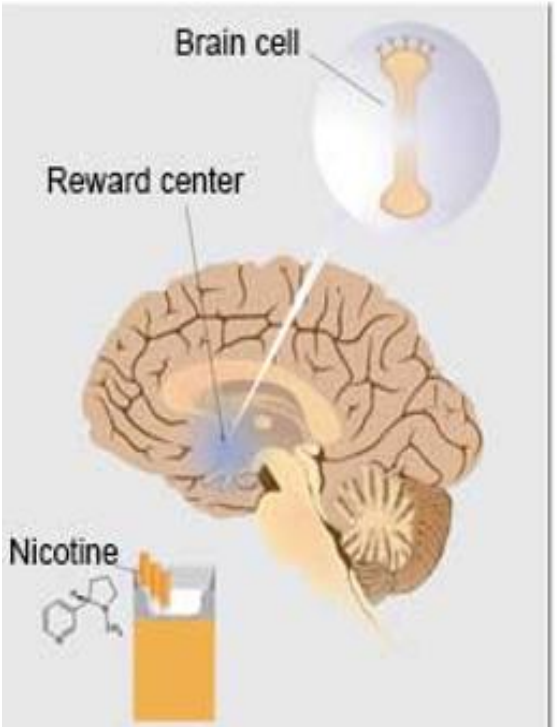
- **Bupropion is a weak NAT and DAT inhibitor**
- **It inhibits the reuptake of NA and DA and hence called a NA and DA Reuptake inhibitor (NDRI)**

Stahl, S. M.,(2013). *Stahl's essential psychopharmacology: neuroscientific basis and practical applications.* Cambridge university press.

- • **Varenicline** is a partial agonist that binds selectively to nicotinic acetylcholine receptors with a greater affinity than nicotine, producing a lesser response than nicotine.

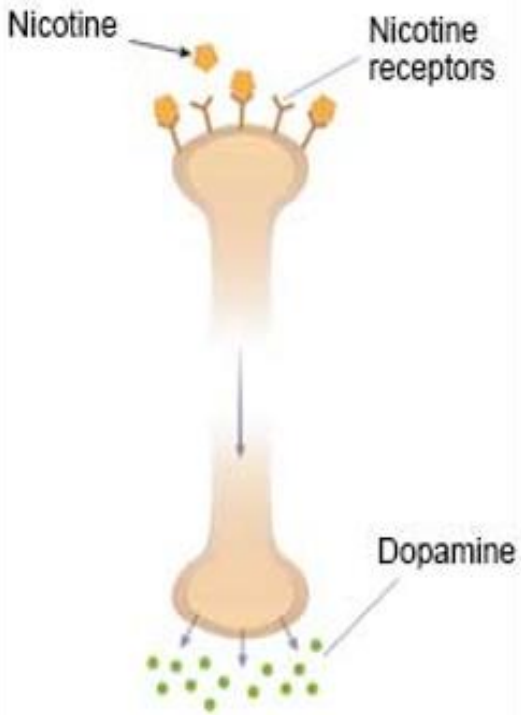


- It is also FDA-approved for 6 months of maintenance therapy. It may result in a higher rate of cessation than bupropion and single forms of NRT. It may be equally effective with combination NRT.
- ✓✓**Side effects** include suicidal thoughts and erratic and aggressive behavior. It may also be associated with a small increased risk of cardiovascular events.



When you smoke, nicotine activates cells in the reward center of the brain.

Brain cell when smoking



Nicotine attaches to brain cell receptors.

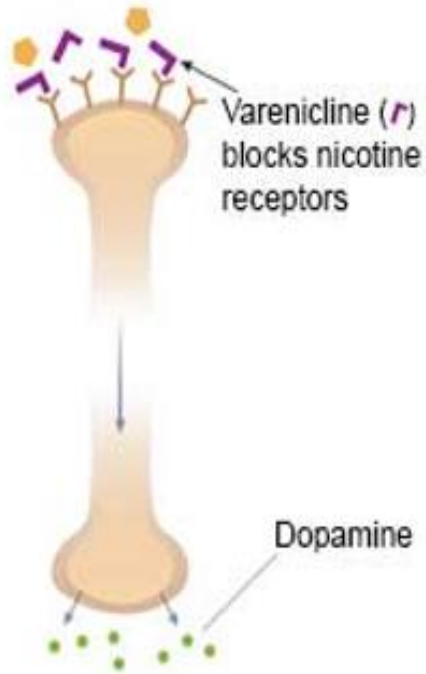
This causes dopamine to release, making you feel good.

Brain cell when not smoking

When you quit smoking, there is no nicotine attaching to the receptors.

Less dopamine is released, which can cause withdrawal symptoms and cravings.

