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KNOWN WHATS WRONG WITH CIGRATTE SMOKING AND INFECTION

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ABSTRACT

Infectious diseases may rival cancer, cardiovascular disease, and chronic lung disease as sources of morbidity and mortality from smoking. The factor for premature mortality thanks to cancer, upset, and chronic obstructive pulmonary disease. Cigarette smoking also appears to be a serious risk factor for tract and other systemic infections. Both active and passive cigarette smoke exposure increases the chance of infections. The morbidity and mortality of infectious diseases because of smoking aren't widely appreciated by physicians. The mechanism of increased susceptibility to infections in smokers is multi-factorial and includes alteration of the structural and immunologic host defenses. The aims of this text are to review the mechanisms by which smoking increases the danger of infection, to review the epidemiology of smoking-related in- infections, and to debate.

KEYWORDS: Cigarette smoking, Epidemiology of smoking-related in- infections,

I INTRODUCTION / METHODS

All relevant English-language articles published between 1978 and 2003 within the MEDLINE database were searched, by using the terms cigarette smoking and system, cellular immunity, humeral immunity, white corpuscle, cytokine, and chemotaxis, furthermore as cigarette smoking with various specific infectious diseases. Selected references contained in these ar- articles were also reviewed. Studies were included if they seemed to be scientifically valid; however, no formal quality classification system was accustomed to screen articles for inclusion.

MECHANISMS BY WHICH SMOKING MAY PREDISPOSE TO INFECTION

The specific mechanisms by which cigarette smoking increases the danger of systemic infections are incompletely understood. They're multi factorial and possibly interactive in their effects. They include structural and immunologic mechanisms Mechanical and Structural Changes Caused by Smoking Cigarette smoke and plenty of its components produce structural changes within the tract. A number of components of cigarette smoke, including acrolein, ac- acetaldehyde, formaldehyde, free radicals produced from chemical reactions within the cigarette smoke, and gas, may contribute to the observed structural alterations within the airway epithelial cells.2, 3 Immunologic Mechanisms.

CELL-MEDIATED IMMUNE RESPONSES.

Cell Counts and Distribution in Peripheral Blood. Smokers on the average exhibit an elevated peripheral white vegetative cell count, about 30% on top of of nonsmokers. All major cell types are increased.6-10 Taylor et al11 found a big relationship between the overall white vegetative cell count in smokers and also the plasma concentration of nicotine. Fried- man et al9 suggested that nicotine-induced catecholamine release may be the mechanism for this effect The authors suggested that pro inflammatory factors released . alalveolar macrophages, like tumor necrosis factor α, interleukin (IL) 1, IL-8, and granulocyte-macrophage colony-stimulating factors, are probably liable for the stimulation of bone marrow by cigarette smoking. Vanuxem et al13 found that white somatic cell count in smokers was associated with the carboxy hemoglobin concentration reflecting exposure to cigarette smoke. Tell et al14 showed the identical relationship between cigarette smoking and increased leukocyte count in adolescents, indicating that there appears to be a rapid effect of cigarette smoking on white somatic cell count that's unlikely to result to smoking-induced chronic disease conditions as seen in adult smokers. Reports of the consequences of smoking on the various subsets of lymphocyte T cells are conflicting. The influence of cigarette smoking on lymphocyte T-cell subpopulations within the peripheral blood has been investigated by means of monoclonal antibodies. Light to moderate smokers (history of but 50 pack-years) were reported to possess a significant increase in CD3+ and CD4+ counts and a trend toward in- creased CD8+ lymphocyte count. The observed increase within the ratio of CD4+ to CD8+ lymphocytes in light smokers was because of the rise of CD4+ cells.6,10,15-17 Two to 4 years af- ter smoking cessation, the rise in CD4+ cells disappeared.15,18 against this, studies of heavy smokers (≥50 pack-years) reported a decrease in CD4+ and a major increase in CD8+ cell counts. Thus, the decrease observed within the ratio of CD4+ to CD8+ lymphocytes in heavy smokers was due predominantly to a rise of CD8+ cells. Other studies have reported no difference within the CD4+ and CD8+ lymphocyte counts among moderate smokers.19 Since CD4+ cells facilitate B-cell proliferation and differentiation and immunoglobulin synthesis, the decrease during this subset observed in heavy smokers might contribute to the increased susceptibility to infections during this population. a rise in CD8+ cells, like that observed in heavy smokers, has been associated with both neoplasia and infection.20 Studies on Lung Fluids. The re-results of studies of broncho alveolar fluid from smokers differ from findings within the peripheral blood. Broncho alveolar lavage studies19,21,22 have demonstrated a marked decrease within the percentage and absolute number of CD4+ cells, and a rise in CD8+ cells with a lower CD4+/CD8+ cell ratio Thus, changes in lymphocyte population within the broncho alveolar lavage in smokers may disclose pathologic changes ahead of in blood. Moreover, these findings suggest that smokers have a deficit in cell-mediated immunity within the lung alveolus, a site critical within the first-line defense against infection. Smoking is additionally related to significant increases within the percentage of macrophages22 in broncho alveolar lavage fluid.

