☆ Effects of Nicotine on Human Health ☆

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Abstract :-

Nicotine addiction is a worldwide problem. This review information on adverse effects of nicotine. Nicotine is known as an addiction component. Tobacco is the leading cause of death, killing nearly six million people worldwide each year. India is the second largest consumer of tobacco globally. Tobacco problem in consumption of various smokeless and smoking forms. Tobacco smoke contains over 9000 chemicals including many carcinogens and toxins which accounts for approximately one six of the world tobacco related deaths. There are increased risks of cardiovascular, respiratory, gastrointestinal disorders, decreased immune response and also effects on human reproductive health. It affects the cell proliferation, oxidation stress apoptosis, DNA mutation by various mechanisms which leads to cancer.

Key Words :-

Addiction, nicotine and cancer, cardiovascular, gastrointestinal, respiratory, reproductive.

Introduction :-

Nicotine is derived from the tobacco plant. Tobacco contains products such as cigarettes, cigars, pipe tobacco and chewing tobacco. These are some nicotine containing smoking. Cessation products are patches and gums.[1] Addiction to tobacco kills one person every six seconds And long term smokers largely in low and middle countries will die from tobacco addiction.[2] WHO estimated around 1.27 billion tobacco users and tobacco consumption alone accounts for nearly 5.4 million deaths per years.[3]

An Intentional treaty spearheaded by WHO in 2003 and signed by 170 countries aims to encourage governments to reduce the sales, production, and promotion of tobacco products. Study process in achieving its goal of comprehensive tobacco control around the world.[4]

Forms of Tobacco :-

Nicotine's effects depend on every user on how the nicotine enters the body thus , before discussing the criteria for addiction or how nicotine addiction develops it is useful to understand different forms for centuries. Historically tobacco was mostly chewed or smoked in pipes. Today's most commonly tobacco used in manufactured cigarettes.[5]

▪ Tobacco products are generally categorized as:-

1. Combustible (tobacco that is smoked)
   - Cigarettes
   - Cigars
   - Pipes and Water Pipes (E – Cigarettes)
   - Bidis
   - Kretek
2. Non- Combustible (Chewing Tobacco Snuff)
   - Chewing tobacco
   - Moist and Dry Snuff

1.Combustible Tobacco (Smoked) :-

Cigarettes :-

Cigarettes are commonly used in tobacco products. Tobacco blend rolled in a thin sheet of paper. The tobacco portion of regular cigarettes is 60 mm (2.2 in) in length and filtered cigarettes Have a 25 mm (~1 in) filter and short length of tobacco. Cigarettes contain 1 -2 mg of nicotine. Some brands of cigarettes containing flavoring agents (eg. Flavoring agent menthol) menthol cigarettes mostly used in Africa, Americans . Mostly more women are use menthol cigarettes than men.[6]

Cigarettes

Cigars :-

Cigars consist of tightly rolled dried tobacco leaves wrapped in leaf. Cigars have popularity with both men and women.[7] Cigars have very wide diameter and length.

Eg.

i] Winchester little cigar is 8mm in diameter and 60 mm in length .it containing 5.9 mg nicotine.

ii] Cuesta – Rey no :- 1 is 20 mm in diameter and 211 mm in length. It containing 335.2 mg nicotine.[8]

Cigars

E- Cigarettes:-

E-cigarettes or (electronic nicotine delivery systems) electronic nicotine vaporizers often shaped like cigarettes. E-cigarettes are heaters attached to atomizers and components reduce liquid into a fine spray. Liquid containing nicotine and propylene glycol plugs into atomizers. Today's many e-cigarettes containing flavoring, such as fruits and candy flowers.[8]

E-cigarette

Bidis :-

Bidis are thin , hand – rolled , filterless cigarettes containing flavoured or unflavored tobacco are wrapped. In temburni leaf .Bidis contain higher concentrations of nicotine tar and carbon monoxide. Bidis are mostly used in India.[7]

Bidis

2. **Non – combustible :-**

Chewing Tobacco :-

Chewing tobacco is called as the plug , loose – left, gutkha, and twist chewing tobacco is orally by placing a pinch between the cheek and gum and continously chewing and suckin. [7] masala contain tobacco , areca nuts, slaked lime , sweetening agent , flavoring agents are wrapped in betel leaf varieties of a pans include kaddipudi gund , pattiwala, kadapam, Zarda, kiawam and mishri. Chewing tobacco used in India more than half women's (56%) chewing tobacco.[7]