Brain cell with varenicline

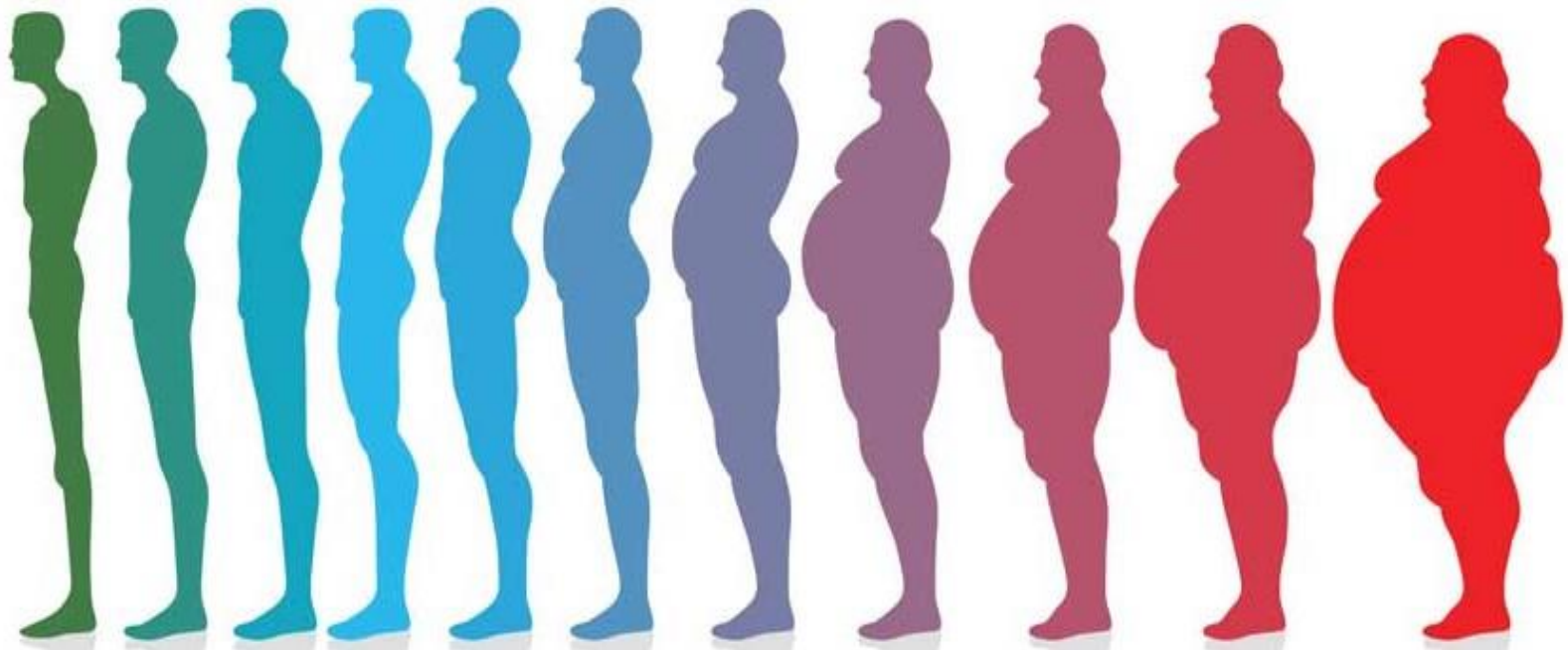


If you use varenicline to quit smoking, it blocks the nicotine receptors.

But varenicline still triggers some dopamine release, so you don't feel as bad.

Drug	Dosing	Duration	Comments/Monitoring Parameters
Non-nicotine replacement options			
Bupropion (Zyban)	150 mg by mouth daily × 3 days then 150 mg by mouth bid (dosing interval should be >8 hours)	3–6 months	Do not exceed 300 mg/day Recommend initiating therapy 1–2 weeks prior to set "quit" day Black box warning for neuropsychiatric warning and suicide warnings removed in 2016; downgraded to warning Pregnancy Category: C, excreted into breastmilk Monitor patients with renal/hepatic impairment Neuropsychiatric adverse events: black box warning removed in December 2016, warning remains Counseling points: might cause dry mouth, could cause insomnia
Varenicline (Chantix)	Start with dose titration: Days 1–3: 0.5 mg by mouth once daily Days 3–7: 0.5 mg by mouth twice daily Week 2 until end of treatment: 1 mg by mouth twice daily	3–6 months	Recommended to begin varenicline 1 week prior to quit day Maintenance up to 6 months of therapy is approved Renal impairment dosing for CrCl ≤30 mL/min (0.5 mL/sec) No dosing adjustment needed in hepatic impairment If patient has difficulty with cessation, recommend taper smoking by 50% each month with a goal of smoking abstinence in 12 weeks, continue varenicline for another 12 weeks for a full 24 week therapy Neuropsychiatric adverse events: black box warning removed in December 2016, warning remains Most common side effects: nausea, sleep problems, constipation, gas, vomiting Patients with intolerable insomnia might improve with lower doses

OBESITY IS NOW A GLOBAL EPIDEMIC!