EFFECTS ON PMN FUNCTION.

The motility and chemotaxis of PMNs are depressed within the mouth of smokers compared with nonsmokers.24,26 Which constituents of smoke are answerable for these effects remains unclear. Bridges et al27 demonstrated that whole cigarette smoke, its gas phase, and therefore the water-soluble fraction were potent inhibitors of PMN chemotaxis. Of the water-soluble fraction of cigarette smoking, the unsaturated aldehydes (acrolein and crotonaldehyde) were the most important contributors to the inhibitor properties The nonvolatile component failed to inhibit migration. A relationship was observed between the polarity of a fraction and its inhibitory potency; thus, the inhibition of PMN chemotaxis couldn't be attributed to either nicotine or the polycyclic hydrocarbons. Thus, the immuno- suppressive effects of the macro- phages on cell-mediated immunologic response are increased in smokers.30 the discharge of cytokines from macrophages may additionally be altered in smokers.31 Twigg and

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coworkers32 showed that cigarette smoking de- creases the secretion of the pro inflammatory cytokines like IL-1 and IL-6. Wewers et al22 showed de- creased production of tumor necro- sis factor α. Ouyang et al33 and Hagiwara et al34 reported that cigarette smoking also suppresses IL-2 and interferon γ production. Hydroqui- none, the phenolic compound in cigarette tar, had the foremost potent inhibitory effect of those cytokines, whereas nicotine had little effect. On the opposite hand, IL-10 production by human mononuclear cells was inhibited by treatment with nicotine patches in patients with inflammatory bowel disease.35 Recently, Matsunaga et al36 reported that nicotinic acetylcholine receptors are involved within the cytokine responses of alveolar macrophages to Le- gionella pneumophila infection. The cytokines IL-1 and IL-6 are important within the host defense against infection.37, 38 Animal studies have shown that depletion of those cytokines increases susceptibility to bacterial pneumonia. Systemic infections, including bacterial pneumonia. Effects on Lymphocyte Functions. Natural killer (NK) cell activity in peripheral blood has been reported to be reduced in smokers compared with nonsmokers.6, 15,39-41 employing a cytotoxicity assay, Ginns et al16 found that smokers had 47% of the NK activity of nonsmokers.

As little as 6 weeks.15,17 Since NK cells are important within the early surveillance response against viral infections and resistance against microbial infections,43,44 impairment of NK cell activity by cigarette smoking could be a potential One suggested mechanism was through activation of protein tyrosine kinases and therefore the depletion of inositol-1,4,5-trisphosphate–sensitive calcium stores in T cells.47 Humoral system. The results of cigarette smoking on humeral immunity are studied extensively.4,5 Several studies have found that smokers had serum immunoglobulin levels (IgA, IgG, and IgM) 10% to twenty under this implies that the effect was reversible, with a return toward the immunoglobulin levels of nonsmokers. pained either by stimulation of local immunoglobulin production or by exudation of plasma immunoglobulin into alveolar spaces in re-response to inhaled cigarette smoke.53 the supply of opsonic anti-microbial antibodies is crucial for the optimal function of phagocytes to require up and contain bacteria.54 The antibody response to a range of antigens, like influenza virus in- fiction and vaccination55 and Aspergillus fumigatus,56 is depressed in cigarette smokers.

SUMMARY OF IMMUNOLOGIC EFFECTS OF CIGARETTE SMOKING.

In summary, cigarette smoking is related to a range of alterations in cellular and humeral system function. These alterations in- include a decreased level of circulating immune globulins, a depression of antibody responses to certain antigens, a decrease in CD4+ lymphocyte counts, a rise in CD8+ lymphocyte The pathogenesis of smoking's effects on the system isn't well understood. Some investigators have demonstrated an antigenic role of gear in cigarette smoking, leading to the event of antigen-antibody complexes. These complexes are capable of causing pulmonary and peripheral changes in responses of the humeral and cell-mediated system. Hersey et al18 and Costabel et al19 suggested that the antigen-antibody complexes may in- duce localized alterations of the immune status of the saliva and also the broncho alveolar fluid and predispose to tract infections. Smoking, via the results of nicotine, can stimulate catecholamine and corticosteroid release. These mediators might increase CD8+ lymphocytes within the cellular-mediated system17 and suppress the host defense against infections. it's important to acknowledge that several of the immunologic abnormalities in smokers resolve within 6 weeks after smoking cessation, supporting the thought that smoking cessation is effective within the area a awfully short time within the prevention of infections. The results of several studies suggest that nicotine is a very important immunosuppressive component of cigarette smoke, but other components also appear to possess a task.