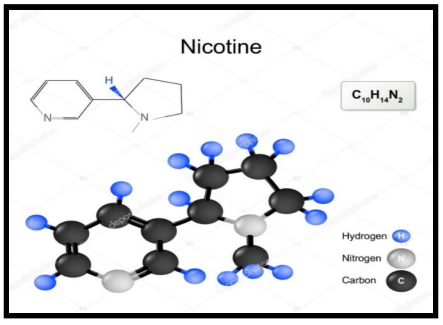
Chewing tobacco

Moist and Dry Snuff :-

Dry snuff is a powdered tobacco they taken orally and inhaled through nose.[7]

Moist and dry snuff

Chemical Properties :-



- Nicotine chemical formula = $C_{10}H_{14}N_2$.
- Molar mass = 162.23 g/mol g. mol^{-1}
- Melting point = -79° C (-110° F)
- Boiling point = 240 C (477 F)

Nicotine is a strong alkaloid and its pure form is a clear liquid. It is water soluble.[9,10] Nicotine are found in the family solanaceae, such as potatoes, tomatoes and eggplant [9,11] Absorb nicotine high amount can be more harmful nicotine are diabesis compound and

absorption in human body depends upon the PH of the solution. The increase Ph of the solution cause easily pass through all biological membranes.[10] Chemical dependency on nicotine is more powerful than alcoholism , crystal meth or heroin addiction dependency researchers report that nicotine may be the most perfectly designed drug of addition.[12]

Metabolism of Nicotine:-

Nicotine is metabolized to a number of metabolites by the liver, derivative, is converted to cotinine. The transformation involves two phases :- Phase I and Phase II.

Phase I :-

There is microsomal oxidation of nicotine. This leads to formation of various metabolites cotinine and narc nicotine, dimethyl cotinine, trans - 3 – hydroxy – cotinine and d – (3 – pyridyl) – 9 – methylamino butyric acid .[14,15]

Phase II :-

There is `N' and 'O' glucuronidation of the metabolites and excretion via urine, faces, bile, saliva, sweat .[16,17] 5 – 10 % elimination by renal excretion of unchanged nicotine.[18]

The rate of metabolism of nicotine can be measured by blood levels after administration of a known dose of nicotine, the total nicotine average is about 1200 ml min -1. Nonrenal clearance represents about 70% of liver blood flow. The most nicotine is metabolized by the liver. This means 70% drug is extracted from blood in each through liver.[15]

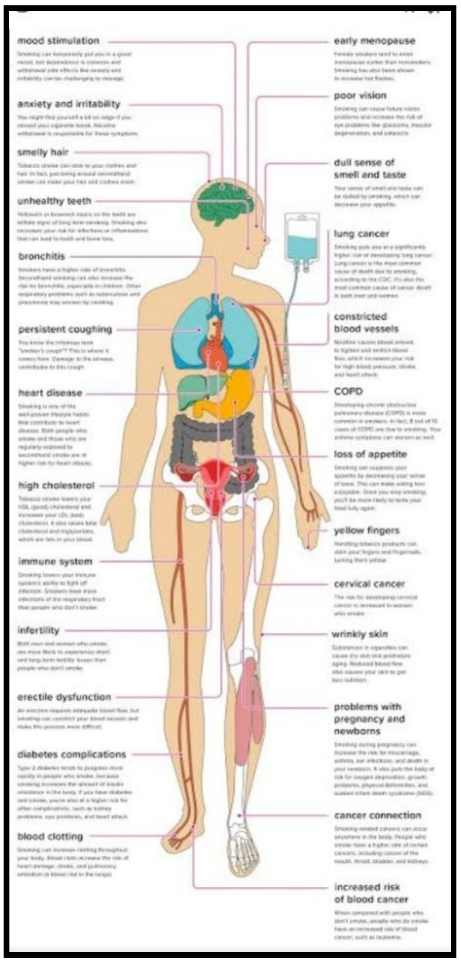
Mechanism of Action :-

Nicotine acts as a three major mechanism produce physiological and pathological effects on variety of organ systems .[21,22]

1. Ganglionic transmission.
2. Nicotine acetylcholine receptors (nAChRs) on chromaffin cells via catecholamines.
3. Central nervous system (CNS) stimulation of nAChRs.