- **Overweight** and **obesity** are terms used to describe weight measurements greater than what is considered healthy for a given height.

Health Risks of Being
OVERWEIGHT OR OBESE

TYPE 2
DIABETES

HIGH BLOOD
PRESSURE

HEART
DISEASE
AND STROKE

HIGH
CHOLESTEROL

GALLBLADDER
DISEASE

SLEEP
APNEA

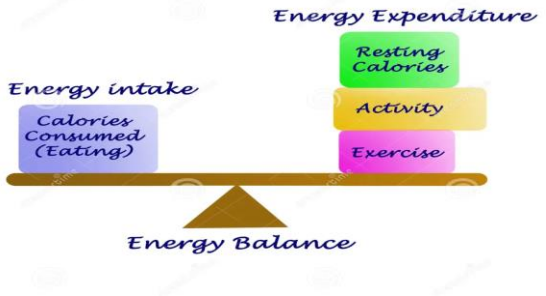
OSTEOARTHRITIS

FATTY
LIVER
DISEASE

CANCER

PATHOPHYSIOLOGY

- The key factor in the development of overweight and obesity is the **imbalance** that occurs between energy intake and energy expenditure.
- The extent of obesity is determined by the length of time this imbalance has been present.
- **Energy intake** is affected by *environmental influences*, including social, behavioural, and cultural factors, whereas *genetic composition* and *metabolism* affect **energy expenditure**.



- Of the three macronutrients (i.e., carbohydrate, protein, and fat), **fat** has received the most attention, given its desirable texture and its ability to augment the flavour of other foods. Food high in fat promotes weight gain, in comparison with the other macronutrients, because fat is more energy dense.
- When compared with carbohydrate and protein, more than twice as many calories per gram are contained in fat.
- In addition, fat is stored more easily by the body compared with protein and carbohydrate.

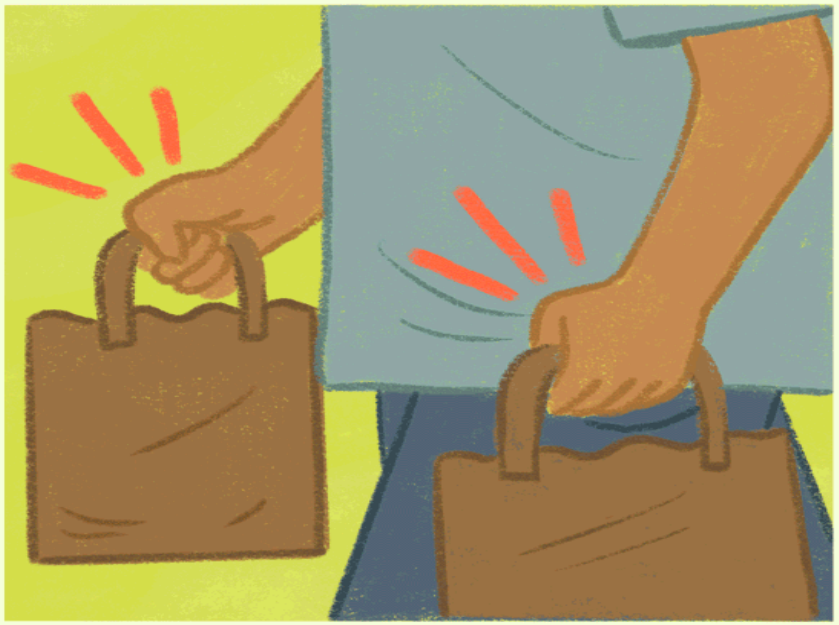
Energy Expenditure

- A person's metabolic rate is the primary determinant of energy expenditure. The metabolic rate is enhanced after food consumption and is directly related to the amount and type.
- Total daily energy expenditure (TDEE) consist of : Basal metabolic rate, Non-exercise activity thermogenesis, Exercise activity and Thermic effect of food.
- Physical inactivity may predispose an individual to overweight and obesity.
- In addition, endocrine-related disorders (e.g., hypothyroidism and Cushing syndrome) may *lower the metabolic rate*, further contributing to the development of overweight and obesity.