SMOKING AND CLINICAL INFECTIOUS DISEASES

General Considerations Concerning Epidemiologic Studies Compared with non-smokers, cigarette smoking is related to

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lower socioeconomic status, different diet, greater alcohol and drug use, lower levels of physical ac- activity, and more risk-taking behaviors, including risky sexual behaviors. Most studies have controlled for factors like age, sex, race/ethnicity, alcohol consumption, sexual habits, etc, although not every study has controlled for each possible confounder.

BACTERIAL INFECTIONS PNEUMOCOCCAL PNEUMONIA.

Cigarette smoking may be a substantial risk factor for pneumonia, especially in patients with chronic obstructive pulmonary disease. How- ever, even without chronic obstructive pulmonary disease, smoking may be a major risk factor. during a population-based surveillance study conducted in Dallas County, Texas, in 1995,57 smoking was strongly related to invasive pneumococcal disease in otherwise healthy young and middle-aged adults (30 to 64 years of age), for whom pneumococcal vaccination isn't currently recommended. Among such individuals with invasive pneumococcal disease, 47% were current smokers

In vitro adherence of Streptococcus pneumoniae to buccal epithelial cells is increased in cigarette smokers.60 This increased adherence may persist for up to three years after smoking cessation. Since increased adherence of bacteria to sur- face cells is a longtime pathogenic step for bacterial colonization and in-fiction in both lung and other organs, this could contribute to the increased risk of respiratory tract infection that exists in cigarette smokers.

LEGIONNAIRES DISEASE.

Legion-names disease is life-threatening bronchopneumonia answerable for 1% to three of community-acquired pneumonia . Meningococcal Disease Active Smokers. during a case-control study by Fischer et al,63 36% of patients with the meningococcal disease were current smokers, while 14% were nonsmokers (OR, 2.4; 95% CI, 0.9-6.6). During an epidemic of sero-group C meningococcal disease among college students, 4 of 6 cases were in cigarette smokers, a prevalence much above that of ex- posed controls (OR, 7.8; 95% CI, 1.3-64.4).64 Exposure to Secondhand Tobacco Smoke. Secondhand tobacco smoke exposure has also been related to an increased risk of meningococcal disease. in an exceedingly case-control study, Fischer et al63 established a robust epidemiologic link between smoking and meningococcal disease in children. for youngsters younger than 18 years, having a mother who smoked was the strongest independent risk factor for invasive meningococcal infection compared with other risk factors like maternal education, no primary physician, or humidifier use (OR, 3.8; 95% CI, 1.6-8.9). Thirty-seven percent of the infections might be attributed to maternal smoking. the amount of smokers living within the home and also the number of packs smoked per day had a major linear relationship with the danger of meningococcal disease. No such association was observed for paternal smoking during this study. In the Norwegian population sur- very, Caugant et al66 found a doubling of carriage rate for passive smokers (OR, 2.30; 95% CI, 1.21-4.37).

OTITIS MEDIA AND EXPOSURE TO SECONDHAND TOBACCO SMOKE.

Long-term tobacco smoke exposure may be a risk factor for otitis and bronchitis in children.3 in an exceedingly prospective study, 175 children with recurrent otitis were compared with an age-matched group of 175 children to work out the role of passive cigarette smoking on the incidence of this disease.

PERIODONTAL DISEASE.

Tobacco use could be a substantial risk factor for periodontitis.73,74 Smokers are 2.5 to six times more likely to develop disease than nonsmokers, and there's an on the spot relationship between the amount of cigarettes smoked and therefore the risk of developing disease.

THE PATHOGENESIS OF ULCER DISEASE IS MULTIFACTORIAL.

Helicobacter pylori in-fiction and smoking are well-established risk factors. Quite 95% of duodenal ulcers are related to H pylori infection, and treatment of H pylori markedly reduces ulcer recurrence rates. Smokers are more

