



TOBACCO AND NEOPLASIA

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Islamic University of Indonesia, Yogyakarta

TOBACCO AND NEOPLASIA

I. GOAL OF MODULE: Provide students with knowledge about the harmful effects of tobacco on the body leading to various carcinomas and the mechanism causing carcinogenic tobacco effects on the body; provide skills to address smoking and to provide smoking cessation counseling for patients with different cancers.

II. TARGET AUDIENCE

- a. Undergraduate students
- b. 4th/5th semester—*Course or Subject: Community Medicine/ Radiotherapy (Surgery)*

III. LEARNING OBJECTIVES

- To understand that there are different powerful carcinogens in cigarette smoke.
- To understand the mechanism of how the carcinogens in cigarettes cause cancer through DNA mutation
- To understand how smoking causes lung cancer, is a risk factor for digestive cancer, causes urogenital cancer, has adverse effects on cancer management, and effects of tobacco cessation on risk and management of cancers.

IV. CURRICULUM STANDARDS ADDRESSED:

India: 5–6th semester during surgical speciality postings. Under surgery and its allied specialities are 138 hours allotted to radiotherapy, wherein there are:

- Lectures of 10 hours
- Practicals of 128 hours are allotted

Objectives are:

- Students shall be able to identify symptoms and signs of various cancers and their steps of investigation and management and be aware of radiation therapy, its advancement, and management of cancers.
- Students will develop skills to take detailed clinical history of cases having malignant diseases and assist in administration of anticancer drugs and application of radiotherapeutic equipment for cancer management.

V. MINI-LECTURES

MINI LECTURE 1: TOBACCO AND CARCINOGENESIS

CORE SLIDES

1. Carcinogenic Content of Cigarettes
2. Tobacco Carcinogenesis Mechanism (1)
3. Tobacco Carcinogenesis Mechanism (2)
4. Behavioural Model of Tobacco Addiction

OPTIONAL SLIDES

1. Nicotine addiction and invasive cancers

MINI LECTURE 2: TOBACCO AND RESPIRATORY CANCERS

CORE SLIDES

1. Which Cancers Occur at a Higher Rate in Smokers?
2. Smoking and Lung Cancer
3. Tobacco and Asbestos
4. SHS and Lung Cancer
5. Smoking Reduction Reduces Risk
6. Cessation and Lung Cancer

OPTIONAL SLIDES

1. Lung Cancer Mechanism

MINI LECTURE 3: TOBACCO AND CANCERS OF THE DIGESTIVE TRACT

CORE SLIDES

1. Tobacco and Digestive Cancers
2. Tobacco and Digestive Cancer Risk (1)
3. Tobacco and Digestive Cancer Risk (2)
4. Smokeless Tobacco and GI Cancers
5. Alcohol and Smoking: Combined Effects
6. Alcohol and Smoking: Combined Rehabilitation

MINI LECTURE 4 : TOBACCO AND UROGENITAL CANCER

CORE SLIDES

1. Tobacco and Risk of Urogenital Cancers
2. Tobacco and Bladder Cancer
3. Tobacco Kidney Cancer
4. Cessation and Bladder Cancer

OPTIONAL SLIDES

1. Tobacco and Urogenital Cancers: Mechanism

MINI LECTURE 5: TOBACCO CESSATION AS AN IMPORTANT PART OF CANCER MANAGEMENT

CORE SLIDES

1. Smoking Affects Cancer Treatment
2. Impact of Smoking Cessation on Cancer Management
3. Barriers to Smoking Cessation in Cancer Patients
4. Cessation and Cancer Prevention

5. Cessation in Cancer Survivors
6. Screening—A Must Do!

VI. CASE DISCUSSION / CLINICAL SCENARIO

CASE SCENARIO—asking patient about smoking

Overview

In this module, students are asked to practice integrated communication during case discussion under supervision of instructors, in order to develop their smoking cessation skills. Students will be trained to routinely ask about patients' smoking status in every case. After obtaining patients' current smoking status, students will then practice how to assess patients' readiness to quit, advise and assist patients to quit smoking, and also arrange follow ups to monitor patients' smoking cessation progress. Therefore, students will also learn how to deliver efficient encouragement and provide proper explanation about the harm of tobacco on health and to help patients on their smoking cessation attempts.