How to Increase Energy Expenditure

Exercise

Most effective way to boost energy expenditure

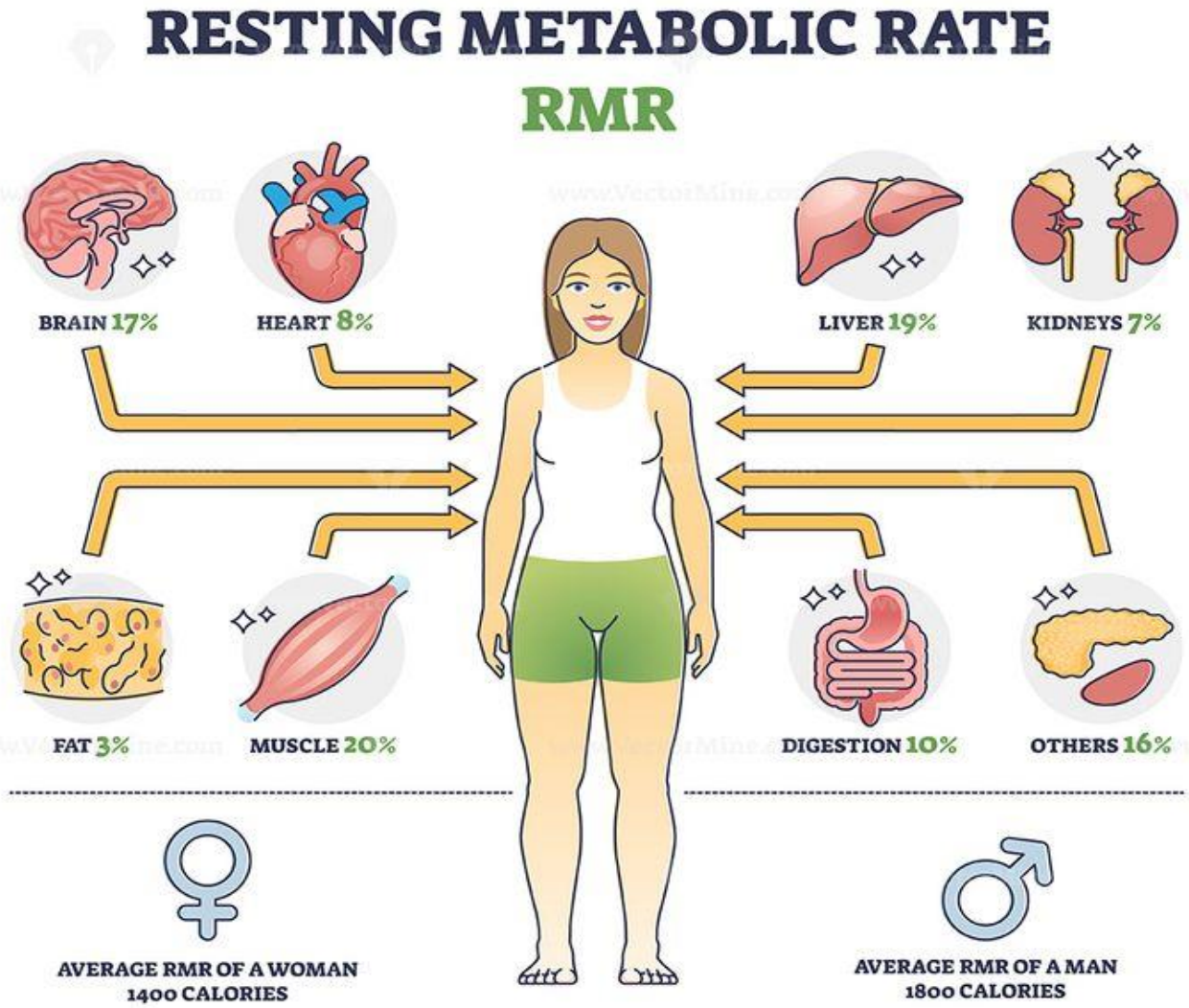


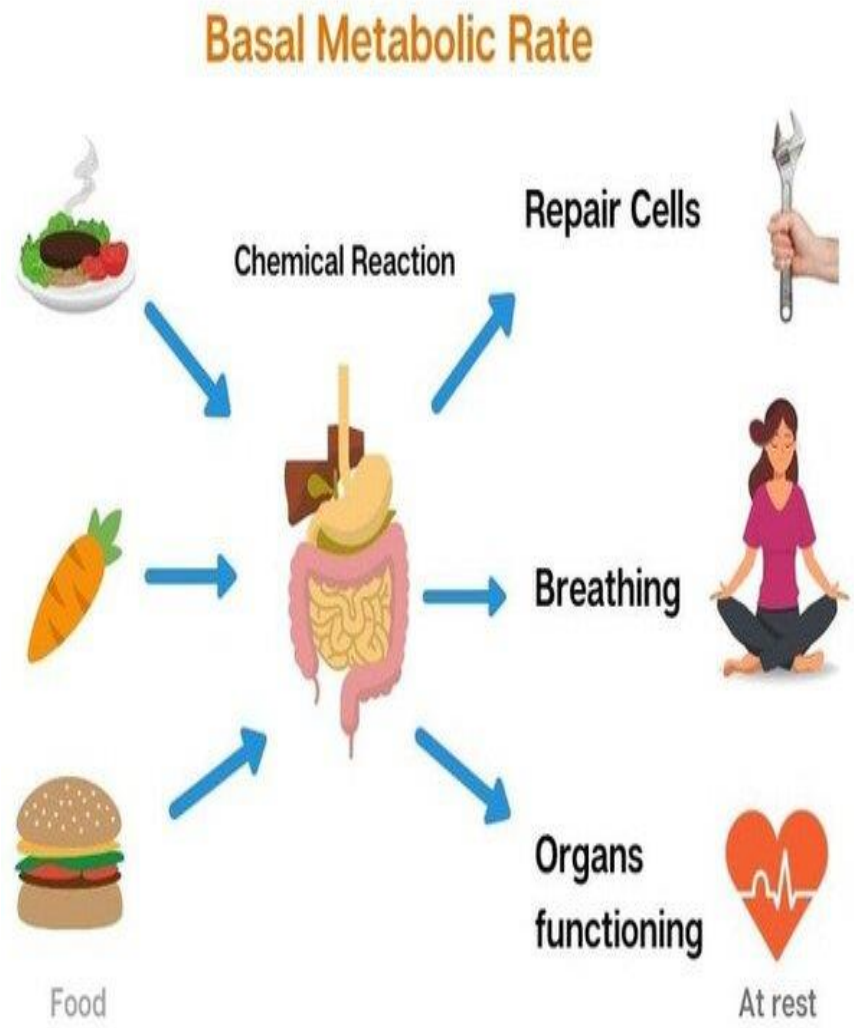
Non-Exercise Activity Thermogenesis (NEAT)