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likely to develop ulcers.81 Ulcers in smokers take longer to heal82 and relapse more often in smokers compared with nonsmokers.83-85 Moskowitz et al86 found that gastric and duodenal ulcers were more prevalent in smokers than non-smokers (gastric, 4.1% vs 1.8%; duodenal, 50% vs 39.8%, respectively; P<.05). Bateson,87 in an exceedingly prospective study, reported that 51.8% of patients with duodenal ulcers and 48.8% of these with gastric ulcers were smokers, compared with 31.8% of the controls. This study reported an association between current smoking and H pylori infection in patients with normal results of endoscopy. Current cigarette smokers had the next rate (49.6%) of H pylori infection than nonsmokers and ex-smokers (35.5%) (P<.01). In another study, 73% of H pylori-positive smokers had a duodenal or peptic ulcer, whereas only 27% of seropositive nonsmokers had ulcers.88 Recently, Nakamura et al89 re- ported an increased risk of severe atrophic gastritis and intestinal metaplasia related to smoking (OR, 9.31; 95% CI, 3.85-22.50; and OR, 4.91; 95% CI, 1.90-12.68) within H pylori-positive subjects. Viral Infections Common Cold. Large epidemiologic studies support the association between smoking and therefore the prevalence of colds and lower tract symptoms. in a very prospective co- short study, Blake et al93 examined an oversized group people Army recruits (1230 soldiers) and located that 22.7% of smokers had upper infection compared with 16% of nonsmokers; relative risk of 1.5 (95% CI, 1.1-1.8). Cohen et al94 showed that smoking status was predictive of the de- velopment of clinical colds after they exposed 400 healthy volunteers intranasally to an occasional dose of 1 of 5 respiratory viruses. Viral suspensions were installed into the nares and infections were diagnosed supported viral isolation, virus-specific antibody, and clinical findings. Smokers had a significantly higher incidence of acute infection (clinical cold) than non-smokers, with an OR of two.23 (95% CI, 1.03-4.82). Among virologically confirmed infected individuals, smoking was related to the next likelihood of symptoms lead- ing to a clinical diagnosis (OR, 1.83; 95% CI, 1.00-3.36). Influenza. Several studies have confirmed the connection between cigarette smoking and also the risk of influenza infections.97 Influenza infections are more severe, with more cough, acute and chronic phlegm production, breathlessness, and wheezing in smokers. Female smokers within the Israeli Army had a 60% risk of in- influenza compared with 41.6% in nonsmokers (OR, 1.44; 95% CI, 1.03-2.01). They also had a 44% increase in complications (visited the clinic more frequently) during a scourge influenza illness caused by the A(H1N1) subtype.98 In another study of 336 healthy young male re- fruits within the Israeli unit conducted by Kark et al,99 the incidence of influenza was 68.5% among smokers and 47.2% among non-smokers (P<.001). The OR was 2.42 (95% CI, 1.53-3.83). Influenza was more severe among smokers, with a dose-related increase in rate: 30% in nonsmokers, 43% in light smokers, and 54% in heavy smokers (P <.001). Work loss occurred in 50.6% of smokers and 30.1% of non-smokers. Overall, 31.2% (95% CI, 16.5-43.1) of influenza cases were attributed to cigarette smoking. Varicella. In adults, varicella infection is related to a considerable incidence of complications. one amongst these complications is varicella pneumonitis, that smokers appear to be at greater risk. Ellis et al104 showed that among 29 adults with varicella infection, 7 of the 19 smokers were hospitalized with pneumonitis, but none of the ten nonsmokers developed pneumonia. Later, Grayson and Newton-John105 reported a 15-fold risk of varicella pneumonitis in smokers compared with nonsmokers and varicella (P<.001). Human Papillomavirus Infections. Human papillomavirus (HPV) in- fection of the lower genital tract is one in every of the foremost common sexually transmitted diseases and is that the reason for cervical intraepithelial neoplasia. Although the human papillomavirus is that the agent, the clinical manifestations of HPV are a function of the interaction of the virus and other factors like the pa- tient's cell-mediated and humoral system, further as patient characteristics like smoking.106 Human Immunodeficiency infection. some studies have investigated cigarette smoking as a cofactor for AIDS in individuals infected with the human immunodeficiency virus (HIV). the primary association between smoking and AIDS was observed by Newell et al.113 Later, Royce and

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Winkelstein114 reported an elevated risk of AIDS and a more rapid progression in seropositive smokers compared with nonsmoker.

SUMMARY AND IMPLICATIONS

Cigarette smoking remains an enormous unhealthiness and is that the principal reason behind several preventable diseases and far premature death. Generally, physicians consider cancer, atherosclerotic disorder, and chronic obstructive pulmonary disease because the major health problems caused by smoking. Infectious diseases may rival cancer, cardiopathy, and chronic lung disease as sources of morbidity and mortality from smoking. We have reviewed the strength of the association between smoking and infections as measured by relative risk and therefore the presence of a dose- response effect. The possible mechanisms by which smoking increases the danger of infections include structural changes within the tract and a decrease in immune response, both systemically and locally within the lungs. Cigarette smoking could be a substantial risk factor for important bacterial and viral infections. To high- light a number of the more common and heavy links between smoking and infection, smokers incur a 2- to 4-fold increased risk of invasive pneumococcal disease, a disease related to high mortality. Influenza risk is several fold higher and far more severe in smokers compared with non-smokers. Perhaps the best public health impact of smoking on infection is that the increased risk of tuberculosis. the best rates of tuberculosis and associated mortality are among the poor and folks in under- developed countries. The prevalence of smoking is high among the poor in developed countries and is in- creasing rapidly in underdeveloped countries. Thus, it's likely that smoking contributes substantially to the worldwide disease burden of tuberculosis

1. Smoking cessation should be a part of the therapeutic plan for people with any serious communicable disease, periodontitis, or positive results of tuberculin skin tests.
2. Secondhand smoke exposure should be controlled in children to re- duce the risks of meningococcal dis- ease and otitis and in adults to scale back the risks of influenza and meningococcal disease.