Nicotine is an amine. Nicotine binds to the receptor called as " nicotinic acetylcholine receptors" (nAChRs).[19] chemical messengers that move between nerves, muscles or glands to affects many body function mood and behaviour.[19,20] Nicotine receptors found in adrenal medulla and autonomic ganglia. Nicotine receptors are the ion channel receptors. They have four subunits.[23]

Side Effects of Nicotine :-



effects of nicotine

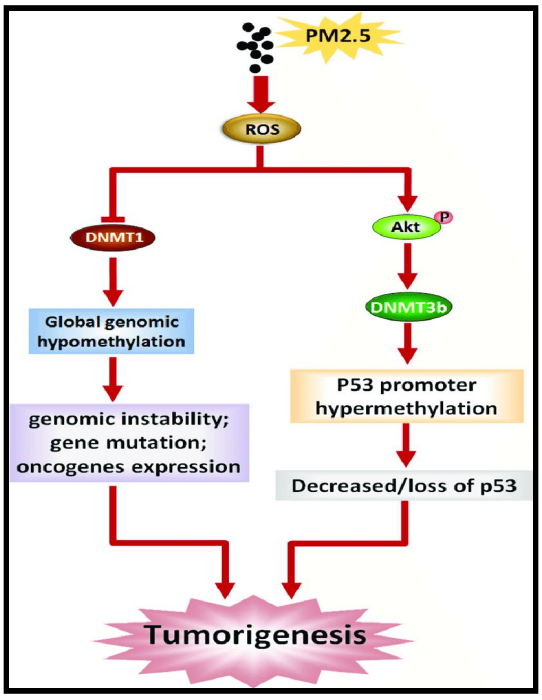
Nicotine also causes plasma free fatty acids, hyperglycemia and increase in the level of catecholamines in the blood. Reduce the coronary blood flow but increase skeleton muscle blood flow. Increase the rate of respiration causes hypothermia, hypercoagulable state , decrease skin temperature and increase the blood viscosity.[26,27,28] Death may occur from paralysis of respiratory muscle / or central respiratory failure with a LD50 in adults of around 30 – 60 mg of nicotine. In children the LD50 around 10 mg .[29]

Nicotine and Cancer :-

Cancer is a disease that occurs when dangerous cells grow in the body. These cells grow anywhere, including the brain, lungs, pancreas and more. Cancerous cells form a mass called à tumor.[30] It is shown nitrosation of nicotine could lead to formation of NNN and NNM. This effect of nicotine may be important because of its high concentration in tobacco and nicotine replacement products.[31]

In normal cells, nicotine can stimulate properties consistent with cell transformation and early stages of cancer formation, such as increased cell proliferation, decreased cellular dependence on the extracellular matrix for survival.[34]

Lungs Carcinogenesis :-



Tumorigenesis

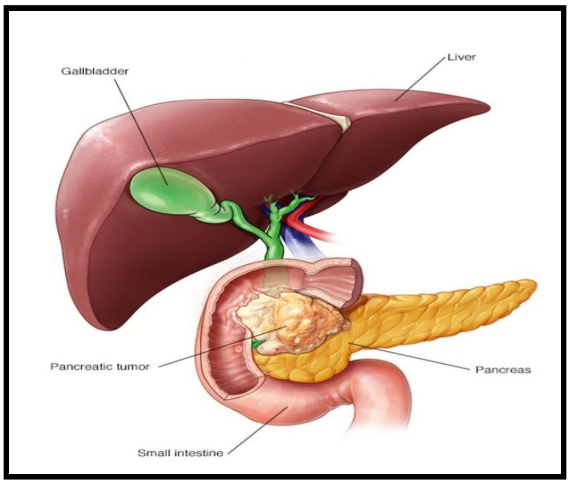
Human lungs carcinogenesis and tumorigenesis is associated with alteration of several genes, such as k- ras ,P53 and K4A /Arf . This genetically modified lungs tumor mouse model is developed on the basis of function of these genes in particular P53 mutations play an important role in tobacco smoke related carcinogenesis.[36] Nuclear translocation of ARBI. Gene by nicotine has been found in proliferation and progression of non small – cell lung cancer. Several studies has been shown that nicotine has significant role in tumor progression and metastasis via CXCR4 and increased angiogenesis.[33,37] Smokers carrying the gene CHRNA3 and CHRIS.[38]