Movements made during the day, not including exercise

Thermic Effect of Food (TEF)

Amount of energy it takes to chew and digest food


RESTING METABOLIC RATE
RMR
BRAIN 17%
HEART 8%
LIVER 19%
KIDNEYS 7%
FAT 3%
MUSCLE 20%
DIGESTION 10%
OTHERS 16%
AVERAGE RMR OF A WOMAN
1400 CALORIES
AVERAGE RMR OF A MAN
1800 CALORIES


Basal Metabolic Rate
Chemical Reaction
Repair Cells
Breathing
Organs
functioning
Food
At rest

Metabolic factors

-  **Age**: The older you get, the slower your metabolic rate.
-  **Body Size**: The bigger the body, the more calories burned.

-  **Outside temperature**: If body exposed to cold, it burns more calories.
-  **Muscle Mass**: The greater your muscle mass, the more calories you burn.
-  **Movement**: The more active you are, the more calories you burn. Metabolism speeds up accordingly.
-  **Hormones**: Hypothyroidism can slow down metabolic rate and increase your risk of weight gain.

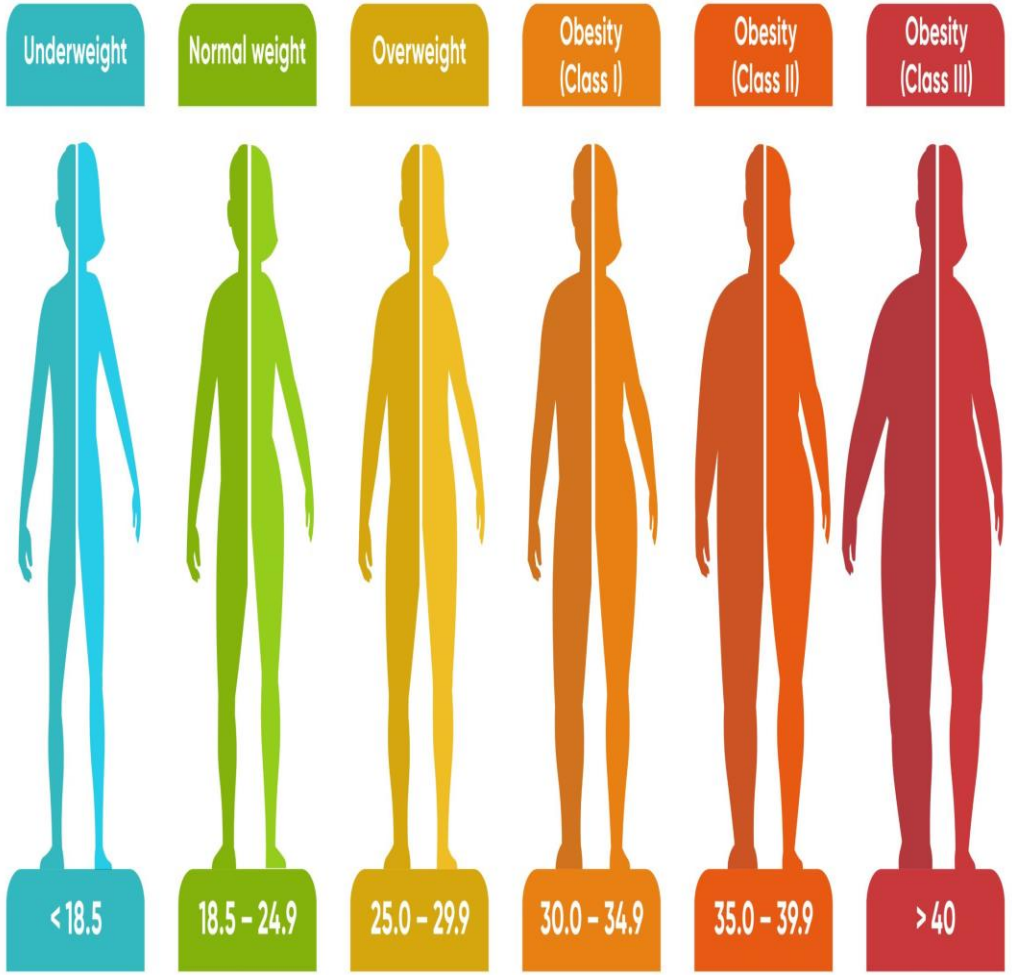
CLINICAL PRESENTATION AND DIAGNOSIS

- *Body mass index (BMI), waist circumference (WC), comorbidities, are used in the assessment of overweight or obese patients.*