Introduction

It has been well documented that smoking has a direct and indirect association with various cancers, including (but not limited to) lung cancer, oral cancer, cancer of the larynx and esophagus; digestive cancers; and urogenital cancers (bladder, cervix, and kidneys). Notably, 30% of all cancer deaths and up to 90% of all lung cancer deaths are attributable to smoking. Tobacco cessation is extremely important in cancer management.

Learning Objectives

Upon the completion of this skills laboratory practice, students are expected to be able to:

- Routinely ask all patients about their smoking status
- Assess patients' readiness to quit
- Advise patients with cardiovascular problems to quit smoking
- Assist the patients to quit
- Arrange follow ups on patients' smoking cessation progress
- Explain the harm of smoking on cardiovascular system

Asking the patients' smoking history

The health consequences of cigarette smoking are well known as is the fact that there is no part of the human body that is not affected by tobacco.

In a survey done by QTI, 77% of Indian doctors did not routinely ask patients about smoking. 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 (Fiore et al. 2000).

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 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 of the patients' smoking status in the medical record (maybe you can indicate patients' smoking status in your patients' card). Women and children should not be excluded and they should also be asked about passive smoking.

Case Scenario

A 40 year old man has a history of heartburn for six months. He has been experiencing difficulty swallowing and inability to swallow solid foods (eventually liquids also) for one week. He also has pain with swallowing and considerable weight loss in the past month. Investigations show a growth in the pharynx.

He has been a smoker for the last 15 years and smokes 5–6 cigarettes a day. He consumes alcohol moderately (up to 5 drinks every day). Patient is a government employee and his wife is a home maker. He has a 12 year old son in school.

Vital Signs

Blood Pressure: 140/90 mm of Hg

Pulse: 76/min

Body Weight: 75kg

Temperature: 98.4 F

Smoking Status: 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 patient 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

- Since the growth was screened and diagnosed early, it may be treated by surgery or radiation. One of the main reasons for the growth is smoking. Stopping smoking is very important even at time of diagnosis to get early cure and to minimize discomfort.
- **Smoking causes post operative complications.** Smoking delays wound healing after surgery and may cause infections at wound sites. If smoking continues, healing of the operation site will take a longer time and discomfort like pain, nausea, irritation will be greater.
- **Smoking can cause second malignancies.** Moreover, the other parts of mouth are also unhealthy and hence vulnerable for new cancerous growth. Continued smoking or chewing any tobacco product will result in new growth in those parts also. Quitting smoking will help the unhealthy areas to recover. Therefore it is important to quit smoking at once.
- **Smoking also reduces efficacy of treatment drugs and radiation.** Smoking also affects the treatment efficacy of the drugs and how the body responds to the radiation due to the presence of toxins in the tobacco smoked or chewed.
- It is also not advisable to continue drinking because **alcohol and smoking have a synergistic effect** causing cancers and inhibiting treatment. Therefore it is advisable to stop alcohol too with smoking.

FACT SHEETS TO SUPPORT DISCUSSION (STUDENT HANDOUTS)