Gastro Intestinal Carcinogenesis :-

Cancer is a major public health problem and at the beginning of the 19th century, gastric cancer was second most common cancer worldwide.[39] Every years there are 900000 new cases and 700000 gastric cancer - related deaths in the world.[40]

The carcinogenic role may be mediated by the MARK / COX – 2 Pathways, alpha 7 nAChR and beta – adrenergic receptor expression and mi RNAS alpha – BTX antagonist.[41] Nicotine affects the periostin gene. Alpha - 7 – nAChR and e – cadherin suppression which explains the mechanism of gastric cancer growth, invasion and metastasis.[42,43]

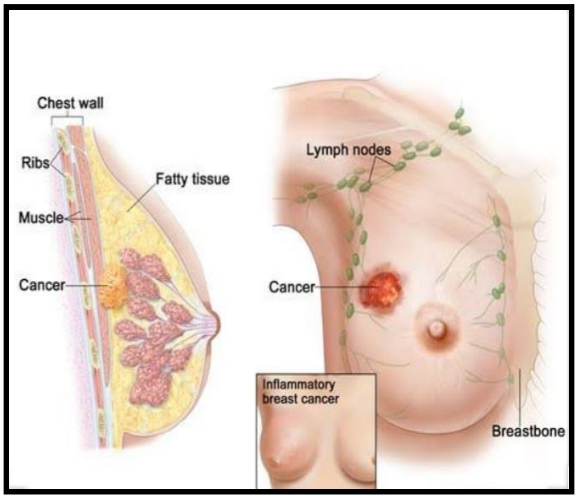
Pancreatic Cancer :-



Pancreatic cancer

Pancreatic cancer begins in the tissue of your pancreas an organ in your abdomen that lies behind the lower part of your stomach.[44] In another study nicotine promoted the growth of non small cell lung cancer and pancreatic cancer in a receptor dependent fashion.[45] The MVC - 4 upregulation ,NF – KB and GRP78 activation and Id1 expression by src dependent manner are probable mechanism leading to tumour growth , metastasis and chemotherapeutic drug resistance.[45,46] Pancreatic cancer is affected the parts that makes digestive substance (exocrine) or the part that makes insulin and other hormones (endocrine).[43]

Breast Cancer :-



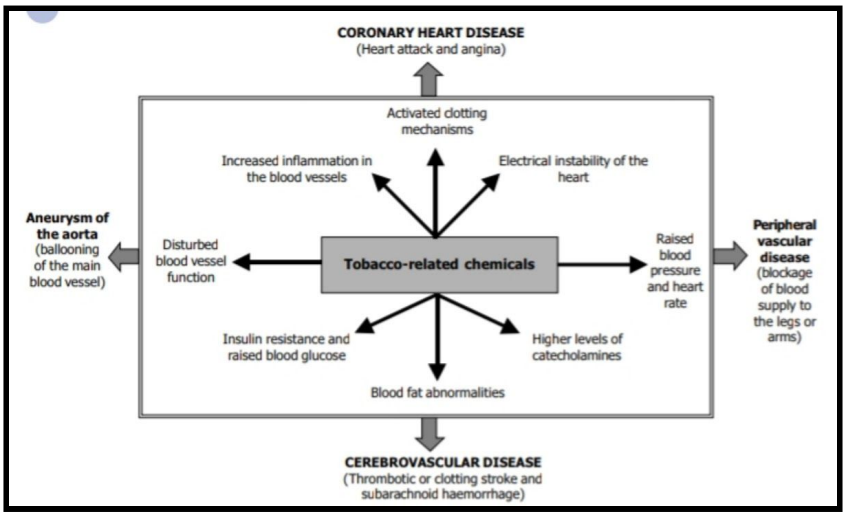
Breast cancer

Breast cancer is cancer that develops in breast cells. Cancer can also occur in the fatty tissue or the fibrous connective tissue within the breast. Uncontrolled cancer cells after inviting other healthy breast tissue can travel to the lymph nodes under the arms. The lymph nodes are primary pathway that help the cancer cells move to other parts of the body.[48]

Several studies have found that alpha 9 – nAChR mediated mechanism leads to increased tumor growth.[49,50]

