TOBACCO AND THE NERVOUS SYSTEM

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Funding for Quit Tobacco International is provided by the U.S. National Institutes of Health, Fogarty International Centre (R01 TW05969-01, RO1TW007944-01).

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TOBACCO AND THE NERVOUS SYSTEM

I. GOAL OF MODULE: Provide students with knowledge and skills on tobacco issues related to the nervous system

II. TARGET AUDIENCE

a. Level of Student/Learner: 4th Semester
b. Suggested Course or Subject: Dept. of General Medicine

III. LEARNING OBJECTIVES

- To understand how tobacco causes stroke
- To understand the effect of tobacco on different types of stroke
- To understand the effect of smoking cessation on stroke
- To understand the pathways of nicotine action on the brain
- To understand how nicotine causes craving and addiction
- To understand the effect of smoking on the risk of developing multiple sclerosis and its progression
- To understand the effect of smoking on Alzheimer's disease
- To understand the effect of smoking on Parkinson's disease
- To understand why smoking cessation is important

IV. CURRICULUM STANDARDS ADDRESSED:

The General Medicine department has the broad goal of teaching undergraduate medical students the knowedge, skills, and behavioural attributes to function effectively as a first contact physician. It has a total of 180 hours, of which 20 hours are for neurological diseases. Time from this slot can be used for this module.

- The student will be able to diagnose common clinical disorders, outline various modes of management, propose and interpret diagnostic and investigative procedures, and provide first level management of acute emergencies.

Skills:

- The student will develop clinical skills for various common medical disorders and emergencies, perform simple routine investigations, assist in common bed-side investigative procedures, and be able to refer a patient to secondary or tertiary level health care.

V. MINI-LECTURES

MINI LECTURE 1: TOBACCO AND STROKE

CORE SLIDES

1. Smoking and Stroke: Causation
2. Smoking and Cerebral Blood Flow
3. Smoking and Ischemic Stroke
4. Smoking and SAH
5. Smoking Cessation and Stroke
6. Stroke Patients Continue to Smoke

OPTIONAL SLIDES:

1. Smoking and Hemorrhagic Stroke
2. Nicotine and Cerebral Vasculature (1–3)

MINI LECTURE 2: NEURO-PHARMACOLOGY OF NICOTINE

CORE SLIDES

1. Nicotine
2. Pathways of Nicotine Action
3. How Nicotine Acts in the Brain (1-4)

OPTIONAL SLIDES

1. Nicotine and Nicotinic Receptors
2. Alternate Pathway: GABA

MINI LECTURE 3: TOBACCO AND NEURODEGENERATIVE DISEASES

CORE SLIDES

1. Smoking and Multiple Sclerosis Risk
2. Smoking and MS Progression
3. Secondhand Smoke and MS
4. Smoking and Alzheimer's Disease
5. Smoking and Parkinson's Disease
6. Discussion: Smoking vs. Quitting

OPTIONAL SLIDES

1. Smoking and MS: Mechanisms (1–2)

VI. CASE DISCUSSION / CLINICAL SCENARIO AND SKILLS CHECKLIST

CASE SCENARIO

- Ask smoking status in a patient coming with a neurological problem.

Overview

In this module, students are trained to practice the following aspects of communication, e.g., exploration of patient's background, identity, and life style. The students are also expected to be able to explore the background, identity, and lifestyle of the spouse or immediate family. One of the most important lifestyle aspects that needs to be asked of the patient and his/he spouse is about their smoking status.

Introduction

To control the tobacco epidemic, all parties should work together in a strategic and sustainable way, including health professionals. Simple advice from a physician has been shown to increase the abstinence rate significantly (by 30%) compared to no advice. Likewise, nursing-led interventions for smoking cessation increase by 50% the chances of successfully quitting. To be able to give advice, doctors must ask every patient about tobacco use.

