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THE BANALITY OF IMMUNITY, DEATH AND DISTRESS OF TOBACCO SMOKING --("STRIKE THE RIGHT")

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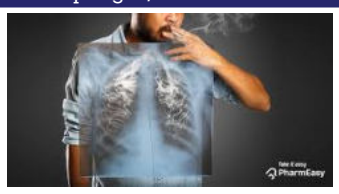
ABSTRACT WHO stated that Tobacco Control is "To protect present and future generations from the devastating health, social, environmental and out-turn of exposure to tobacco smoke".

Tobacco plants are indigenous to American abstinent and they knew of its cultivation thousands of years ago. Christopher Columbus brought this plant to European countries. Portuguese traders brought tobacco plants to India Tobacco put to use in the forms of smoking, chewing, or snorting. Bronchial accounts for more than 50% of all male deaths from malignant disease. It is four times more common in men than in women. Cigarette smoking for most cases of bronchial carcinoma, and the increased risk is directly proportional to the amount smoked and to the tar content of the cigarettes. Smoking puffs of any kind, disclosed to nicotine, have pernicious consequences on immune system.

Nicotine escalates cortisol concentration, while curtail B cell antibody development and T cells' response to antigens. Smoking bumps one and the other innate and adaptive immunity and operates challenge roles in synchronize immunity

KEYWORDS : T helper cells, CD8+ T cells, B cells and memory cells, inflammatory cytokines, Dendritic cells, Macrophages, and Natural Killer cells, Nicotine acetylcholine receptors (nAChR).Harlequin's nails,



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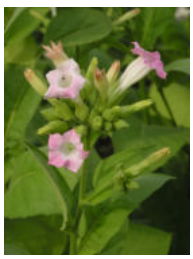

INTRODUCTION

Smoke contains numerous harmful chemicals, CO, NO, Cd and, nicotine. (1)

Exposure of smoke is an important cause of death worldwide (2)

Smoking produces many inflammatory mediators. (3)

Cigarette smoking effects on inflammation.(4,5)

Inflammation of the airways and the lungs is thought to play a major role in the pathogenesis of COPD (6)

Several studies have reported that CS can cause elevated levels of TNF-α, TNF-α receptors, interleukin (IL)-1, IL-6, IL-8, and granulocyte-macrophage colony-stimulating factor (7)

Smoking instigate cellular impairment and serves as an immunosuppressant (8)

Exposure to CS affects the respiratory immune system (9)

Exposure of mononuclear cells to CS declines RNA-cytotoxic function (10,11).

Smoking affect Th1/Th2/Th17, CD4+CD25+ regulatory T cells.(12)

T lymphocytes (T cells) are a major subset of immune cells mediating adaptive immunity.(13)

Nicotine (NT), a major component of cigarette smoke, has been shown to suppress various parameters of the immune system (14)

Chronic NT administration of rats by subcutaneously or intracerebroventricularly implanted mini osmotic pumps (15)

History

Tobacco has long been used in the Americas, with some cultivation sites in Mexico,1400–1000 BCE (16)

American tribes traditionally grow and use tobacco. (17,18)

In some domestic society, tobacco is seen as a gift from the Creator (19)

The English colony, Jamestown used tobacco as a cash crop(20)

The astronomer Thomas Harriot, on his 1585 expedition to Roanoke Island, thought that the plant "openeth all the pores and passages of the body" (21)

Manufacturing of tobacco became a major industry in Europe (22)

Tobacco has been a major cash crop in Cuba and in other parts of the Caribbean islands. (23)

James Bonsack invented a machine cigarette manufacturing (24)

Table-1

Healthy lungs	Smokers lungs
Pink	Gray or black
Normal size	Hyperinflated
No inflammation	Patches of inflammation
Dome-shaped diaphragm	Diaphragm muscle loss

Immunity

Immunity is concerned with resistance to infection. This is carried out by the process of recognition and disposal of no self or foreign material that enters the body.

Adaptive immunity

Adaptive immunity is also called acquired immunity. It is mediated by either B cells (antibody) or T cells (cell-mediated immunity). As a core function it recognizes antigenic molecules where antigens can be "foreign" or "self" and against that cytokines (messengers) are produced.