3.we've got 3 recommendations for prevention of specific diseases:

- Pneumococcal and influenza vaccine all told smokers
- Acyclovir treatment for varicella in smokers
- Yearly Papanicolaou smears in women who smoke. Accepted for Publication: Novem- ber 28, 2003. This study was supported partly by Public Health Service grants DA02277 and DA12393 from the National Insti- tutes of Health, Bethesda, Md, and also the Flight Attendants' Medical Re- search Institute, Miami, Fla.

REFERRENCE

1. Dye JA, Adler KB. Effects of cigarette smoke on epithelial cells of the respiratory tract. *Thorax*. 1994;49:825-834.

2. Marcy TW, Merrill WW. Cigarette smoking and respiratory tract infection. *Clin Chest Med*. 1987; 8:381-391.

3. Richardson MA. Upper airway complications of cigarette smoking. *J Allergy Clin Immunol*. 1988; 81:1032-1035.

4. Sopori ML, Goud NS, Kaplan AM. Effect of to- bacco smoke on the immune system. In: Dean JH, Luster AE, Kimer M, eds. *Immunotoxicol- ogy and Immunopharmacology*. New York, NY: Raven Press; 1994:413-432.

5. Sopori ML, Kozak W, Savage SM, et al. Effect of nicotine on the immune system: possible regu- lation of immune responses by central and pe- ripheral mechanisms. *Psychoneuroendo- crinology*. 1998;23:189-204.

Pro. Dravid Hillton[1]; *[1,] PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh***;** *drags_637@gmail.com.*

6. Tollerud DJ, Clark JW, Brown LM, et al. The effects of cigarette smoking on T cell subsets: a population-based survey of healthy caucasians. *Am Rev Respir Dis*. 1989;139:1446-1451.

7. Yeung MC, Buncio AD. Leukocyte count, smoking, and lung function. *Am J Med*. 1984;76: 31-37.

8. Corre F, Lellouch J, Schwartz D. Smoking and leucocyte-counts: results of an epidemiological survey. *Lancet*. 1971;2:632-634.

9. Friedman GD, Siegelaub AB, Seltzer CC, Feldman R, Collen MF. Smoking habits and the leukocyte count. *Arch Environ Health*. 1973; 26:137-143.

10. Mili F, Flanders WD, Boring JR, Annest JL, Destefano F. The associations of race, cigarette smoking, and smoking cessation to measures of the immune system in middle-aged men. *Clin Immunol Immunopathol*. 1991;59:187-200.

11. Taylor RG, Woodman G, Clarke SW. Plasma nicotine concentration and the white blood cell count in smokers. *Thorax*. 1986;41:407-408.

12. van Eeden SF, Hogg JC. The response of hu- man bone marrow to chronic cigarette smoking. *Eur Respir J*. 2000;15:915-921.

13. Vanuxem D, Sampol J, Weiller PJ. M'Barki M, Grimaud C. Influence of chronic smoking on leukocytes [in French]. *Respiration*. 1984;46: 258-264.

14. Tell GS, Grimm RH Jr, Vellar OD, Theodorsen L. The relationship of white cell count, platelet count, and hematocrit to cigarette smoking in adolescents: the Oslo Youth Study. *Circulation*. 1985; 72:971-974.

15. Hughes DA, Haslam PL, Townsend PJ, Turner-Warwick M. Numerical and functional alterations in circulatory lymphocytes in cigarette smokers. *Clin Exp Immunol*. 1985;61:459-466.

16. Ginns LC, Goldenheim PD, Miller LG, et al. T-lymphocyte subsets in smoking and lung can- cer: analysis of monoclonal antibodies and flow cytometry. *Am Rev Respir Dis*. 1982;126: 265-269.

17. Miller LG, Goldstein G, Murphy M, Ginns LC. Reversible alterations in immunoregulatory T cells in smoking: analysis by monoclonal antibodies and flow cytometry. *Chest*. 1982;82:526- 529.

18. Hersey P, Prendergast D, Edwards A. Effects of cigarette smoking on the immune system: fol- low-up studies in normal subjects after cessation of smoking. *Med J Aust*. 1983;2:425-429.

19. Costabel U, Bross KJ, Reuter C, Ruhle KH, Matthys H. Alterations in immunoregulatory T-cell subsets in cigarette smokers: a phenotypic analysis of bronchoalveolar and blood lymphocytes. *Chest*. 1986;90:39-44.

20. Reinherz EL, Rubinstein A, Geha RS, Strelkauskas AJ, Rosen FS, Schlossman SF. Abnormalities of immunoregulatory T cells in disorders of immune function. *N Engl J Med*. 1979;301:1018-1022.

21. Leatherman JW, Michael AF, Schwartz BA, Hoidal JR. Lung T cells in hypersensitivity pneumonitis. *Ann Intern Med*. 1984;100:390- 392.

22. Wewers MD, Diaz PT, Wewers ME, Lowe MP, Nagaraja HN, Clanton TL. Cigarette smoking in HIV infection induces a suppressive inflammatory environment in the lung. *Am J Respir Crit Care Med*. 1998;158:1543-1549.