Tobacco and Neoplasia

1. Smoking increases the risks for many cancers and is known as the cause of cancers in the respiratory tract, urinary bladder, pancreas, and kidneys.¹
2. There is sufficient evidence to show the casual relationship between smoking and the following cancers: lung cancer; laryngeal cancer; oral cavity and pharyngeal cancer esophageal cancer; pancreatic cancer; renal cell, renal pelvis, and bladder cancer; cervical cancer; gastric cancer; and acute myeloid leukemia.¹
3. Tobaccos smoke has more than 50 carcinogens, the most potent of which are polycyclic aromatic hydrocarbons (PAHs) and tobacco specific nitrosamines (TSNs).²
4. Women who are exposed to second hand smoke from their husbands are 1.2 times more likely to suffer from lung cancer.¹
5. The evidence is suggestive to infer causal relationship between exposure to second hand smoking and breast cancer and nasal sinus cancer.¹
6. The cause of lung cancer is tobacco smoking in as many as 90% of patients.³
7. The development of lung cancer is directly related to the number of cigarettes smoked, the length of smoking history, and the tar and nicotine content of the cigarettes, and is highest among current smokers and lowest among nonsmokers.⁴
8. Lung cancer risk increased by as much as 5 times in asbestos exposure.⁵
9. Non-smokers have a statistically significant greater risk of lung cancer if their spouses are smokers than if their spouses are non-smokers.⁶
10. Nondrinkers who smoked 25 or more cigarettes per day had a seven-fold increased risk of oral and pharyngeal cancer compared with nonsmokers.⁷
11. Alcohol when combined with cigarette smoke increases the risk of cancer in the upper aero-digestive tract significantly.⁸
12. Smoking has been shown to increase the risk of cancers of the uterine cervix, urinary bladder, and penis.⁹
13. Cigarette smoking, both past and present, is responsible for approximately 20% of kidney cancer cases among men, and for 10% of cases among women.¹⁰
14. Smokers' under cancer treatment are at increased risk of experiencing postoperative complications, such as delayed wound healing, and pulmonary and cardiovascular complications, as compared to non-smokers or former smokers. It also affects radiation therapy adversely.¹¹
15. The longer the interval between smoking cessation and initiation of cancer treatment, the better the prognosis.¹²
16. Ten to 15 years after giving up smoking, the ex-smoker faces the same low risk of developing cancer of the upper digestive tract, the lungs, the pancreas, and the urinary tract as the nonsmoker.¹³

References:

1. U.S. Department of Health and Human Services. The Health Consequences of Smoking: A Report of the Surgeon General. Atlanta: U.S. Department of Health and Human

- Services, Centers for Disease Control and Prevention, National Center for Chronic Disease Prevention and Health Promotion, Office on Smoking and Health, 2004
2. Shields PG. Epidemiology of tobacco carcinogenesis *Curr Oncol Rep.* 2000; 2(3): 257–62.
 3. Quit-Smoking-Stop.com. 2011. Available at <http://www.quit-smoking-stop.com/lung-cancer.html>
 4. Tan WW, Farina GA, Huq S, Maghfoor I, Perry M, Ramnarine M. Non-small cell lung cancer. Available at <http://emedicine.medscape.com/article/279960-diagnosis>. 2008; updated: Mar. 30, 2011.
 5. Veys CA. Education and debate ABC of work related disorders: occupational cancers. *BMJ.* 1996; 313:615–9.
 6. Vineis P, Airolidi L, Veglia F, Olgiati L, Pastorelli R, Autrup H, Dunning A, et al. Environmental tobacco smoke and risk of respiratory cancer and chronic obstructive pulmonary disease in former smokers and never smokers in the EPIC prospective study. *BMJ.* 2005; 330(277), doi:10.1136/bmj.38327.648472.82 (published 28 January 2005).
 7. Pelucchi C, Gallus S, Garavello W, Bosetti C, La Vecchia C. Cancer risk associated with alcohol and tobacco use: focus on upper aerodigestive tract and liver. *Alcohol Res Health.* 2006; 29(3):193–8.
 8. Schlecht NF, Franco EL, Pintos J, Negassa A, Kowalski LP, Oliveira BV, et al. Interaction between tobacco and alcohol consumption and the risk of cancers of the upper aero-digestive tract in Brazil, *Am J Epidemiol.* 1999; 150(11):1129–37.
 9. Harish K, Ravi R. The role of tobacco in penile carcinoma. *Br J Urol.* 1995; 75(3):375–7.
 10. Scélo G, Brennan P. The epidemiology of bladder and kidney cancer, *Nat Clin Pract Urol.* 2007; 4(4):205–17. Available at www.nature.com/clinicalpractice/uro.
 11. Cooley ME, Sipples RL, Murphy M, Sarna L. Smoking cessation and lung cancer: oncology nurses can make a difference. *Semin Oncol Nurs.* 2008; 24(1):16–26.
 12. Gritz ER, Fingeret MC, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: smoking cessation in cancer patients. *Cancer.* 2006; 106(1):17–27.
 13. Wynder EL, Hoffmann D. Tobacco and tobacco smoke. *Semin Oncol.* 1976; 3(1):5–15.