T lymphocytes

T-lymphocytes alter theratio of helper and suppressor cells and lowers the NK cell activity.Reduces the production of IFN-gamma

T lymphocytes (T cells) are mediating adaptive immunity, and these cells exert in response to specific antigens. Previous research explained the impacts of cigarette smoking on T cells and their release of proinflammatory substances. Tobacco smoking produces many diseases, and specifically, major cause of COPD and results the airflow obstruction (25)

Forsslund et al. (26) analysed T cells in Broncho alveolar lavage (BAL) fluid (27)

T-cell populations from non-smokers proved that passive smoking was positively correlated with the prevalence of CD3+ T cells (28)

CD8+ T cells

CD8+ T cells play an important role in host immune defense. CD8+ T cells serve as a key mediator of COPD.

Current research proved that CD8+ T cells facilitated the production of macrophage elastase, contributing to elastin fragmentation and pulmonary injury (29)

Nadigal et al. (30) found an increase in cytokine expression in human CD8+ T cells, from lung tissue of COPD patients Biochemical analysis of clinical specimens from 9 smokers with COPD and 7 healthy smokers for lung showed that CD8+ T cells were also increased in the peripheral airways of COPD patients compared with healthy smokers (31), and their proliferation was induced by CSE (32)

Study on emphysema mice demonstrated that cigarette smoke not only increased the percentage of IL-21+ Th17 and IL-21R+ CD8+ T cells in peripheral blood, but also enhanced their expressions of IL-17 and IL-21 (33)

Effects of cigarette smoking on the pulmonary alveolar macrophage

Macrophages are responsible for the presentation of antigen to the immunocompetent cells.

Alveolar macrophage is the key phagocytic cell in the normal lung (34)

Exposure to cigarette smoke also changes the macrophage phenotype (35)

The phagocytic function of macrophage is grossly reduced by cigarette smoke, capacity of the macrophage to clear the inflammatory cells and debris from the lungs (36,37)

Effects of cigarette smoking on alveolar lymphocytes and NK cells

Cigarette smoking alters the T cell responses, which has been associated with increased susceptibility to respiratory tract infections.

Production of cytokines was significantly suppressed by cigarette smoke (38)

Ferson et al. observed that lymphocytes from healthy smokers have a low natural killer-cell activity

Active immunity

The immunity which results from exposure to an antigen results in natural infection, Vaccination, Passive immunity. Immune components from an exposed individual are transferred to and individual without immunity. Usually antibodies. Occasionally cellular Cytokines.

Tobacco impact on immunity

The chronic inhalation of tobacco contains chemicals that have toxic and/or carcinogenic activity. These chemicals have been implicated in immune or inflammatory mediators, pro and anti-inflammatory.

The main metabolite from benzene is hydroquinone, which inhibits the progression of T lymphoblasts. Tobacco smoking has an impact on both the innate and adaptive immunity.

The cells involved in the innate immunity are mainly dendritic cells, macrophages, and Natural Killer cells. **(39,40,41)**

ADAPTIVE IMMUNITY	
Cells	*Effect*
T helper cell 1 (Th1)	Increase cell percentage. Altered: IFN-gamma increased
T helper cell 17 (Th17)	Increase ROR-gammat, cell percentage, IL-6, IL-23, IL-17A. Decrease IL-17+ cell percentage in colitis