Pro. Dravid Hillton[1]; *[1,] PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh***;** *drags_637@gmail.com.*

23. Fisher GL, McNeill KL, Finch GL, Wilson FD, Golde DW. Functional evaluation of lung macrophages from cigarette smokers and nonsmokers. *J Reticuloendothel Soc*. 1982;32:311-321.

24. Noble RC, Penny BB. Comparison of leukocyte count and function in smoking and nonsmoking young men. *Infect Immun*. 1975;12:550-555.

25. Corberand J, Nguyen F, Do AH, et al. Effect of tobacco smoking on the functions of polymorphonuclear leukocytes. *Infect Immun*. 1979; 23:577-581.

26. Eichel B, Shahrik HA. Tobacco smoke toxicity: loss of human oral leukocyte function and fluid-cell metabolism. *Science*. 1969;166:1424- 1428.

27. Bridges RB, Kraal JH, Huang LJ, Chancellor BM. Effects of tobacco smoke on chemotaxis and glucose metabolism of polymorphonuclear leukocytes. *Infect Immun*. 1977;15:115-123.

28. Bridges RB, Hsieh L. Effects of cigarette smoke frac- tions on the chemotaxis of polymorphonuclear leukocytes. *J Leukoc Biol*. 1986;40:73-85.

29. Sasagawa S, Suzuki K, Sakatani T, Fujikura T. Effects of nicotine on the functions of human polymorphonuclear leukocytes in vitro. *J Leukoc Biol*. 1985;37:493-502.

30. Holt PG. Immune and inflammatory function in cigarette smokers. *Thorax*. 1987;42:241-249.

31. McCrea KA, Ensor JE, Nall K, Bleecker ER, Hasday JD. Altered cytokine regulation in the lungs of cigarette smokers. *Am J Respir Crit Care Med*. 1994;150:696-703.

32. Twigg HL III, Soliman DM, Spain BA. Impaired alveolar macrophage accessory cell function and reduced incidence of lymphocytic alveolitis in HIV-infected patients who smoke. *AIDS*. 1994; 8:611-618.

33. Ouyang Y, Virasch N, Hao P, et al. Suppression of human IL-1β, IL-2, IFN-γ, and TNF-alpha production by cigarette smoke extracts. *J Allergy Clin Immunol*. 2000;106:280-287.

34. Hagiwara E, Takahashi KI, Okubo T, et al. Cigarette smoking depletes cells spontaneously secreting Th(1) cytokines in the human airway. *Cytokine*. 2001;14:121-126.

35. Madretsma S, Wolters LM, van Dijk JP, et al. In-vivo effect of nicotine on cytokine production by human non-adherent mononuclear cells. *Eur J Gastroenterol Hepatol*. 1996;8:1017-1020.

36. Matsunaga K, Klein TW, Friedman H, Yama- moto Y. Involvement of nicotinic acetylcholine receptors in suppression of antimicrobial activity and cytokine responses of alveolar macrophages to *Legionella pneumophila* infection by nicotine. *J Immunol*. 2001;167: 6518-6524.

37. Smith KA. Interleukin-2: inception, impact, and implications. *Science*. 1988;240:1169-1176.

38. Luster MI, Simeonova PP, Gallucci R, Mathe- son J. Tumor necrosis factor α and toxicology. *Crit Rev Toxicol*. 1999;29:491-511.

39. Ferson M, Edwards A, Lind A, Milton GW, Hersey P. Low natural killer–cell activity and immunoglobulin levels associated with smoking in human subjects. *Int J Cancer*. 1979;23:603- 609.

Pro. Dravid Hillton[1]; *[1, PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh*; *drags_637@gmail.com.*

40. Nair MP, Kronfol ZA, Schwartz SA. Effects of alcohol and nicotine on cytotoxic functions of human lymphocytes. *Clin Immunol Immunopathol*. 1990;54:395-409.

41. Tollerud DJ, Clark JW, Brown LM, et al. Association of cigarette smoking with decreased numbers of circulating natural killer cells. *Am Rev Respir Dis*. 1989;139:194-198.

42. Silverman NA, Potvin C, Alexander JC Jr, Chretien PB. In vitro lymphocyte reactivity and T- cell levels in chronic cigarette smokers. *Clin Exp Immunol*. 1975;22:285-292.

43. Herberman RB, Holden HT. Natural cell– mediated immunity. *Adv Cancer Res*. 1978; 27:305-377.

44. Herberman RB. *Natural Cell–Mediated Immu- nity Against Tumors*. New York, NY: Academic Press; 1980.

45. Geng Y, Savage SM, Johnson LJ, Seagrave J, Sopori ML. Effects of nicotine on the immune response, I: chronic exposure to nicotine im- pairs antigen receptor–mediated signal trans- duction in lymphocytes. *Toxicol Appl Pharmacol*. 1995;135:268-278.

46. Geng Y, Savage SM, Razani-Boroujerdi S, Sopori ML. Effects of nicotine on the immune response, II: chronic nicotine treatment induces T cell anergy. *J Immunol*. 1996;156:2384-2390.