- The BMI a measure of body fat is calculated using the measured weight in kilograms divided by the height in meters squared (kg/m2) for all adult patients regardless of gender.

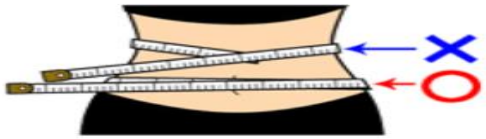
$$\text{BMI} = \frac{\text{Weight in kilogram}}{\left(\text{Height in meter}\right)^2}$$

BMI Classification

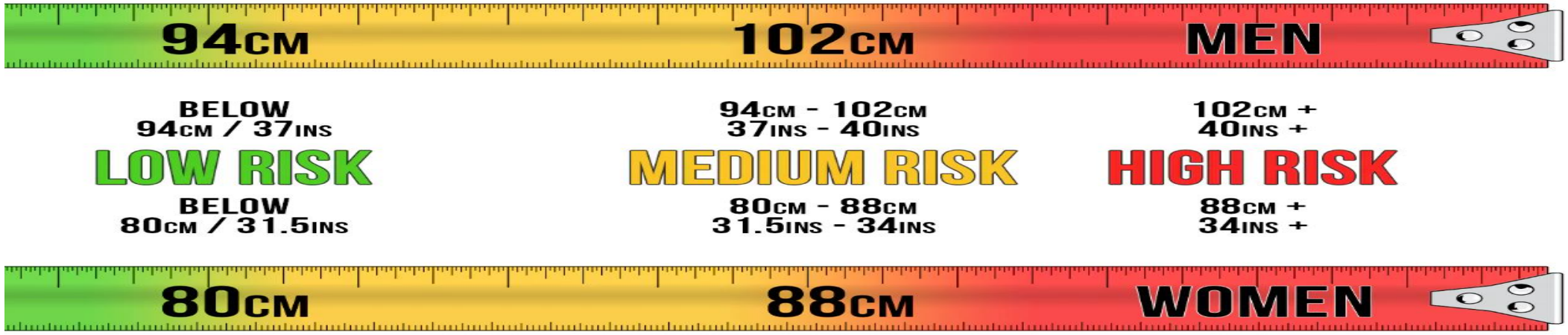
- Underweight < 18.5 kg/m2
- Normal weight 18.5–24.9 kg/m2
- Overweight 25–29.9 kg/m2
- Obesity (Class 1) 30–34.9 kg/m2
- Obesity (Class 2) 35–39.9 kg/m2
- Extreme obesity (Class 3) ≥ 40 kg/m2



- Waist circumference(WC) should also be determined no less than annually for adult patients by placing a **measuring tape** at the top of the right iliac crest and proceeding around the abdomen, ensuring that the tape is tight but not constricting the skin. The value is measured after normal expiration.



Important points
- Waist circumference is NOT measure around the narrowest part of the waist.
- Measure horizontally around the waist at the level of the navel. Do not compress the skin with the tape.



Nonpharmacologic Therapy

- The imbalance between energy intake and energy expenditure is key factor for developing overweight and obesity, weight loss therapy requires the creation of an energy deficit.