T helper cell (Th2)	Increase IL-4, IL-5, IL-13, cell percentage, activated GATA3/Lck/ERK 1/2. Decrease cell percentage by nicotine
Cytotoxic T lymphocytes CD8+ (CTL)	Increase IP-10 (increase macrophage elastase), perforin, granzyme B, IFN-gamma, IL-6. Altered: cell percentage, chemotaxis.
Regulatory T cell (Treg)	Decrease Foxp3, IL-10. Altered: cell percentage
B cells	Increase IgE and memory B cells. Decreased IgA, IgG, IgM, percentage and development.
INNATE IMMUNITY	
Cells	*Effect*
Macrophages	Increase cell percentage, TLR 2 and TLR4. Higher levels of oxygen radicals and myeloperoxidase activity. Decrease RANTES, CCL5, TLR&, phagocytosis (Staphylococcus aureus and Listeria monocytogenes). Altered: IL-1beta, IL-6, TNF-alpha, IL-8.
Natural killer cells	Increase IL-17A. Altered: IFN-gamma, cell percentage. Decrease TNF-alpha and perforins.
Dendritic cells	Increase TLR2 and TLR4. Decrease IFN-alpha, TLR-7, CCR7, TLR7, CD45, MHC II, IDO. Altered: cell percentage and function.

Smoking, and DNA damage

Tobacco smoking contains over 60 carcinogenic chemicals that, as they are inhaled, provokes a massive influx of neutrophils and macrophages to the respiratory system, damaging its DNA by somatic mutations and methylation. Nicotiner. Has a high affinity to the nicotine acetylcholine receptors (nAChR). This receptor is responsible in the autocrine-proliferation mechanism involved in the growth of cancerous cells by up regulating growth factors; example vascular endothelial growth factors (VEGF) responsible for angiogenesis, and the fibroblast growth factors (FGF) responsible in the stroll tissue growth. Misapplication of the DNA causes an increased load of somatic mutations, each leaving a mutation signature. Signature 4 was found in those type of cancers where the epithelia is directly exposed to tobacco smoking and is likely the responsible for the direct mutational consequences of mis replication of DNA damage induced by the carcinogens in tobacco (42,43)

Cancer Type	**Total number of mutational signatures found in the cancer type**	**Signature 4 found in cancer type**
Small cell lung carcinoma	6	Yes
Lung squamous carcinoma	8	Yes
Lung adenocarcinoma	7	yes
Larynx	5	Yes
Pharynx	5	Yes
Oral cavity	5	Yes
Esophagous squamous carcinoma	9	Yes
Bladder cancer	5	No
Liver cancer	19	Yes
Stomach cancer	13	No
Acute myeloid leukemia	2	No
Ovarian cancer	3	No
Cervical cancer	8	No
Kidney cancer	6	No
Pancreatic cancer	11	No
Colorectal cancer	4	No

Smoking-Lung immunity

World No Tobacco Day is 31st May. It aims at tobacco's repercussions and highlights a world without tobacco with fewer deaths. The most significant risk factor for lung cancer is smoking. It can also cause cancers of the mouth, throat, larynx, oesophagus, bowel, bladder, cervix, kidney, liver, stomach and pancreas. Smoking primarily affects the lungs.

Tobacco-Skindiseases

The integumentary system has faced the brunt of nicotine usage with both positive and inverse associations resulting in aggravation and improvement of the disease process. Dermatological hazards of tobacco can be due to direct alteration of the biophysical properties of the epidermis and dermis and indirectly via the bloodstream. Heavy smokers can typically be identified by characteristic cutaneous and mucosal manifestations. Skin, hair, nails, and mucosa can be the targets affected by tobacco. One-third of smokers have visible oral pigmentation(Gingival) pigmentation. Yellow discoloration demarcation lines on the fingernails (harlequin's nails) are classical presentations (52)

The most common and socially distressing manifestation of smoking is precocious aging with a characteristic plethoric complexion of smokers face.

Cigarette smoking could be a risk factor for squamous cell carcinoma. Smoking aggravates existing dermatoses like contact dermatitis, Psoriasis, SLE, Immune Blistering disorders, cutaneous ulcers. Even nicotine patches themselves can elicit allergic and irritant contact dermatitis. On the other side of coin nicotine has been used as a therapeutic modality in Behcets, Beurger disease, Pyoderma gangrenosum, etc (53)

Tobacco is an incompatible partner that damages the integumentary system and quitting it ameliorates the hazardous consequences on the skin.

Tobacco –Viral diseases

Tobacco -- COVID-19

The effect of Corona virus can be worse for people who use tobacco. Smokers had escalated developing COVID-19 contrast to those who do not smoke, It brings about an abundance of smokers who want to quit tobacco. The severity of COVID-19 disease is higher among smokers.