VII. REFERENCE LISTS FOR MODULES

Mini Lecture 1: Tobacco and carcinogenesis

1. Shields PG. Epidemiology of tobacco carcinogenesis *Curr Oncol Rep.* 2000; 2(3): 257–62.
2. Van Duuren BL. Tobacco carcinogenesis. *Cancer Res.* 1968; 28(11):2357–62.
3. Hecht SS Tobacco smoke carcinogens and lung cancer. *J Natl Cancer Inst.* 1999; 91:1194–1210.
4. Tsurutani J, Castillo SS, Brognard J, Granville CA, Zhang C, Gills JJ, et al. Tobacco components stimulate Akt-dependent proliferation and NFκB-dependent survival in lung cancer cells. *Carcinogenesis.* 2005; 26(7):1182–95.
5. Hoffmann D, Hecht SS. Nicotine-derived JV-nitrosamines and tobacco-related cancer: current status and future directions. *Cancer Res.* 1985; 45:935–44.
6. Hiatt RA, Rimer BK. A new strategy for cancer control research. *Cancer Epidemiol Biomarkers Prevent.* 1999; 8:957–64.

7. Hecht SS. Cigarette smoking and lung cancer: chemical mechanisms and approaches to prevention. *Lancet Oncol.* 2002; 3:461–9.

Mini Lecture 2: Tobacco & Respiratory Cancers

1. Vineis P, Alavanja M, Buffler P, Fontham E, Franceschi S, Gao YT, et al. Tobacco and cancer: recent epidemiological evidence. *J Natl Cancer Inst.* 2004; 96(2):99–106.
2. Quit-Smoking-Stop.com. 2011. Available at <http://www.quit-smoking-stop.com/lung-cancer.html>
3. Tan WW, Farina GA, Huq S, Maghfoor I, Perry M, Ramnarine M. Non-small cell lung cancer. Available at <http://emedicine.medscape.com/article/279960-diagnosis>. 2008; updated: Mar. 30, 2011.
4. Veys CA. Education and debate ABC OF work related disorders: occupational cancers, *BMJ.* 1996; 313:615–19.
5. Vineis P, Airoidi L, Veglia F, Olgiati L, Pastorelli R, Autrup H, et al. Environmental tobacco smoke and risk of respiratory cancer and chronic obstructive pulmonary disease in former smokers and never smokers in the EPIC prospective study. *BMJ.* 2005; 330:277 (5 February), doi:10.1136/bmj.38327.648472.82 (published 28 January 2005).
6. Godtfredsen NS, Prescott E, Osler M. Effect of smoking reduction on lung cancer risk. *JAMA.* 2005; 294:1505–10.
7. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Doll R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two case-control studies. *BMJ.* 2000; 321:323–29.
8. Halpern MT, Gillespie BW, Warner KE. Patterns of absolute risk of lung cancer mortality in former smokers. *J Natl Cancer Inst.* 1993; 85(6):457–64.
9. Hecht SS. Tobacco smoke carcinogens and lung cancer. *J Natl Cancer Inst.* 1999; 91:1194–1210.