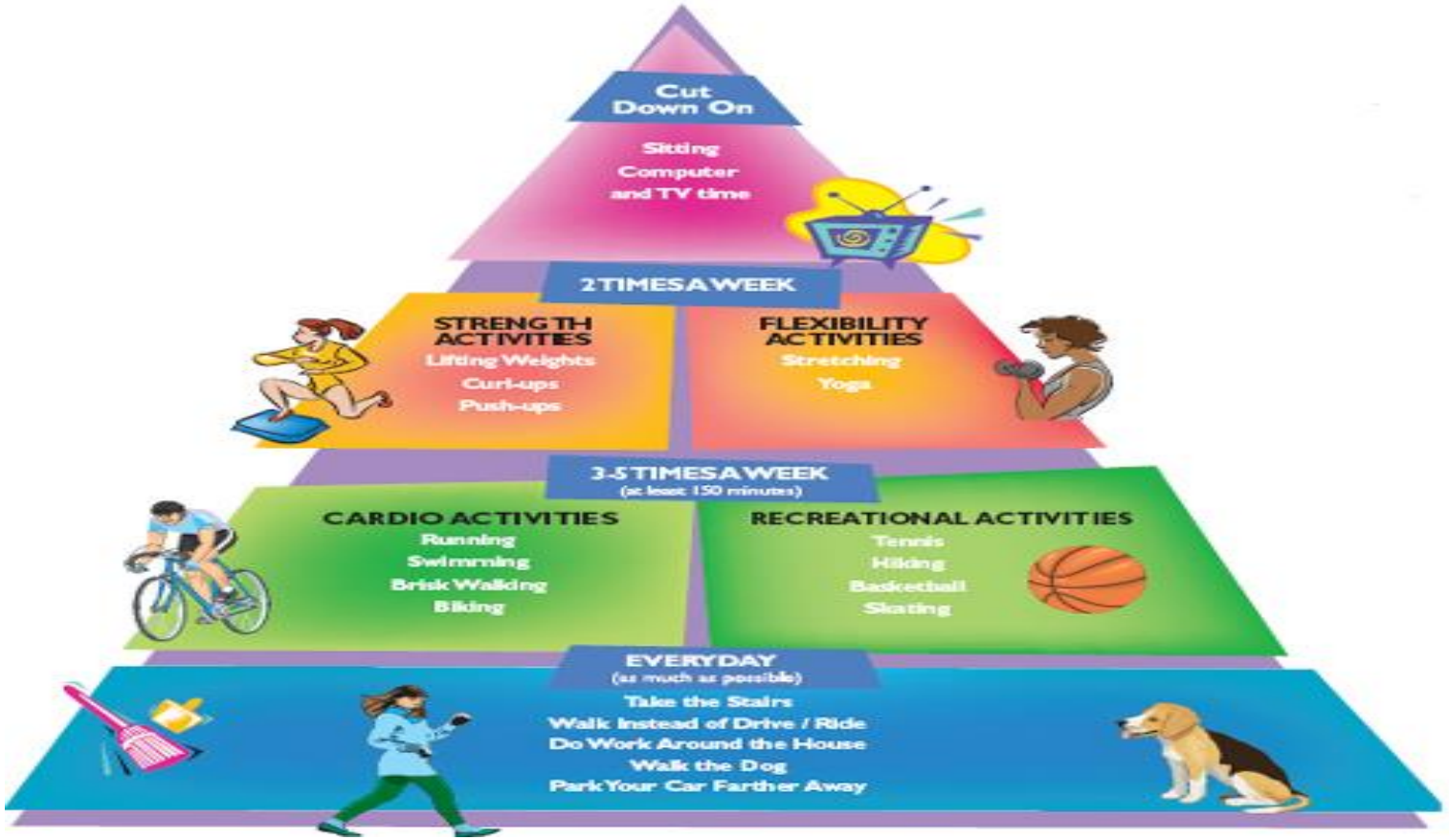
- This may be achieved through daily caloric restriction and increased physical activity. Both therapeutic strategies are part of a comprehensive lifestyle intervention program as well as behavioral therapy to facilitate compliance diet and exercise

A) *Reduced-Calorie Diet*

- Techniques to reduce dietary energy intake include adoption of a target energy intake less than that required for energy balance. This can usually be accomplished by reducing the energy intake by **500 kcal/day** or greater. Recommend **1200–1500** for women or **1500–1800** kcals/day for men.
- The choice of calorie-restricted diet is based on patient preference and current health status. A variety of diets, including but not limited to high protein, low carbohydrate, low fat
- The daily limit should be considered after assessing a patient's normal daily caloric intake and ensuring that the initial caloric restriction does not exceed **500 to 1000 kcal/ day**.

B) *Increased Physical Activity*

- Although <u>diet</u> and <u>exercise</u> contribute to **weight loss**, combining a reduced-calorie diet with increased physical activity results in greater weight loss compared with either therapy alone.



- Slow titration of both the amount and intensity of aerobic physical activity is recommended for most patients.
- A program that incorporates brisk walking daily is a viable option for most patients.
- **200 to 300 minutes** per week of aerobic physical activity are recommended for weight maintenance or prevention of weight regain.