Learning Objectives

Upon the completion of this case scenario practice, students are expected to be able to:

1. Routinely ask and integrate assessment of the smoking status of the patient and spouse.
2. Advise the patient/spouse to quit smoking.
3. Advise the patient to avoid second hand smoke.
4. Explain to the patient about the harmful effects of tobacco.
5. Explain to the patient about nervous system problems and their association with smoking.

Asking the patients' smoking history

Research studies show that if doctors have a reminder to ask about smoking, e.g., smoking status is part of the vital signs, doctors are three times more likely to advise patients to quit. Simple advice from a physician has been shown to increase abstinence rates significantly (by 30%) compared to no advice.

There are several important factors that should be considered when we are asking the patients'smoking history, i.e. 1) asking the smoking status of all patients (including women and teenagers); 2) if the patient does not smoke, they should be asked if they have ever smoked (because even after quitting, a smoker can start again); 3) questions should be delivered in a non-critical manner; 4) evaluate the patients' smoking history as to how many cigarettes they smoke daily, do they use any other forms of tobacco; and 5) make a note on the patients' smoking status in the medical record. Women and children should not be excluded and they should also be asked about passive smoking.

Case Scenario

A 49 year old lawyer was admitted with complaints of weakness of left upper and lower limbs. The episode was sudden and he was unconscious for about 5 minutes. He has been a diabetic for the past three years and hypertensive for the past five years and has been on regular medication for the same. He has been a smoker for the past 30 years, smoking an average of 12–15 cigarettes per day. He consumes alcohol occasionally.

Vital Signs
Blood Pressure: 150/100 mm Hg
Pulse: 80/min
Body Weight: 78 kg
Temperature: 97 F

Smoking Status
Smoking status of patient: Smoker Ex-Smokers Never Smoke (Circle one)
Smoking status of spouse: Smoker Ex-Smokers Never Smoke (Circle one)

Checklist for Case Scenario

S.No.	Aspects	Please tick if student has covered this aspect
	Ask	
1.	• Ask patients whether he/she smokes or not	
2.	• If the patient doesn't smoke, ask whether he/she ever smoked before	
3.	• If the patient smokes, ask how many cigarettes he/she takes per day	
	Assess	
4.	• Assess patient's readiness to quit	
	Advise	
5.	• Advise patient to quit smoking	
6.	• Personalize advice by using the tobacco user's health status/disease	
	Assist	
7.	• Assist the patient to quit by giving him/her pamphlets, brochures	
	Arrange for Follow-up	
8.	• Arrange to follow up on tobacco use	

Points for Discussion

- Cigarette smoking is a preventable risk factor for ischemic stroke. The physician should discuss that smoking is a risk factor for stroke and strongly encourage the patient to quit.
- Approximately one in three cases of sub-arachnoid hemorrhage (SAH) could be attributed to current smoking with a clear dose-dependent effect, but risks decline quickly after smoking cessation. This information can be used to emphasize to patients the benefits of quitting.
- Research also shows that emphasizing the benefits of quitting may have a stronger impact on patients than simply discussing the hazards and dangers of tobacco.

FACT SHEET

The fact sheets are to be used by the tutor to supplement the discussion about the scenario. This fact sheet will address background information on tobacco that could be relevant to the scenario.

Tobacco and Stroke

- Cigarette smoking is a preventable risk factor for ischemic stroke. Nicotine has been shown to alter the function of the blood–brain barrier (BBB) and stimulate DNA synthesis, which leads to endothelial cell proliferation.[1]
- Cigarette smoking, diabetes mellitus, ischemic heart disease, and valvular heart disease are causal risk factors for ischemic stroke and the association is strong, consistent, biologically plausible, and independent of other factors that were measured and analyzed.[2]
- Approximately one in three cases of sub-arachnoid hemorrhage (SAH) could be attributed to current smoking with a clear dose-dependent effect, but risks decline quickly after smoking cessation.[3]
- Past smokers had no increase in risk of total hemorrhagic stroke, intra-cranial hemorrhage, or SAH compared with never smokers.[4,5]
- Nicotine disrupts the tight junctions of the BBB and has numerous detrimental effects on endothelial components in the brain including mediators of thrombosis and leukocyte migration.[1]