47. Kalra R, Singh SP, Savage SM, Finch GL, So- pori ML. Effects of cigarette smoke on immune response: chronic exposure to cigarette smoke impairs antigen-mediated signaling in T cells and depletes IP3-sensitive Ca(2+) stores. *J Pharma- col Exp Ther*. 2000;293:166-171.

48. Dales LG, Friedman GD, Siegelaub AB, Selzer CC. Cigarette smoking and serum chemistry tests. *J Chronic Dis*. 1974;27:293-307.

49. Gulsvik A, Fagerhoi MK. Smoking and immunoglobulin levels [letter]. *Lancet*. 1979;1:449.

50. Gerrard JW, Heiner DC, Ko CG, Mink J, Meyers A, Dosman JA. Immunoglobulin levels in smokers and non-smokers. *Ann Allergy*. 1980; 44:261-262.

51. Andersen P, Pedersen OF, Bach B, Bonde GJ. Serum antibodies and immunoglobulins in smok- ers and nonsmokers. *Clin Exp Immunol*. 1982; 47:467-473.

52. Onari K, Seyama A, Inamizu T, et al. Immunological study on cigarette smokers, part I: se- rum protein pattern in smokers. *Hiroshima J Med Sci*. 1978;27:113-118.

53. Warr GA, Martin RR, Sharp PM, Rossen RD. Normal human bronchial immunoglobulins and proteins: effects of cigarette smoking. *Am Rev Respir Dis*. 1977;116:25-30.

54. Reynolds HY. Immunoglobulin G and its func- tion in the human respiratory tract. *Mayo Clin Proc*. 1988;63:161-174.

55. Finklea JF, Hasselblad V, Riggan WB, Nelson WC, Hammer DI, Newill VA. Cigarette smoking and hemagglutination inhibition response to influ- enza after natural disease and immunization. *Am Rev Respir Dis*. 1971;104:368-376

56. Gruchow HW, Hoffmann RG, Marx JJ Jr, Emanuel DA, Rimm AA. Precipitating antibodies to farmer's lung antigens in a Wisconsin farming population. *Am Rev Respir Dis*. 1981;124:411-415.

Pro. Dravid Hillton[1]; *[1,] PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh***;** *drags_637@gmail.com.*

57. Pastor P, Medley F, Murphy TV. Invasive pneumococcal disease in Dallas County, Texas: re- sults from population-based surveillance in 1995. *Clin Infect Dis*. 1998;26:590-595.

58. Nuorti JP, Butler JC, Farley MM, et al; Active Bacterial Core Surveillance Team. Cigarette smok- ing and invasive pneumococcal disease. *N Engl J Med*. 2000;342:681-689.

59. Almirall J, Gonzalez CA, Balanzo X, Bolibar I. Pro- portion of community-acquired pneumonia cases attributable to tobacco smoking. *Chest*. 1999; 116:375-379.

60. Raman AS, Swinburne AJ, Fedullo AJ. Pneumococcal adherence to the buccal epithelial cells of cigarette smokers. *Chest*. 1983;83:23-27.

61. Doebbeling BN, Wenzel RP. The epidemiology of *Legionella pneumophila* infections. *Semin Respir Infect*. 1987;2:206-221.

62. Straus WL, Plouffe JF, File TM Jr, et al; Ohio Legionnaires Disease Group. Risk factors for domestic acquisition of legionnaires disease. *Arch Intern Med*. 1996;156:1685-1692.

63. Fischer M, Hedberg K, Cardosi P, et al. Tobacco smoke as a risk factor for meningococcal disease. *Pediatr Infect Dis J*. 1997;16:979-983.

64. Imrey PB, Jackson LA, Ludwinski PH, et al. Outbreak of serogroup C meningococcal disease associated with campus bar patronage. *Am J Epidemiol*. 1996;143:624-630.

65. Stuart JM, Cartwright KA, Robinson PM, Noah ND. Effect of smoking on meningococcal carriage. *Lancet*. 1989;2:723-725.

66. Caugant DA, Hoiby EA, Magnus P, et al. Asymptomatic carriage of *Neisseria meningitidis* in a randomly sampled population. *J Clin Microbiol*. 1994;32:323-330.

67. Blackwell CC, Tzanakaki G, Kremastinou J, et al. Factors affecting carriage of *Neisseria meningitidis* among Greek military recruits. *Epide- miol Infect*. 1992;108:441-448.

68. Haneberg B, Tonjum T, Rodahl K, Gedde-Dahl TW. Factors preceding the onset of meningococcal disease, with special emphasis on pas- sive smoking, symptoms of ill health. *NIPH Ann*. 1983;6:169-173.

69. Tappero JW, Reporter R, Wenger JD, et al. Meningococcal disease in Los Angeles County, California, and among men in the county jails. *N Engl J Med*. 1996;335:833-840.