Cardiovascular Systems :-

Cardiovascular disease (CVD) major contributors to death and disability many of the deaths due to cardiovascular disease occurs at younger ages in India compared to other countries. In India 42% of the deaths by 2020 are projected to be due to cardiovascular causes. [79]



effects of tobacco on cardiovascular system

The acute hemodynamic effect of cigarette smoking or smokeless tobacco are mediated primarily by sympathomimetic action .[51] The nicotinic receptors are present on peripheral chemoreceptors cells.[52] Nicotine acetylcholine receptors actions on vascular smooth muscle proliferation and plaque neovascularization increase the risk of peripheral arterial disorders.[32]

Cardiovascular effects of smoking include aggravation of stable angina pectoris, intermittent claudication vasospastic angina and restenosis after thrombolysis or angioplasty of coronary or peripheral arteries.[53] Nicotine cause increase blood pressure (BP), heart rate (HR), and sympathetic nerve activity to muscle circulation (MSNA), in response to hypoxia.[52] It reduces blood flow in cutaneous and coronary vessels increase blood flow in skeletal muscle.[27]

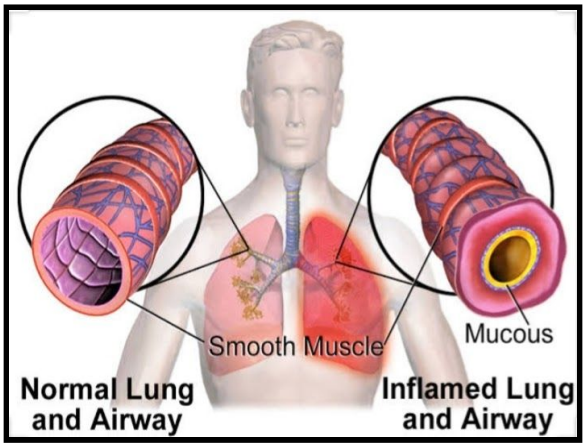
Respiratory System :-

Smokers are far more likely than non-smoker to develop diseases such as lung cancer. In developed countries, smoking is estimated to cause over 90% of lung cancer in men and about 70% cancer among women. In this countries 56% - 80% of death due to chronic respiratory disease globally attributable fractions for mortality due to tobacco

smoking about 66% for cancer of trachea, branches and lung cancer combined and 38% for chronic respiratory disease.[78]

Respiratory disease :-

Respiratory effects in childhood and adolescence : decreased physical fitness, potential retardation in the rate of lung growth and the level of maximum lung function among children and adolescents. Other respiratory effects increased cough, phlegm production wheezing respiratory infections and dyspnoea. [79]



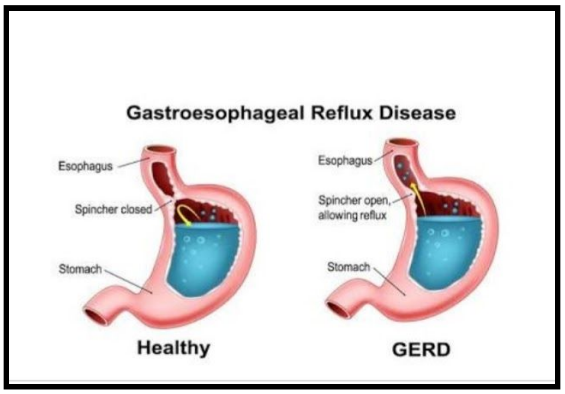
Effects on respiratory system

The effects of nicotine on the respiratory system are two years old. One, directly by local exposure of lungs to nicotine through smoking or inhaled nicotine and second via a central nervous system (CNS) mechanism.[54]

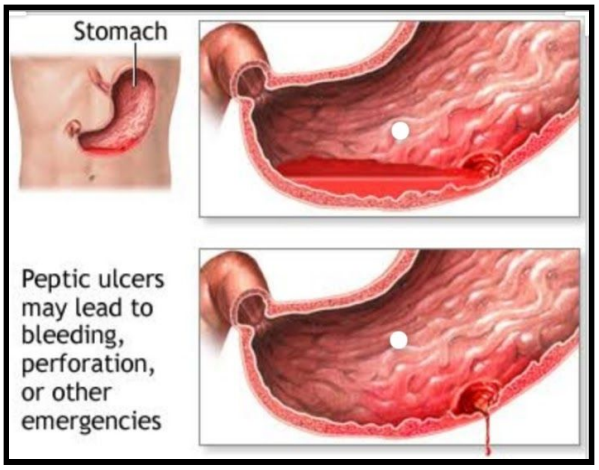
The effect of tobacco smoke on the respiratory system includes reduced lung function and breathlessness due to swelling and narrowing of the lung passages irritation of the trachea (windpipe) and larynx (voice box). Increased risk of lungs infection and symptoms such as coughing and sneezing. Permanent damage to the air sacs of the lungs.[55]