Mini Lecture 3: Tobacco and Digestive Tract Cancers

1. Polesel J, Talamini R, La Vecchia C, Levi F, Barzan L, Serraino D, et al. Tobacco smoking and the risk of upper aero-digestive tract cancers: a reanalysis of case-control studies using spline models. *Int J Cancer.* 2008; 122(10):2398–402.
2. Lagergren J, Bergström R, Lindgren A, Nyren O. The role of tobacco, snuff and alcohol use in the aetiology of cancer of the oesophagus and gastric cardia. *Int J Cancer.* 2000; 85:340–6.
3. Pelucchi C, Gallus S, Garavello W, Bosetti C, La Vecchia C. Cancer risk associated with alcohol and tobacco use: focus on upper aerodigestive tract and liver. *Alcohol Res Health.* 2006; 29(3):193–8.
4. American Cancer Society article 2002 available at http://www.cancer.org/docroot/NWS/content/NWS_1_1x_Large_Study_Links_Tobacco_To_Stomach_Cancer.asp
5. Slattery ML, Potter JD, Friedman GD, Ma K, Edwards S. Tobacco use and colon cancer. *Int J Cancer.* 1997; 70:259–64.
6. Dikshit RP, Kanhere S. Tobacco habits and risk of lung, oropharyngeal and oral cavity cancer: a population-based case-control study in Bhopal, India. *Int J Epidemiol.* 2000; 29(4):609–14.

7. Phukan RK, Zomawia E, Narain K, Hazarika NC, Mahanta J. Tobacco use and stomach cancer in Mizoram, India. *Cancer Epidemiol Biomarkers Prev.* 2005; 14(8):1892–6.
8. Gangane N, Chawla S, Anshu, Gupta SS, Sharma SM. Reassessment of risk factors for oral cancer. *Asian Pacific J Cancer Prev.* 2007; 8:243–8.
9. Bhonsle RB, Murti PR, Gupta PC. Tobacco habits in India. In: Gupta PC, Hamner JE III, Murti PR, editors. *Tobacco related cancer and other diseases.* Bombay: Oxford University Press; 1992. P. 25–46.
10. Schlecht NF, Franco EL, Pintos J, Negassa A, Kowalski LP, Oliveira BV, et al. Interaction between tobacco and alcohol consumption and the risk of cancers of the upper aero-digestive tract in Brazil. *Am J Epidemiol.* 1999; 150(11):1129–37.

Mini Lecture 4: Tobacco and Urogenital Cancer

1. Harish K, Ravi R. The role of tobacco in penile carcinoma. *Br J Urol.* 1995; 75(3):375-7.
2. Scélo G, Brennan P. The epidemiology of bladder and kidney cancer. *Nat Clin Pract Urol.* 2007; 4(4):205–17.
3. Bjerregaard BK, Raaschou-Nielsen O, Sørensen M, Frederiksen K, Christensen J, Tiønnealand A, et al. Tobacco smoke and bladder cancer—in the European Prospective Investigation into Cancer and Nutrition. *Int J Cancer.* 2006; 119(10):2412–6.
4. Jiang X, Yuan JM, Skipper PL, Tannenbaum SR, Yu MC, Environmental tobacco smoke and bladder cancer risk in never smokers of Los Angeles County. *Cancer Res.* 2007; 67(15):7540–5.
5. Hemminki K, Chen B. Parental lung cancer as predictor of cancer risks in offspring: clues about multiple routes of harmful influence? *Int J Cancer.* 2006; 118(3):744–8.
6. Brennan P, Bogillot O, Cordier S, Greiser E, Schill W, Vineis P, et al. Cigarette smoking and bladder cancer in men: a pooled analysis of 11 case-control studies. *Int J Cancer.* 2000; 86(2):289-94.
7. Hughes DA, Haslam PL, Townsend PJ, Turner-Warwick M. Numerical and functional alterations in circulatory lymphocytes in cigarette smokers. *Clin Exp Immunol.* 1985; 61:459–66.
8. Lahat N, Alexander B, Levin D, Moskovitz B. The relationship between clinical stage, natural killer activity and related immunological parameters in adenocarcinoma of the prostate. *Cancer Immunol Immunother.* 1989; 28:208–12.