C) *Behavioural change*

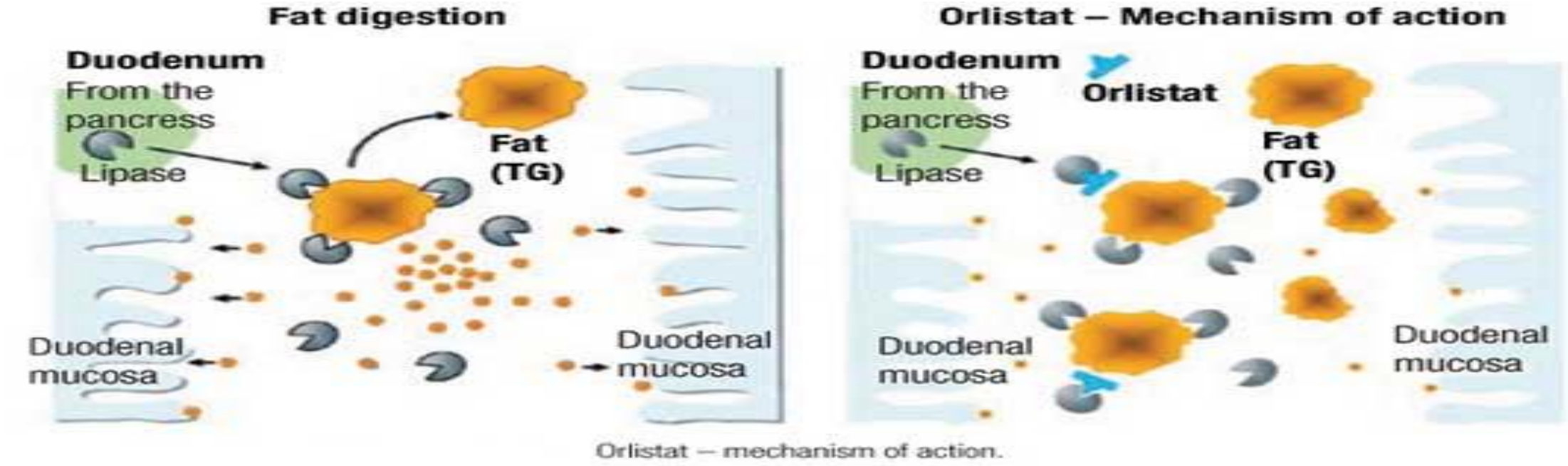
- Nonadherence with recommended lifestyle changes may result in unsuccessful weight loss for adults. Successful behavioural therapy includes regular self-monitoring of food intake, physical activity, and weight.

These include:

- •• Limit the consumption of sugar-sweetened beverages.
- •• Limit the amount of screen time (television, computer, etc) to 2 hours or less per day.
- •• Limit the number meals eaten at restaurants, especially those serving fast food.
- •• Parents should limit portion size when preparing and serving meals.

ORLISTAT (The only OTC medicine approved and licensed by the FDA for weight loss)

- *Orlistat* inhibits gastric and pancreatic lipases as well as triglyceride hydrolysis so causes less fat to be digested and absorbed and more to be excreted in the faeces.



Orlistat – mechanism of action.

- *Orlistat* 60 mg capsules can be purchased OTC by individuals aged 18 years and over with a BMI of 28 kg/m2 or greater, to be used in conjunction with a reduced calorie diet that is low in fat, and with suitable exercise.

- It is intended to be taken three times daily with or after food. It is used to make the weight loss through diet and exercise more effective.
- A realistic target for weight loss is 0.5–1 kg (1–2 lb) a week for adults.

Previous medical history

- Patient Kidney disease, or renal stones, is a contraindication to *orlistat*.
- Patients with chronic malabsorption syndrome and those with cholestasis (bile flow from the liver is blocked) should not take OTC *orlistat*.
- It is contraindicated in pregnancy and in women who are breastfeeding.
- Patients on *warfarin* or other oral anticoagulants should not be supplied with OTC *orlistat*. *Orlistat* may be prescribed by a doctor to those on these drugs with a requirement to monitor anticoagulant effects.

- Other medicines where the patient needs to check with their GP before starting ***orlistat*** are *amiodarone*, *acarbose*, *ciclosporin.*
- Patients with hypothyroidism on thyroxine should be referred to the doctor if they wish to take *orlistat*, as it can reduce control of the condition.
- There is also an **interaction** with antiepileptic drugs, so people on these will need to be referred to their doctor.
- Patients on the combined oral contraceptive will need to use additional contraception if they develop severe diarrhoea while taking *orlistat*.

Side effects

- Gastrointestinal (GI) adverse effects are common (e.g. oily spotting, abdominal discomfort, flatulence, faecal urgency, fatty stools).
- These are usually reduced with continued use of *orlistat* and can often be reduced by limiting fat intake.
- It is important to have adopted the low-fat diet a few days before introducing *orlistat*. Oily stools and flatulence can be controlled by reducing the dietary fat content to somewhere in the region of 15 g per meal, and it has been suggested that and adoption of a low-fat diet. The daily intake of fat should be spread throughout the day.
- Taking drugs for diarrhoea (such as *loperamide*) will not control these symptoms.

- *Orlistat* **reduces** the absorption of fat-soluble vitamins. When it is supplied, a multivitamin supplement is advised at bedtime.