Gastrointestinal System :-

Nicotine use has been associated with gastro esophageal reflux disorder (GERD) and peptic ulcer disorder (PUD).[36,56] It also increases risk of Crohn's disease and possibly gallstones. Smoking seems after the liver too by changing the way it handle drugs and alcohol.[57] Nicotine causes smooth muscle relaxation by action endogenous nitric oxide as a non-adrenergic non-cholinergic neurotransmitter.[58]



gastroesophageal reflux disorder (GERD)



peptic ulcer disorder (PUD)

Immunological Systems :-

Nicotine has been known to be immunosuppressive through central and peripheral mechanisms. T- cells population is reduced due to arrests of cell cycles. Decrease the epithelization and cell adhesion and there delayed wound heating as well as increased risk of infection in nicotine exposed individuals.[59] Treatment with nicotine has been shown to influence all aspects of the immune system, including alteration in humoral and cellular immunity.[60]

The sympathetic and parasympathetic pathways affect the immune system. The adrenocorticotropic hormone (ActH) secretion pathway and corticotropin release is affected and causes immunological systems.[61]

Ocular (Eye) System :-

The effects of smoking on the eyes and ophthalmic disease was first reported in the late 1970s when linked between smoking habit and age related macular degeneration

nicotine and reactive oxygen species contribute to vasocontraction, reduced oxygen availability and chronic inflammation. Cigarettes smoking in also important factor in the pathogenesis and progression of disease of eyes, including AMD, cataracts and graves ophthalmopathy.[63]

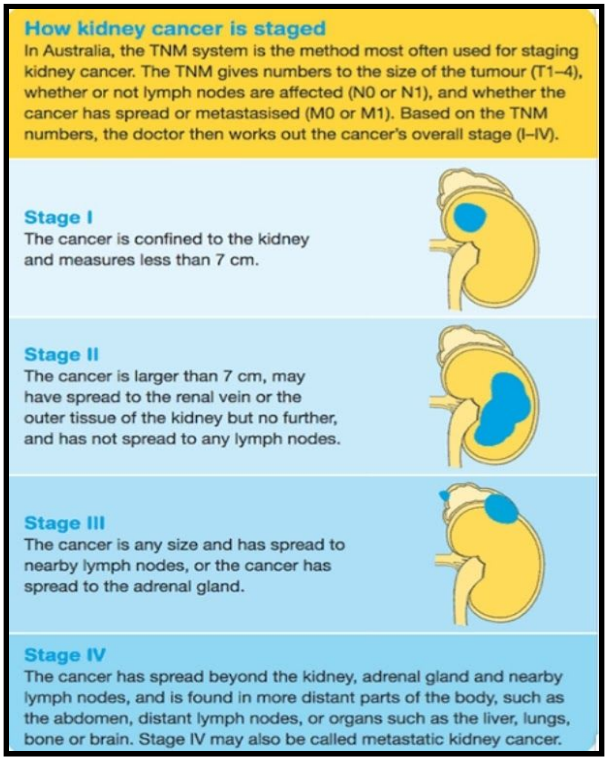
In animal model, spraguely drawley rates with type I diabetes treated with nicotine the relationship between nicotine and glucose which increase the risk of diabetes mellitus.[64]

Renal System :-

The risk of kidney disease in smokers is high cigarette smoking are increase albumin excretion in urine, decrease glomerular filtration rate.[64] The smoker with health conditions like diabetes or high blood pressure progress to kidney disease.[65]