Neuro-pharmacology of Nicotine

- The tobacco in manufactured cigarettes contains between 6 and 12 mg of nicotine. On average, a cigarette smoker absorbs into the body about 1 mg of nicotine per cigarette smoked.[6]
- Nicotine is shaped like the neurotransmitter acetylcholine so, it can fit in the nicotinic receptors and act just like acetylcholine.[7]
- Activation of nicotinic receptors could modulate the immune response either by activation of the hypothalamus–pituitary–adrenal axis or activation of the autonomic nervous system through sympathetic and parasympathetic innervations.[8]
- Nicotine attaches to the core neurons of the brain's reward system situated in the ventral tegmental area (VTA), where beneficial behaviors are rewarded and reinforced.[9]
- Nicotine activates dopamine systems within the brain by stimulating nicotinic receptors and triggering the production of dopamine in the nucleus accumbens (NAc).[9]

Tobacco and Neurodegenerative Diseases

- The risk of Alzheimer's disease decreased as the number of cigarettes smoked daily increased.[10]
- The protective association between smoking and Alzheimer's disease was restricted to patients with a family history of dementia and was independent of cardiovascular history and potential confounding variables such as age, sex, and alcohol consumption.[10]

- Smoking was found to increase in the risk of multiple sclerosis (MS)[11,12] and clinical MS progression and the incidence increased with cumulative exposure to smoking.[12]
- Parental smoking at home was associated with a significant increase in the risk of first episode of MS in children.[12]
- A variety of mechanisms have been suggested to explain the association between smoking and multiple sclerosis, including immune stimulation or suppression, direct effect of cigarette smoke components on the blood–brain barrier, nicotine effect on microvascular blood flow in the brain, direct toxic effects on the central nervous system through cigarette smoke components like cyanide and NO, etc.[11,12]

References:

1. Hawkins BT, Brown RC, Davis TP. Smoking and ischemic stroke: a role for nicotine? Trends Pharmacol Sci. 2002; 23:78–82.
2. Hankey GJ. Potential new risk factors for ischemic stroke: what is their potential? Stroke. 2006; 37:2181–8.
3. Anderson CS, Feigin V, Bennett D, Lin RB, Hankey G, Jamrozik K. Active and passive smoking and the risk of subarachnoid hemorrhage: an international population-based case-control study. Stroke. 2004; 35:633–7.
4. Kurth T, Kase CS, Berger K, Schaeffner ES, Buring JE, Gaziano JM. Smoking and the risk of hemorrhagic stroke in men. Stroke. 2003; 34:1151–5.
5. Kurth T, Kase CS, Berger K, Gaziano JM, Cook NR, Buring JE. Smoking and risk of hemorrhagic stroke in women. Stroke. 2003; 34:2792–5.
6. Benowitz NL. Cotinine as a Biomarker of Environmental Tobacco Smoke Exposure. Epidemiol Rev. 1996; 18:188–204.
7. National Institute on Drug Abuse. Brain Power! Challenge: Grades 6-9; Module 2: Legal Doesn't Mean Harmless. Available at: http://www.drugabuse.gov/JSP4/MOD2/page3.html
8. Sopori M. Figure 3. A simplified schematic of possible communication between the CNS and the immune system through nicotinic acetylcholine receptors. In: Effects of cigarette smoke on the immune system. Nat Rev Immunol. 2002; 2:372–7. Available at: http://www.nature.com/nri/journal/v2/n5/fig_tab/nri803_F3.html
9. School of Chemistry, Bristol University, UK. The Metabolism of Nicotine. Available at: http://www.chm.bris.ac.uk/motm/nicotine/E-metabolisme.html
10. van Duijn CM, Hofman A. Relation between nicotine intake and Alzheimer's disease. BMJ. 1991; 302:1491–4.
11. Hawkes CH. Smoking is a risk factor for multiple sclerosis: a metanalysis. Mult Scler. 2007; 13:610–15.
12. Mikaeloff Y, Caridade G, Tardieu M, Suissa S on behalf of the KIDSEP study group. Parental smoking at home and the risk of childhood-onset multiple sclerosis in children. Brain. 2007; 130:2589–95:1–7.