Mini Lecture 5: Tobacco Cessation as an Important Part of Cancer Management

1. Cooley ME, Sipples RL, Murphy M, Sarna L. Smoking cessation and lung cancer: oncology nurses can make a difference. *Semin Oncol Nurs.* 2008; 24(1):16–26.
2. Gritz ER, Fingeret MC, Vidrine DJ, Lazev AB, Mehta NV, Reece GP. Successes and failures of the teachable moment: smoking cessation in cancer patients. *Cancer.* 2006; 106(1):17–27.
3. McBride CM, Ostroff JS. Teachable moments for promoting smoking cessation: the context of cancer care and survivorship. *Cancer Control.* 2003; 10(4):325–33.
4. Wynder EL, Hoffmann D. Tobacco and tobacco smoke. *Semin Oncol.* 1976; 3(1):5–15.
5. Brennan P, Bogillot O, Cordier S, Greiser E, Schill W, Vineis P, et al. Cigarette smoking and bladder cancer in men: a pooled analysis of 11 case-control studies. *Int J Cancer.* 2000; 86(2):289–94.

6. Ebbert JO, Yang P, Vachon CM, Vierkant RA, Cerhan JR, Folsom AR, et al. Lung cancer risk reduction after smoking cessation: observations from a prospective cohort of women. *J Clin Oncol*. 2003; 21(5):921–6.
7. Peto R, Darby S, Deo H, Silcocks P, Whitley E, Dol R. Smoking, smoking cessation, and lung cancer in the UK since 1950: combination of national statistics with two casecontrol studies. *BMJ*. 2000; 321(7257):323–9.
8. Frobisher C, Winter DL, Lancashire ER, Reulen RC, Taylor AJ, Eiser C, et al. Extent of smoking and age at initiation of smoking among adult survivors of childhood cancer in Britain. *J Natl Cancer Inst*. 2008; 100:1068–81.

VIII. INSTRUCTOR KEY RESOURCES/REFERENCES

Mini Lecture 1

1. Hecht SS. Cigarette smoking and lung cancer: chemical mechanisms and approaches to prevention. *Lancet Oncol*. 2002; 3:461–9.

Mini Lecture 2

1. Vineis P, Alavanja M, Buffler P, Fontham E, Franceschi S, Gao YT, et al. Tobacco and cancer: recent epidemiological evidence. *J Natl Cancer Inst*. 2004; 96(2):99–106.
2. Tan WW, Farina GA, Huq S, Maghfoor I, Perry M, Ramnarine M. Non-small cell lung cancer. Available at <http://emedicine.medscape.com/article/279960-diagnosis>. 2008; updated: Mar. 30, 2011.

Mini Lecture 3

1. Polesel J, Talamini R, La Vecchia C, Levi F, Barzan L, Serraino D, et al. Tobacco smoking and the risk of upper aero-digestive tract cancers: a reanalysis of case-control studies using spline models. *Int J Cancer*. 2008; 122(10):2398–402.
2. Schlecht NF, Franco EL, Pintos J, Negassa A, Kowalski LP, Oliveira BV, et al. Interaction between tobacco and alcohol consumption and the risk of cancers of the upper aero-digestive tract in Brazil. *Am J Epidemiol*. 1999; 150(11):1129–37.

Mini Lecture 4

1. Scélo G, Brennan P. The epidemiology of bladder and kidney cancer. *Nat Clin Pract Urol*. 2007; 4(4):205–17.

Mini lecture 5

1. Cooley ME, Sipples RL, Murphy M, Sarna L. Smoking cessation and lung cancer: oncology nurses can make a difference. *Semin Oncol Nurs*. 2008; 24(1):16–26.

IX. INSTRUCTOR WEB-SITE RESOURCES