Quitting tobacco can be a challenge, especially showing up the supplementary social and economic stress that has come with the pandemic. The 2021 canvas of the World No Tobacco Day intends to support tobacco users in their attempt to quit (WHO)

Tobacco--fungal diseases

The cigarette smokers develop respiratory and oral bacterial infections.

Cigarette smoke contributes to yeast infection. oropharyngeal mucosal candidiasis is an opportunistic infection in immunocompromised persons (54)

Candida albicans, a commensal dimorphic yeast that colonizes up to more than half of normally healthy individuals,and causes Candidiasis (55)

invasive candidiasis is the most frequent fungal diseases, go round with aspergillosis and Pneumocystis pneumonia (56,57) The main jeopardy for IFD incorporates hematological cancers, neutropenia, HIV infection, immunodeficiencies, diabetes, kidney diseases (58)

The residents may be at risk for IFD, as a result of exposures,

such as climate and agricultural profession, and lifestyle habits, such as smoking (59)

Tobacco research

Cigarette smoking is a major contributing factor in the development of a large number of fatal and crippling disorders. While burning tobacco, the hot air causes nicotine and other volatile components to evaporate. The volatile components, and nicotine, condense onto smoke particles. The nicotine-rich aerosol, rapidly absorbed into the systemic blood. Besides nicotine, a burning cigarette generates thousands of many other toxic compounds. Cigarette smoke undergoes complex chemical reactions. The toxins generated can deviate from cigarette to cigarette. (60)

Discovery without boundaries

Cigarette smoke extremely affects the immune system, understanding the host's potential to ascend suitable immune and inflammatory responses against microbial agents.

Future directions and challenges

Cigarette smoke is an aerosol of liquid particles be contained for the most part of nitrogen, oxygen, carbon monoxide and carbon dioxide "Major classes of chemicals in the tobacco are toxic and carcinogenic. Tobacco-specific biomarkers (nicotine and nitrosamines) have been approved as quantitative allotments of exposure to tobacco smoke.

1. Boost in leaf tax
2. Cautioning symbols on packaging,
3. Decreasing of tobacco product publication
4. Constitution to demoralize young people to quit tobacco.
5. Export of leaf products by youth and tobacco jurisdiction approach are crucial challenges.

Shortened version of large work

Cigarette smoking affects enzyme levels throughout the body. Smoking is a risk factor for hypertension, heart disease, peripheral vascular disease, chronic obstructive pulmonary disease, and cancers of lung, colon, larynx,oral cavity, oesophagus, bladder, pancreas and kidney. Nicotine escalates cortisol concentration, while curtailing B cell antibody development and T cells' response to antigens. Adaptive immune cells damaged by smoking primarily include T helper cells CD8+ T cells, B cells and memory T/B lymphocytes but innate immune cells encountered by smoking are essentially the macrophages and NK cells. Several studies have reported that CS can cause elevated levels of TNF-□, TNF-□ receptors, interleukin (IL)-1, IL-6, IL-8, and granulocyte-macrophage colony-stimulating factor. Exposure to cigarette smoke also changes the macrophage phenotype.

An opinion arrived at through a process of reasoning

Cigarette smoke is susceptible to all cells and mechanisms, and debilitates the cellular immunity and humoral immunity. Cigarette smoke vitiates the normal defensive function of the immune system. Smoking plays a harmful role. Cigarette smoke principally weakens immunity against infections, and on the other hand stimulates autoimmunity. Smoking makes the lungs more vulnerable to infection and disease. Quit smoking and boost your immunity and don't weaken it. Smoking damages the immune system and increases the chances of suffering from diseases like cancer. Chemicals in smoke reduces the activity of the immune system. Smoking may cause inflammatory bowel disease. Smoking can causes damage to every part of the body. It causes lung, stomach, kidney, pancreas, colon and bladder cancers. It produces chronic diseases like stroke, heart diseases, pneumonia, asthma, hardening of arteries, and reduced fertility. The last cigarette you smoked should be your last.

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