1. REFERENCE LIST FOR MODULE

MINI LECTURE 1 *[Tobacco and Stroke]*

1. Hawkins BT, Brown RC, Davis TP. Smoking and ischemic stroke: a role for nicotine? Trends Pharmacol Sci. 2002; 23:78–82.
2. Hankey GJ. Potential new risk factors for ischemic stroke: what is their potential? Stroke. 2006; 37:2181–8.
3. Naess H, Nyland HI, Thomassen L, Aarseth J, Myhr KM. Etiology of and risk factors for cerebral infarction in young adults in western Norway: a population-based case-control study. Eur J Neurol. 2004; 11:25–30.
4. Feigin V, Parag V, Lawes CM, Rodgers A, Suh I, Woodward M, et al. Smoking and elevated blood pressure are the most important risk factors for subarachnoid hemorrhage in the Asia-Pacific region: an overview of 26 cohorts involving 306,620 participants. Stroke. 2005; 36:1360–5.
5. Anderson CS, Feigin V, Bennett D, Lin RB, Hankey G, Jamrozik K. Active and passive smoking and the risk of subarachnoid hemorrhage: an international population-based case-control study. Stroke. 2004; 35:633–7.
6. Bak S, Sindrup SH, Alslev T, Kristensen O, Christensen K, Gaist D. Cessation of smoking after first-ever stroke: a follow-up study. Stroke. 2002; 33(9):2263–9.
7. Ballard J, Kreiter KT, Claassen J, Kowalski RG, Connolly ES, Mayer SA. Risk factors for continued cigarette use after subarachnoid hemorrhage. Stroke. 2003; 34(8):1859–63.
8. Kurth T, Kase CS, Berger K, Schaeffner ES, Buring JE, Gaziano JM. Smoking and the risk of hemorrhagic stroke in men. Stroke. 2003; 34:1151–5.
9. Kurth T, Kase CS, Berger K, Gaziano JM, Cook NR, Buring JE. Smoking and risk of hemorrhagic stroke in women. Stroke. 2003; 34:2792–5.

MINI LECTURE 2 [*Neuro-Pharmacology of Nicotine]*

1. Benowitz NL. Cotinine as a Biomarker of Environmental Tobacco Smoke Exposure. Epidemiol Rev. 1996; 18:188–204.
2. National Institute on Drug Abuse. Brain Power! Challenge: Grades 6-9; Module 2: Legal Doesn't Mean Harmless. Available at: http://www.drugabuse.gov/JSP4/MOD2/page3.html (accessed: June 5, 2009)
3. Sopori M. Figure 3. A simplified schematic of possible communication between the CNS and the immune system through nicotinic acetylcholine receptors. In: Effects of cigarette smoke on the immune system. Nat Rev Immunol. 2002; 2:372–7. Available at: http://www.nature.com/nri/journal/v2/n5/fig_tab/nri803_F3.html
4. School of Chemistry, Bristol University, UK. The Metabolism of Nicotine. Available at: http://www.chm.bris.ac.uk/motm/nicotine/E-metabolisme.html
5. National Institute on Drug Abuse. Nicotine's multiple effects on the brain's reward system drive addiction. Available at: http://www.drugabuse.gov/NIDA_Notes/NNVol17N6/Nicotine.html