70. Kitchens GG. Relationship of environmental tobacco smoke to otitis media in young children. *Laryngoscope*. 1995;105:1-13

71. Ilicali OC, Keles N, Deger K, Savas I. Relationship of passive cigarette smoking to otitis media. *Arch Otolaryngol Head Neck Surg*. 1999;125: 758-762.

72. Stathis SL, O'Callaghan DM, Williams GM, Najman JM, Andersen MJ, Bor W. Maternal ciga- rette smoking during pregnancy is an indepen- dent predictor for symptoms of middle ear disease at five years' postdelivery [serial online]. *Pediatrics*. 1999;104:e16.

Pro. Dravid Hillton[1]; *[1,] PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh***;** *drags_637@gmail.com.*

73. Barbour SE, Nakashima K, Zhang JB, et al. Tobacco and smoking: environmental factors that modify the host response (immune system) and have an impact on periodontal health. *Crit Rev Oral Biol Med*. 1997;8:437-460.

74. Arbes SJ Jr, Agustsdottir H, Slade GD. Environmental tobacco smoke and periodontal disease in the United States. *Am J Public Health*. 2001; 91:253-257.

75. Tomar SL, Asma S. Smoking-attributable periodontitis in the United States: findings from NHANES III: National Health and Nutrition Examination Survey. *J Periodontol*. 2000;71: 743-751.

76. Muller HP. Smoking and periodontal health [in German]. *Gesundheitswesen*. 2000;62:400- 408.

77. Genco RJ. Current view of risk factors for periodontal diseases. *J Periodontol*. 1996;67: 1041-1049.

78. van der Weijden GA, de Slegte C, Timmerman MF, van der Velden U. Periodontitis in smokers and non-smokers: intra-oral distribution of pockets. *J Clin Periodontol*. 2001;28:955-9 mknjkn

79. Shiloah J, Patters MR, Waring MB. The prevalence of pathogenic periodontal microflora in healthy young adult smokers. *J Periodontol*. 2000;71:562-567.

80. Anda RF, Williamson DF, Escobedo LG, Remington PL. Smoking and the risk of peptic ulcer disease among women in the United States. *Arch Intern Med*. 1990;150:1437-1441.

81. Kato I, Nomura AM, Stemmermann GN, Chyou PH. A prospective study of gastric and duode- nal ulcer and its relation to smoking, alcohol, and diet. *Am J Epidemiol*. 1992;135:521-530.

82. Sontag S, Graham DY, Belsito A, et al. Cimetidine, cigarette smoking, and recurrence of duodenal ulcer. *N Engl J Med*. 1984;311:689-693.

83. Korman MG, Hansky J, Eaves ER, Schmidt GT. In- fluence of cigarette smoking on healing and relapse in duodenal ulcer disease. *Gastroenterology*. 1983; 85:871-874.

84. Endoh K, Leung FW. Effects of smoking and nicotine on the gastric mucosa: a review of clinical and experimental evidence. *Gastroenterology*. 1994;107:864-878.

85. Moshkowitz M, Brill S, Konikoff FM, Averbuch M, Arber N, Halpern Z. Additive deleterious effect of smoking on gastroduodenal pathology and clinical course in *Helicobacter pylori*–positive dyspeptic patients. *Isr Med Assoc J*. 2000;2: 892-895.

86. Bateson MC. Cigarette smoking and *Helicobac- ter pylori* infection. *Postgrad Med J*. 1993; 69:41-44.

87. Martin DF, Montgomery E, Dobek AS, Patrissi GA, Peura DA. *Campylobacter pylori*, NSAIDS, and smoking: risk factors for peptic ulcer disease. *Am J Gastroenterol*. 1989;84:1268-1272.

88. Nakamura M, Haruma K, Kamada T, et al. Cigarette smoking promotes atrophic gastritis in *Helicobacter pylori*–positive subjects. *Dig Dis Sci*. 2002;47:675-681.

89. Cover TL, Vaughn SG, Cao P, Blaser MJ. Potentiation of *Helicobacter pylori* vacuolating toxin activity by nicotine and other weak bases. *J In- fect Dis*. 1992;166:1073-1078.

Pro. Dravid Hillton[1]; *[1,] PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh***;** *drags_637@gmail.com.*

90. O’Connor HJ, Kanduru C, Bhutta AS, Meehan JM, Feeley KM, Cunnane K. Effect of *Helicobacter py- lori* eradication on peptic ulcer healing. *Post- grad Med J*. 1995;71:90-93.

91. Borody TJ, George LL, Brandl S, Andrews P, Jank- iewicz E, Ostapowicz N. Smoking does not con- tribute to duodenal ulcer relapse after *Helico- bacter pylori* eradication. *Am J Gastroenterol*. 1992;87:1390-1393. Blake GH, Abell TD, Stanley WG. Cigare

Pro. Dravid Hillton[1]; *[1,] PhD. in Neutraceutical Science and Medicine from Patuakhali Science and Technology University of Bangladesh***;** *drags_637@gmail.com.*