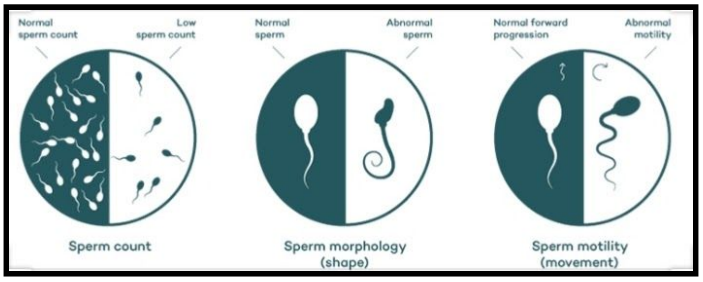
Renal cell cancer is a disease in which malignant cells form in tubules of the kidney. Smoking and misuse of certain pain mediated can affects the risk of cell cancer include blood in urine a lump in the abdomen there are four stages in renal cancer.[66]

1] Stage I
2] Stage II
3] Stage III
4] Stage IV



Four stages of renal cancer

Male Reproductive System :-

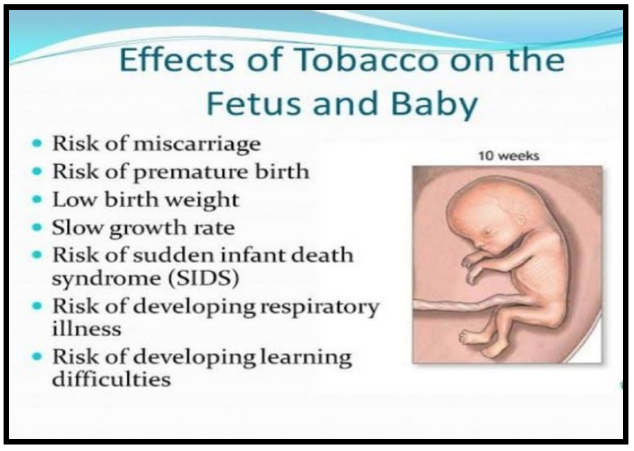


Effects of nicotine on Male fertility

The in vivo productive effects of nicotine have been assessed in many animal studies. In Male reproductive system, nicotine (0.5 mg kg^{-1}) to decrease sperm motility and reduce semen quality fewer normally shaped sperm increase sperm DNA damage.[67]

The studies have shown a 23% decrease in sperm concentration in men who smoke.[68] If sperm cannot swim properly. They have trouble reaching the egg and fertilizing. With a 13 % decrease in sperm motility, the oddly shaped sperm do not swim well to get to the egg. Male smokers have fever healthier shaped sperm than non-smoker.[70] The sperm of smokers has increased DNA fragmentation. DNA damaged sperm may lead to problems with fertilization, embryo development, embryo implantation, increased miscarriage rates, abnormal hormone level levels, which effects fertility, increased risk of birth defects in children of male smokers and increased risk of cancer because damage to sperm DNA.[70]

Reproductive System of Female :-



Effects of tobacco on the fetus and baby

Animal studies have also shown females are addicted to nicotine more quickly.[71] The survey of women of childbearing age found only about 30% knew that smoking they included risk of miscarriage.[71,72] Smoking are increased risk for many cancers, emphysema, heart

disease, number of other health problems. Smoking habits are responsible for fertility. Struggle in 13% of couples. [72]

Menstrual Cycle:-

Smoking habits affect the menstrual cycle. This leads to irregular bleeding.[74] There is an increase in follicular stimulation hormone levels and decrease in estrogen and progesterone. The effects of nicotine in the endocrine system. [34]

Effects Of Oocytes:-

The concentration of nicotine in follicular fluid affects the maturation of oocytes. For in vitro fertilization. The oocytes maturation are reducing up to 50% in women over 40 years.[75] Decreased blood flow to the oviduct nicotine treat oocytes appeared non spherical with rough surface torn and irregular zona pellucida. [76]

PeriNatal Effects **:-**

The material smoking effects on the fetal outcome increased risk of spontaneous abortion, preterm birth, stillbirth, fetal growth restriction and low birthweight.[77]

Conclusion :-

Nicotine is the cause of addiction for tobacco users. Taken together, the obtained results on many types of human cancer. Biological effects to all systems of the body including pancreatic cancer, breast cancer, cardiovascular systems, gastrointestinal system, respiratory system, renal system, reproductive system. The true face of disease, death, and horror. *Needly to say eliminate smoking to bring a smile to many faces in your life. Eliminate tobacco products consumption and be the real hero of your family.*

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