MINI LECTURE 3 *[Tobacco and Neurodegenerative Diseases]*

1. Hawkes CH. Smoking is a risk factor for multiple sclerosis: a metanalysis. Mult Scler. 2007; 13:610–15.
2. Mikaeloff Y, Caridade G, Tardieu M, Suissa S on behalf of the KIDSEP study group. Parental smoking at home and the risk of childhood-onset multiple sclerosis in children. Brain. 2007; 130:2589–95:1–7.
3. van Duijn CM, Hofman A. Relation between nicotine intake and Alzheimer's disease. BMJ. 1991; 302:1491–4.
4. Smoking may double the risk of Alzheimer's: Available at: http://news.bbc.co.uk/2/hi/health/115829.stm
5. Merchant C, Tang MX, Albert S, Manly J, Stern Y, Mayeux R. The influence of smoking on the risk of Alzheimer's disease. Neurology. 1999; 52:1408–12.

2. INSTRUCTOR KEY RESOURCES/REFERENCES

1. Bak S, Sindrup SH, Alslev T, Kristensen O, Christensen K, Gaist D. Cessation of smoking after first-ever stroke: a follow-up study. Stroke. 2002; 33(9):2263–9.
2. Benowitz NL. Cotinine as a biomarker of environmental tobacco smoke exposure. Epidemiol Rev. 1996; 18:188–204.
3. Hawkes CH. Smoking is a risk factor for multiple sclerosis: a metanalysis. Mult Scler. 2007; 13:610–15.

3. SUPPORT KEY REFERNCES

1. Bak S, Sindrup SH, Alslev T, Kristensen O, Christensen K, Gaist D. Cessation of smoking after first-ever stroke: a follow-up study. Stroke. 2002; 33(9):2263–9.
2. Benowitz NL. Cotinine as a biomarker of environmental tobacco smoke exposure. Epidemiol Rev. 1996; 18:188–204.
3. Hawkes CH. Smoking is a risk factor for multiple sclerosis: a metanalysis. Mult Scler. 2007; 13:610–15.

4. INSTRUCTOR WEB-SITE RESOURCES

1. http://www.drugabuse.gov/JSP4/MOD2/page3.html
2. http://www.nature.com/nri/journal/v2/n5/fig_tab/nri803_F3.html
3. http://www.chm.bris.ac.uk/motm/nicotine/E-metabolisme.html
4. http://www.drugabuse.gov/NIDA_Notes/NNVol17N6/Nicotine.html

5. SAMPLE EXAMINATION QUESTIONS

Short Answers

1. Describe the mechanisms by which smoking can cause stroke.
2. How does nicotine act in the brain to induce craving?
3. Describe the effect of smoking on neurodegenerative disorders.

Multiple Choice Questions (Answers in blue font)

1. Which of the following is **false** regarding the effect of smoking on cerebral blood flow?

    a. Increased in right para-hippocampus
    b. Decreases in acute smoking
    c. Decreased in left para-hippocampus
    d. Decreased in chronic smoking
    e. Increased in thalamus & pons

2. Smoking causes stroke through which of the following mechanisms?

    a. Breakdown of the blood brain barrier
    b. Changes in cerebral blood flow
    c. Increases peripheral thrombus formation
    d. None of the above
    e. All of the above

3. Nicotine is shaped like the neurotransmitter _____

    a. Dopamine
    b. GABA
    c. Acetyl choline
    d. Glutamate
    e. None of the above

4. Which of the following reactions is **not** caused by prolonged nicotine exposure?

    a. Decreases dopamine effeiciency
    b. Decreases no. of available receptors
    c. Decreases psychotropic effect of nicotine
    d. Increases no. of available receptors
    e. None of the above

5. Nicotine was **not** found to be protective for which of the following neurodegenerative diseases?

    a. Parkinson's disease
    b. Multiple Sclerosis
    c. Familial Alzheimer's disease
    d. Sporadic Alzheimer's disease
    e. Both b & d

6. Which of the following is **false** regarding the association between smoking and multiple sclerosis?

    a. Increases risk of developing multiple sclerosis
    b. Passive smoking has no effect on risk of multiple sclerosis
    c. Increases risk of severity of disease
    d. Increased incidence with cumulative smoking exposure
    e. None of the above